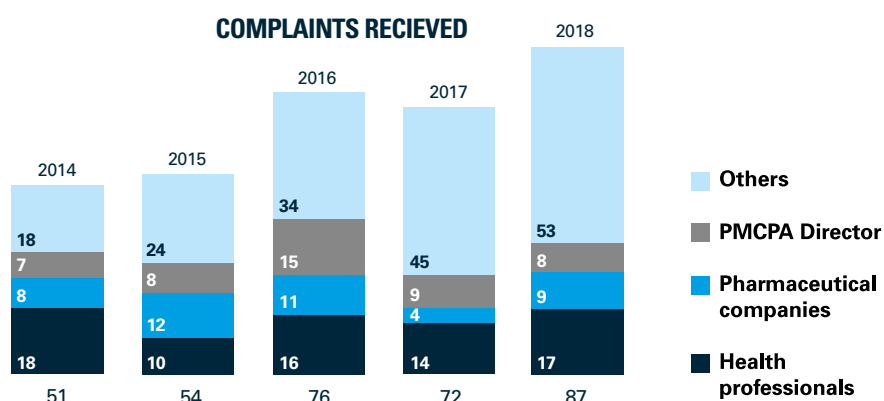


CODE OF PRACTICE REVIEW

The Prescription Medicines Code of Practice Authority (PMCPA) was established by The Association of the British Pharmaceutical Industry (ABPI) to operate the ABPI Code of Practice for the Pharmaceutical Industry independently of the ABPI. The PMCPA is a division of the ABPI which is a company limited by guarantee registered in England & Wales no 09826787, registered office 7th Floor, Southside, 105 Victoria Street, London SW1E 6QT.

COMPLAINTS IN 2018



In 2018 the PMCPA received 87 complaints, compared with 72 in 2017. There were 76 complaints in 2016, 54 complaints in 2015 and 51 in 2014.

There were over 100 cases to be considered in 2018, compared with 77 in 2017 and 100 in 2016. The number of cases usually differs from the number of complaints because some complaints involve more than one company and others, for a variety of reasons, do not become cases at all.

The number of complaints from health professionals in 2018 (17) was more than the number from pharmaceutical companies (both members and non-members of the ABPI) (9). In addition, there were 25 complaints from anonymous health professionals. The more complex cases considered by the Authority are generally inter-company complaints which often raise a number of issues.

Eight complaints were nominally made by the Director, of which 7 arose from voluntary admissions by companies. One arose from the publication of a study looking at disclosure of clinical trial details.

There were 8 complaints made by employees/ex-employees. Two complaints were made by a consultant to a company and 5 complaints were from members of the public.

There were 13 anonymous complaints in addition to the 25 from anonymous health professionals. Three were from anonymous employees.

The details will be included in the PMCPA 2018 Annual report to be published in due course.

COMPLAINTS CONSIDERATION – DELAYS

The PMCPA is very aware that there are a number of complaints that have taken significantly longer to consider than we would have hoped. We realise that this is far from ideal and we are doing all that we can to progress them.

As you will see from the figures for complaints received in 2018 there has been an increase in numbers. Other contributory factors include the number of audits/re-audits and other work required to be done. We are taking a number of steps to improve the situation, including recruiting more staff to the Panel. Also, we delayed publication of the Code of Practice Reviews to allow extra time for the case workload. The individual cases have been published regularly on the website as usual.

PUBLIC REPRIMAND OTSUKA UK AND OTSUKA EUROPE

Otsuka Pharmaceuticals Europe Limited and Otsuka Pharmaceuticals UK Limited have each been publicly reprimanded by the Code of Practice Appeal Board for failing to notify and/or implement changes to the summaries of product characteristics (SPCs) from 2017 for Jinarc (tolvaptan), Samsca (tolvaptan) and Abilify (aripiprazole) and update relevant materials in a timely manner (Cases AUTH/3041/6/18 and AUTH/3042/6/18 respectively). These failings had the potential to adversely impact patient safety. Otsuka Europe was also publicly reprimanded for these failings in a subsequent but overlapping case (Case AUTH/3123/11/18).

In Cases AUTH/3041/6/18 and AUTH/3042/6/18, Otsuka Europe and Otsuka UK were each ruled in breach of the Code, including of Clause 2 for bringing discredit upon, and reducing confidence in, the pharmaceutical industry. It was crucial that health professionals and others could rely upon the industry for up-to-date and accurate information about their medicines. The Code of Practice Panel also had broader concerns about governance within the two companies and it decided to report Otsuka Europe and Otsuka UK to the Code of Practice Appeal Board.

In the subsequent case, Case AUTH/3123/11/18, Otsuka Europe's response to the PMCPA in relation to Case AUTH/3041/6/18 was not transparent as the company had not disclosed relevant internal audit reports. The Panel considered that the further information disclosed in Case AUTH/3123/11/18 now showed that the magnitude of the compliance issues at Otsuka Europe was greater than apparent in Case AUTH/3041/6/18. The Code of Practice Panel ruled breaches of the Code including of Clause 2. The Panel also decided to report Otsuka Europe to the Appeal Board.

The three reports were considered at the same Appeal Board meeting.

Continued overleaf...

CODE OF PRACTICE TRAINING

Training seminars on the Code of Practice, run by the Prescription Medicines Code of Practice Authority and open to all comers, are held on a regular basis in central London.

These full day seminars offer lectures on the Code and the procedures under which complaints are considered, discussion of case studies in syndicate groups and the opportunity to put questions to the Code of Practice Authority.

For dates of the Code of Practice Seminars in 2019 please see the PMCPA website.

Short training sessions on the Code or full day seminars can be arranged for individual companies, including advertising and public relations agencies and member and non member companies of the ABPI. Training sessions can be tailored to the requirements of the individual company.

For further information regarding any of the above, please contact Nora Alexander for details (020 7747 1443 or nalexander@pmcpa.org.uk).

HOW TO CONTACT THE AUTHORITY

Our address is:
Prescription Medicines Code of Practice Authority
7th Floor, Southside, 105 Victoria Street, London SW1E 6QT
www.pmcpa.org.uk

Telephone: 020 7747 8880

Copies of the Code of Practice for the Pharmaceutical Industry and of this Review can be obtained from Lisa Matthews (020 7747 8885 or lmattews@pmcpa.org.uk).

Direct lines can be used to contact members of the Authority.

Heather Simmonds: 020 7747 1438

Etta Logan: 020 7747 1405

Tannyth Cox: 020 7747 8883

Natalie Hanna: 020 7747 8862

The above are available to give informal advice on the application of the Code of Practice.

The Authority rather than the ABPI is the contact point for information on the application of the Code.

PUBLIC REPRIMAND OTSUKA UK AND OTSUKA EUROPE

(Continued from cover)

In Cases AUTH/3041/6/18 and AUTH/3042/6/18 and Case AUTH/3123/11/18 the Appeal Board was very concerned that an overall failure of governance in relation to Otsuka Europe and Otsuka UK's processes in implementing SPC changes, updating prescribing information and updating and withdrawing promotional materials in a timely manner had potential patient safety implications. This was a serious matter. Also at issue in Cases AUTH/3041/6/18 and AUTH/3042/6/18 was the timely update and submission to the Medicines and Healthcare products Regulatory Authority (MHRA) of risk minimisation materials.

In Case AUTH/3123/11/18, the Appeal Board was also concerned that Otsuka Europe had neither referred to nor provided the relevant internal audits of global and European functions in its response to Case AUTH/3041/6/18.

In addition to the public reprimand, the Appeal Board also decided to require an audit of Otsuka Europe's (Case AUTH/3041/6/18 and Case AUTH/3123/11/18) and Otsuka UK's (Case AUTH/3042/6/18) procedures in relation to the Code

Full details of all three cases can be found on the PMCPA website.

DO YOUR WEBSITE AND SOCIAL MEDIA ACTIVITIES MEET THE REQUIREMENTS OF THE CODE?

The Authority has recently received a number of complaints about pharmaceutical companies' websites and social media activities.

Companies need to ensure that they regularly review their websites to ensure they comply with the Code. Concerns raised include issues such as certification, availability and updates to prescribing information and other obligatory information and access. Some of the key considerations are set out below.

Certification Clause 14

Company procedures must ensure that promotional material and certain non-promotional materials are not issued until the final form has been certified.

A key requirement of certification is that signatories have all the pertinent information including how material is to be used. This is particularly important if the material is non-promotional. Certifiers need to be certain that such material is not being used for a promotional purpose.

When certifying dynamic content for websites, care must be taken to ensure the dynamic content meets the requirements of the Code as a standalone item. As the final form of digital material might not be static, consideration needs to be given to the context in which it appears but each possible combination does not need to be certified.

Material which is still in use must be certified at intervals of no more than two years (Clause 14.5); some materials may need more frequent recertification.

Prescribing Information

The prescribing information listed in Clause 4.2 must be provided in a clear and legible manner on all promotional websites; there must be a clear prominent statement as to where it can be found. Companies must ensure that

the hyperlinks work. The prescribing information must be up-to-date and where the current summary of product characteristics (SPC) for the medicine is not used, the information provided must reflect the current SPC. Any changes to the SPC which affects the prescribing information must be made forthwith.

Black triangle

The Authority has received a number of complaints about the lack of, or incorrect colour of the inverted black equilateral triangle symbol.

Clause 4.10 states that when required by the licensing authority, all promotional material must show an inverted black equilateral triangle to denote that additional monitoring is required in relation to adverse reactions.

In addition, Clause 26.3 requires the inverted black triangle symbol together with a statement explaining it to be included on material which relates to a medicine which is subject to additional monitoring and which is intended for a patient taking that medicine.

The black triangle symbol should be located adjacent to the first mention of the product as this is likely to be considered the most prominent display of the name of the product. Companies must ensure that the symbol is black (orange, navy and dark grey are not acceptable) and that its size is easily readable.

Access

A reminder to companies that the supplementary information to Clause 28.1 states that unless access to promotional material about prescription only medicines is limited to health professionals and other relevant decision makers, a pharmaceutical company website or a company sponsored website must provide information for the public as well as promotion to health professionals with the sections for each target audience clearly separated and the intended audience identified. This is to avoid the public needing to access material for health professionals unless they choose to. The MHRA Blue Guide states that the public should not be encouraged to access material which is not intended for them.

Social Media - Like v Share

The Authority has recently received complaints about material on social media including LinkedIn and Twitter. The Code of Practice Panel has noted that LinkedIn is different to some other social media platforms in that it is a business and employment-orientated network and is primarily, although not exclusively, associated with an individual's professional heritage and current employment and interests. In the pharmaceutical industry, an individual's network might, albeit not exclusively, be directly or indirectly associated with the healthcare industry. In the Authority's view, it is of course not unacceptable for company employees to use personal LinkedIn accounts and the Code would not automatically apply to all activity on a personal account; whether the Code applied would be determined on a case-by-case basis taking into account all the circumstances including: the content, any direct or

indirect reference to a product, how the information was disseminated on LinkedIn, the company's role in relation to the availability of the content and whether such activity was instructed or encouraged by the company. If activity was found to be within the scope of the Code, the company would be held responsible.

Material can be disseminated or highlighted by an individual on LinkedIn in a number of ways, by posting, sharing, commenting or liking. In the Panel's view, activity conducted on social media that could potentially alert one's connections to the activity might be considered proactive dissemination of material. In addition an individual's activity and associated content might be visible to others outside his/her network depending on the security settings used. The Authority understands that if an individual 'liked' a post it increases the likelihood that the post will appear in his/her connections' LinkedIn feeds, usually as '[name] likes this'. Companies should remain vigilant and need to ensure that they take reasonable steps to highlight the potential compliance issues that might arise if certain posts are liked and are potentially pushed to others.

NEW IFPMA CODE OF PRACTICE

The new Code of Practice of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) came into effect on 1 January 2019.

eLEARNING MODULE

Unfortunately, as a result of the delays we have had to remove the eLearning module from the current website, as it reflects the 2016 Code. Feedback shows that it is very popular, and so we are in the process of updating and redesigning it and it will be on the new website later in the year.

EFPIA CODES CONSOLIDATED

The three European Federation of Pharmaceutical Industries and Associations (EFPIA) Codes (EFPIA Code on the Promotion of Prescription-Only Medicines to, and Interactions with, Healthcare Professionals – EFPIA Code of Practice on Relationships between the Pharmaceutical Industry and Patient Organisations - EFPIA Code on Disclosure of Transfers of Value from Pharmaceutical Companies to Healthcare Professionals and Healthcare Organisations) have been consolidated into one Code – The EFPIA Code of Practice.

The EFPIA member associations will need to amend their codes to reflect the new EFPIA Code of Practice.

BRISTOL-MYERS SQUIBB AND PFIZER v DAIICHI-SANKYO

Promotion of Lixiana

Bristol-Myers Squibb Pharmaceuticals and Pfizer (The Alliance) made a joint complaint about the promotion of Lixiana (edoxaban) by Daiichi-Sankyo. Lixiana was a direct oral anticoagulant (DOAC) of which there were currently four marketed in the UK: edoxaban, rivaroxaban, dabigatran and apixaban. Apixaban (Eliquis) was marketed by the Alliance.

The detailed response from Daiichi-Sankyo is given below.

The Alliance alleged that Daiichi-Sankyo had failed to include important information from the Lixiana summary of product characteristics (SPC) in promotional material. Section 4.4 (Special warnings and precautions for use) included:

'Renal function in [nonvalvular atrial fibrillation] NVAF

A trend towards decreasing efficacy with increasing creatinine clearance was observed for edoxaban compared to well-managed warfarin (see section 5.1). Therefore, edoxaban should only be used in patients with NVAF and high creatinine clearance after a careful evaluation of the individual thromboembolic and bleeding risk.'

The Alliance further noted that this precautionary wording was unique to Lixiana. Despite the fact that none of the other three DOACs had such wording in their SPCs, there was a consistent, even ubiquitous, omission of any mention of the precautionary wording in any Lixiana promotional material. The Alliance alleged that this misled as to the type and number of patients who might be eligible for Lixiana and misrepresented its risk benefit profile for a significant number of patients who might have a high creatinine clearance.

The Alliance alleged the misleading omission of this precautionary wording in all Lixiana materials but it was particularly notable in two items. The first, a Lixiana 'Initiation Information Guide' stated: 'This booklet contains important summary information designed to help prescribers initiate Lixiana appropriately', specific sections on indications and recommended dose, switching, contraindications, cautions, pregnancy and breastfeeding, hepatic impairment, renal impairment, monitoring, prescribing and dispensing information, storage, missed dose, patient alert card, further information, interactions summary and side-effects. Despite the extremely detailed content there was no mention in any of these sections of the precautionary wording from the SPC about patients with high creatinine clearance levels. This omission was particularly misleading as the 'Cautions' section referred to patients with end stage renal disease. By including

information about patients with low creatinine clearance but not important information about patients with high creatinine clearance gave the misleading impression that there were no important considerations for the latter group of patients. The precaution relating to patients with high creatinine clearance was not a trivial matter. Underdosing of patients with atrial fibrillation with anticoagulants could put them at increased risk of serious outcomes such as stroke or systemic embolism. Such adverse outcomes could be life-changing or even fatal.

Similar allegations were made about the second item at issue, a Lixiana 'Practical Guide', was described in the 'Overview' section as 'specifically for prescribers in relation to the use of Lixiana'.

The Alliance refuted Daiichi-Sankyo's assertion that the precautionary wording at issue was in the prescribing information and thus did not need to be included in the body text of the promotional material itself as the Code required the presentation of an accurate, balanced, complete and fair reflection of all the evidence in order to enable the recipient to form their own opinion of the therapeutic value of the medicine. This was particularly the case where matters of patient safety were concerned. When health professionals were encouraged to initiate a particular medicine, or switch patients from one medicine to another, they needed clear information about those patients who might not be suitable for the new medicine. Thus, promotional material which referred to the benefits of a medicine but omitted any warnings, relying instead on the reader referring to the prescribing information, usually placed at a distance at the back of the material, did not present a complete and balanced case regarding a significant proportion of patients. For example, there was a great deal of prominent information on Lixiana, in the 'Practical Guide' and 'Initiation Guide', discussed above, much of which could also be found in the prescribing information. However, Daiichi-Sankyo had also chosen to include this information prominently in the body of the promotional material itself, just as it had always omitted from the body text the precautionary wording at issue. In short, the appearance of the precautionary wording in the prescribing information alone was not adequate. Presentation of the information about a medicine in this way was unbalanced, misleading and potentially dangerous.

The Alliance stated that the other principal pillar of Daiichi-Sankyo's defence of the omission of this important information was to refer to the National Institute for Health and Care Excellence (NICE) technology appraisal of edoxaban TA355 which it selectively quoted as saying 'there is no reason to make differential recommendations based

on creatinine clearance'. However, The Alliance noted that the NICE committee noted the relevant warning at Section 4.4 of the SPC before concluding that if edoxaban was used in accordance with that SPC there was no reason to make differential recommendations based on creatinine clearance.

The Alliance stated that it was therefore clear that the Committee considered that this wording, contained within the SPC, was an adequate warning but that the clinician needed to take this into consideration before deciding to prescribe. It was on this basis that the Committee decided that it did not need to issue any additional differential recommendations. The Alliance agreed with NICE that edoxaban should be used, and therefore promoted, in accordance with its SPC, which would therefore include any appropriate warnings and precautions.

The Alliance stated that whilst not relevant to the regulatory guidance issued about the use of Lixiana in the UK, it was reflective of the clinical importance of this UK SPC warning statement that in the USA the Food and Drug Administration (FDA) included these considerations as a contraindication black box warning in the Lixiana prescribing information. Details were provided.

In summary, the Alliance stated that the considered and ubiquitous omission from all promotional material of a prominent precautionary statement, found in the SPC, about the use of Lixiana in patients with high creatinine clearance, potentially placed a significant number of patients at risk of stroke or systemic embolism in breach of the Code.

The Panel noted that Lixiana was indicated for the prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation (NVAf) with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack (TIA).

The Panel considered that whether a special warning or precaution needed to be referred to in material depended on a consideration of all of the circumstances including the nature of the warning/precaution, the therapy area and the content and intended use of the material.

The Panel noted the relevant warning Section 4.4 of the Lixiana SPC.

The Panel further noted that a subgroup analysis based on renal function which used 3 categories of creatinine clearance (CrCl) was discussed in the NICE technology appraisal guidance on edoxaban for preventing stroke and systemic embolism in people with NVAf which stated that the subgroup analysis across three categories (normal renal function, mild renal impairment and moderate renal impairment) 'suggested that renal function had a significant impact on the efficacy of edoxaban compared to warfarin ($p=0.0042$)'. The hazard ratios for the primary efficacy endpoint (prevention of stroke or systemic embolic event) were 0.68 (95% CI 0.54-0.85) and 0.86 (95% CI 0.63-1.17) for patients

with mild to moderate renal impairment. In contrast the relative risk of stroke or systemic embolic event was higher with edoxaban than with warfarin in patients with normal renal function (HR 1.31, 95% CI 0.96-1.79). The guidance noted the company's view that these results should be treated with caution because a variety of factors including an unusually low event rate in the warfarin group and the lack of randomisation within the sub-groups could have contributed towards the result. The NICE guidance (Section 4.6) noted evidence that the trend towards decreasing efficacy of edoxaban with increasing creatinine clearance was likely to be because with better renal function edoxaban was removed by the kidneys more quickly leading to a reduction in treatment effect. Evidence was also submitted that this might apply to all newer anticoagulants but data needed to be re-evaluated to confirm this. Evidence was provided to NICE that the proportion of people with good renal function measured by creatinine clearance who would be eligible for treatment with edoxaban was in the region of 5-10% and that these were often younger people. The NICE committee noted the relevant warning at Section 4.4 of the SPC before concluding that if edoxaban was used in accordance with that SPC there was no reason to make differential recommendations based on creatinine clearance. The Panel noted that the relevant clinical data was also discussed at Section 5.1 Pharmacodynamic properties, of the Lixiana SPC which showed event rate data for 6 creatinine clearance sub-groups. The Panel noted that the Lixiana SPC stated in a Section 4.2 under the sub-heading Special populations, assessment of renal function, that renal function should be assessed in all patients by calculating creatinine clearance prior to initiation of treatment with Lixiana, *inter alia*, when deciding on the use of Lixiana in patients with increased creatinine clearance.

The Panel noted that a section on page 2 of the six page Lixiana Initiation Information Guide headed 'CAUTIONS' stated that the use of Lixiana was not recommended in patients with end stage renal disease (ESRD) (CrCl <15 ml/min or on dialysis). On the following page in a section headed renal impairment it stated that in patients with mild renal impairment the recommended Lixiana dose was 60mg once daily, in patients with moderate or severe renal impairment the recommended dose was 30mg once daily and repeated that in patients with ESRD or on dialysis Lixiana was not recommended. It further stated in a subsequent section headed 'Monitoring' that renal function should be monitored before treatment and when clinically indicated during treatment. There was no reference in the body of the booklet to the SPC warning at issue. The Panel noted Daiichi-Sankyo's submission that the warning was not included within the renal impairment section as there was no recommendation for dose alteration in patients with high creatinine clearance. The Panel noted the comments about the nature of the relevant subgroup analysis in the NICE guidance. The Panel noted that based on this data the regulators had decided to include a special warning about decreased efficacy in patients with high creatinine clearance in the SPC. The SPC

clearly stated that edoxaban should only be used in those patients after a careful evaluation of the individual thromboembolic and bleeding risk. The Panel considered that the warning in question did more than 'encourage' prescribers to undertake a careful evaluation, as stated by Daiichi-Sankyo; the warning stated that edoxaban *should only* be used after a careful evaluation of the individual's thromboembolic and bleeding risk (emphasis added), thereby implying in the Panel's view that such an evaluation was a requirement in this patient population. The Panel noted the stated purpose of the booklet in question to help prescribers initiate Lixiana appropriately and considered that failure to include the special warning was misleading and did not encourage the rational use of the medicine. In the Panel's view it was not sufficient to rely on the prescribing information at the back of the guide to provide the warning about the use of Lixiana and the trend towards the decreasing efficacy in patients with NVAF and high creatinine clearance. Material had to be capable of standing alone with regard to the requirements of the Code and could not rely on qualification in either prescribing information or a footnote. The Panel noted the Alliance's submission about the potential life-changing or even fatal consequences of failing to undertake such an evaluation in the relevant patient population. Breaches of the Code were ruled. The Panel considered that Daiichi-Sankyo had failed to maintain high standards and a breach was ruled. The breaches were upheld upon appeal by Daiichi-Sankyo.

In making these rulings the Appeal Board noted that the FDA had contraindicated the use of Lixiana in this group of patients and noted Daiichi-Sankyo's submission that the EMA had assessed the data differently. Nevertheless there was a warning about use in a patient population with normal kidney function which the Appeal Board considered was unusual. Both items at issue referred readers to the SPC for full prescribing information. The Appeal Board considered that prescribers would not necessarily expect patients with high creatinine clearance and thus normal kidney function to be at risk when prescribing a DOAC for NVAF; it was counter intuitive. It was therefore even more important that the SPC warning in question was drawn to their attention, particularly as Lixiana was the only DOAC that had this specific warning. Other warnings from the SPC were included in the main body of the Initiation Information Guide, including in the Appeal Board's view special warnings and precautions with less strong wording and to omit the warning at issue downplayed its relative importance. The Appeal Board considered that given the nature of the warning it was paramount that it appeared prominently in the body of the item at issue.

The Appeal Board thought it odd that, according to the Daiichi-Sankyo representatives, its field force had been trained on the warning at issue yet the company had omitted the warning from the body of the materials.

In relation to the 19 page Lixiana 'Practical Guide', the Panel noted its general comments above about

the warning at Section 4.4 of the SPC, Section 4.2 of the SPC, including comments about the relevant data in the NICE guidance and the prescribing information and considered that they applied here. The Panel noted that the Lixiana Practical Guide covered more matters than the Initiation Information Guide considered above and included discussion of efficacy and safety issues including patients at higher risk of bleeding and special patient populations. The Panel considered that failure to include the special warning at issue, particularly considering there was a page dedicated to special patient populations, was misleading and did not encourage the rational use of the medicine. Breaches of the Code were ruled. The Panel considered that Daiichi-Sankyo had failed to maintain high standards and a breach of the Code was ruled. The breaches were upheld upon appeal by Daiichi-Sankyo.

In making these rulings, the Appeal Board considered that its comments above applied equally to this item. The Appeal Board also noted that the Practical Guide covered more matters than the Initiation Information Guide and included discussion of efficacy and safety issues including patients at higher risk of bleeding and special patient populations. There was a page dedicated to special patient populations and the missing information appeared in the Lixiana SPC under the heading special populations.

The Panel noted the comments in the NICE guidance about the size of the patient population with good renal function (measured by creatinine clearance) who would be eligible for treatment with edoxaban was in the region of 5-10%. The Panel further noted the trend towards decreasing efficacy of edoxaban with increasing creatinine clearance and the consequences of such and considered that Daiichi-Sankyo's failure to include the warning meant that it had potentially put those patients' safety at risk. The Panel considered that patient safety was of the utmost importance and Daiichi-Sankyo's failure in this regard brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled in relation to each item. This was upheld on appeal by Daiichi-Sankyo.

The Appeal Board noted its comments and rulings of breaches of the Code including a breach of Clause 2. The Appeal Board considered that Daiichi-Sankyo's actions had meant that prescribers had been provided with material that failed to highlight an important patient safety consideration and consequently patients might have been put at risk. This was totally unacceptable. The Appeal Board noted that the NHS guidance on the use of DOACs in NVAF provided by the Alliance made no reference to the warning at issue. Consequently, the Appeal Board decided, in accordance with Paragraph 10.6 of the Constitution and Procedure, to require Daiichi-Sankyo to issue a corrective statement to all recipients of the material at issue. In addition, the Appeal Board considered that given the items broad dissemination including that in the Appeal Board's view it was more likely than not that this material would have been shared by prescribers with colleagues, the Appeal Board considered that

the corrective statement should also be sent to relevant UK prescribers. The corrective statement should refer to the case report. Under Paragraph 10.6 details of the proposed content and mode and timing of dissemination of the corrective statement must be provided to the Appeal Board for approval prior to use.

In addition, the Appeal Board decided, in accordance with Paragraph 10.3, to require Daiichi-Sankyo to take steps to recover the material from those who had received it; written details of the action taken must be provided to the Appeal Board. This should be included in the corrective statement. [The corrective statement, which was agreed by the Appeal Board prior to use, appears at the end of this report.]

Bristol-Myers Squibb Pharmaceuticals Limited and Pfizer Limited (The Alliance) made a joint complaint about the promotion of Lixiana (edoxaban) by Daiichi-Sankyo UK Ltd. Lixiana was a direct oral anticoagulant (DOAC) of which there were currently four marketed in the UK: edoxaban, rivaroxaban, dabigatran and apixaban. Apixaban (Eliquis) was jointly marketed by Bristol-Myers Squibb and Pfizer (the Alliance).

COMPLAINT

The Alliance noted that Section 4.4 (Special warnings and precautions for use) of the current Lixiana summary of product characteristics (SPC) contained the following:

‘Renal function in [nonvalvular atrial fibrillation] NVAf

A trend towards decreasing efficacy with increasing creatinine clearance was observed for edoxaban compared to well-managed warfarin (see section 5.1). Therefore, edoxaban should only be used in patients with NVAf and high creatinine clearance after a careful evaluation of the individual thromboembolic and bleeding risk.’

The Alliance further noted that this precautionary wording was unique to Lixiana. Despite the fact that none of the other three DOACs had such wording in their SPCs, there was a consistent, even ubiquitous, omission of any mention of the precautionary wording in any Lixiana promotional material. The Alliance alleged that this misled as to the type and number of patients who might be eligible for Lixiana and misrepresented its risk benefit profile for a significant number of patients who might have a high creatinine clearance.

The Alliance stated that there was a misleading omission of this precautionary wording in all Lixiana materials but it was particularly notable in two items, the first of which was a Lixiana ‘Initiation Information Guide’ (ref EDX/16/0171) which described itself as follows: ‘This booklet contains important summary information designed to help prescribers initiate Lixiana appropriately’. The booklet contained specific sections on indications and recommended dose, switching, contraindications, cautions, pregnancy and breastfeeding, hepatic impairment, renal

impairment, monitoring, prescribing and dispensing information, storage, missed dose, patient alert card, further information, interactions summary and side-effects. Despite the extremely detailed content there was no mention in any of these sections of the precautionary wording from the SPC about patients with high creatinine clearance levels. This omission was particularly misleading as the ‘Cautions’ section referred to patients with end stage renal disease. By including information about patients with low creatinine clearance but not important information about patients with high creatinine clearance gave the misleading impression that there were no important considerations for the latter group of patients. However, the precaution relating to patients with high creatinine clearance was not a trivial matter. Underdosing of patients with atrial fibrillation with anticoagulants could put them at increased risk of serious outcomes such as stroke or systemic embolism. Such adverse outcomes could be life-changing or even fatal.

The second item at issue was a Lixiana ‘Practical Guide’ (ref EDX/15/0091(4)). In its ‘Overview’ section it described itself as ‘specifically for prescribers in relation to the use of Lixiana’ and listed the following section headings: indications, summary of efficacy and safety, dosing recommendations and dose reductions, information on switching patients to or from Lixiana, populations at potentially higher risk of bleeding, special patient populations, temporary discontinuation, perioperative management, overdose, management of bleeding complications, coagulation testing, patient alert card. However, despite this detailed content on the practical considerations on the use of Lixiana, and reference to patients with low creatinine clearance, there was no mention of the precautionary wording about patients with high creatinine clearance.

The Alliance stated that during inter-company dialogue, Daiichi-Sankyo, in defence of its omission of this information, had asserted that the precautionary wording at issue was in the prescribing information and thus did not need to be included in the body text of the promotional material itself. The Alliance refuted this assertion as the Code required the presentation of an accurate, balanced, complete and fair reflection of all the evidence in order to enable the recipient to form their own opinion of the therapeutic value of the medicine. This was particularly the case where matters of patient safety were concerned. When health professionals were encouraged to initiate a particular medicine, or switch patients from one medicine to another, they needed clear information about those patients who might not be suitable for the new medicine. Thus, promotional material which referred to the benefits of a medicine but omitted any warnings, relying instead on the reader referring to the prescribing information, usually placed at a distance at the back of the material, did not present a complete and balanced case regarding a significant proportion of patients. For example, there was a great deal of prominent information on Lixiana, in the ‘Practical Guide’ and ‘Initiation Guide’, discussed above, much of which could also be found in the prescribing information. However, Daiichi-Sankyo had also chosen to include this information

prominently in the body of the promotional material itself, just as it had always omitted from the body text the precautionary wording at issue. In short, the appearance of the precautionary wording in the prescribing information alone was not adequate. Presentation of the information about a medicine in this way was unbalanced, misleading and potentially dangerous.

The Alliance stated that when encouraging health professionals to initiate treatment with a medicine, there was an obligation to point out to them specifically if there was a significant group of patients where particular caution should be exercised. In this instance, Daiichi-Sankyo had failed to do so with appropriate prominence in any of its materials, even ones which purported to give detailed and specific guidance on the initiation and use of its medicine.

The Alliance stated that the other principal pillar of Daiichi-Sankyo's defence of the omission of this important information was to refer to the National Institute for Health and Care Excellence (NICE) technology appraisal of edoxaban TA355 which it selectively quoted as saying 'there is no reason to make differential recommendations based on creatinine clearance'. However, The Alliance noted that the full wording was:

'It [The Committee] also noted the summary of product characteristics which states that, in people with non valvular atrial fibrillation and high creatinine clearance, edoxaban should only be used after careful evaluation of a person's thromboembolic and bleeding risk. The Committee concluded that if edoxaban is used in accordance with the summary of product characteristics, there is no reason to make differential recommendations based on creatinine clearance.'

The Alliance stated that it was therefore clear that the Committee considered that this wording, contained within the SPC, was an adequate warning but that the clinician needed to take this into consideration before deciding to prescribe. It was on this basis that the Committee decided that it did not need to issue any additional differential recommendations. The Alliance agreed with NICE that edoxaban should be used, and therefore promoted, in accordance with its SPC, which would therefore include any appropriate warnings and precautions.

The Alliance stated that whilst not relevant to the regulatory guidance issued about the use of Lixiana in the UK, it was reflective of the clinical importance of this UK SPC warning statement that in the USA the Food and Drug Administration (FDA) had included these considerations as a contraindication black box warning in the Lixiana prescribing information:

'REDUCED EFFICACY IN NONVALVULAR ATRIAL FIBRILLATION PATIENTS WITH CRCL >95 ML/ MIN: SAVAYSA should not be used in patients with CrCL >95mL/min. In the ENGAGE AF-TIMI 48 study, nonvalvular atrial fibrillation patients with CrCL >95mL/min had an increased rate of ischemic

stroke with SAVAYSA 60mg once daily compared to patients treated with warfarin. In these patients another anticoagulant should be used.'

In summary, the Alliance stated that the considered and ubiquitous omission from all promotional material of a prominent precautionary statement, found in the SPC, about the use of Lixiana in patients with high creatinine clearance, potentially placed a significant number of patients at risk of stroke or systemic embolism and represented a clear breach of Clauses 7.2, 7.10, 9.1 and 2.

RESPONSE

Daiichi-Sankyo stated that the edoxaban SPC listed one of the therapeutic indications for Lixiana as 'prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation (NVAf) with one or more risk factors'.

In its complaint, the Alliance had quoted a paragraph from Section 4.4 (Special warnings and precautions for use) of SPC:

'Renal function in NVAf

A trend towards decreasing efficacy with increasing creatinine clearance was observed for edoxaban compared to well-managed warfarin (see section 5.1). Therefore, edoxaban should only be used in patients with NVAf and high creatinine clearance after a careful evaluation of the individual thromboembolic and bleeding risk.'

The Alliance had incorrectly alleged that this precautionary wording had been consistently omitted from all Lixiana promotional materials, including EDX/16/0171 and EDX/15/0091(4). The prescribing information which formed a part of all Lixiana promotional materials contained clear details of this precaution (as required by Clauses 4.1 and 4.2):

'Renal function and NVAf: A trend towards decreasing efficacy with increasing creatinine clearance was observed for edoxaban compared to well-managed warfarin. Edoxaban should only be used in patients with NVAf and high creatinine clearance after a careful benefit risk evaluation.'

This wording was entirely consistent with Section 4.4 of the Lixiana SPC.

Daiichi-Sankyo stated that it had withdrawn the Lixiana Initiation Information Guide for prescribers before it received the complaint from the Alliance and this was communicated to the Alliance in Daiichi-Sankyo UK's initial response letter on 14 November 2017. The item was not specifically discussed during the face-to-face meeting. Subsequently, the Alliance stated in its response on 5 January 2018 that it considered 'all other matters raised in previous correspondence but not discussed at this [face-to-face] meeting to have been resolved'. Daiichi-Sankyo was thus surprised that the Alliance had specifically named this material in its complaint as it knew it had been withdrawn and had stated that it considered the matter resolved.

The Alliance had alleged that not referring to patients with high creatinine clearance in the main body of text in the Initiation Information Guide was misleading because patients with low creatinine clearance were discussed. Daiichi-Sankyo did not agree with this reasoning. The mention of patients with low creatinine clearance (ie moderate or severe renal impairment) was necessary because a dose adjustment was required for patients with creatinine clearance between 15-50ml/min, as per Section 4.2 (Posology and method of administration) of the Lixiana SPC:

‘Renal impairment

In patients with mild renal impairment (CrCL >50 – 80mL/min), the recommended dose is 60 mg Lixiana once daily.

In patients with moderate or severe renal impairment (CrCL 15 – 50mL/min), the recommended dose is 30mg Lixiana once daily (see section 5.2).

In patients with end stage renal disease (ESRD) (CrCL <15mL/min) or on dialysis, the use of Lixiana is not recommended (see sections 4.4 and 5.2).’

Daiichi-Sankyo stated that it was entirely proper and rational that the dose reduction criteria for patients with renal impairment should be mentioned in the main text of the Initiation Information Guide which was intended to help prescribers initiate Lixiana.

Conversely, there was no recommendation for dose alteration in the Lixiana SPC for patients with high creatinine clearance, which was why this group had not been given the same prominence in the main text as patients with renal impairment. Patients with high creatinine clearance were not renally impaired and had normal functioning kidneys. There was, therefore, no requirement to discuss patients with high creatinine clearance in conjunction with discussion around dose modification for patients with renal impairment, as they were very different patient groups. Patients with high creatinine clearance were instead discussed in the prescribing information of the Initiation Information Guide. Daiichi-Sankyo also noted that the front page of the Guide expressly and clearly instructed health professionals to consult the prescribing information and SPC for full information thus:

‘For UK healthcare professionals only in relation to the use of LIXIANA.
Prescribing information can be found on the back cover.
For additional prescriber and patient resources please visit www.lixiana.co.uk.
Please consult the Summary of Product Characteristics (SmPC) for full prescribing information.’

Daiichi-Sankyo noted that the Alliance had also complained that there was no mention in the Lixiana Practical Guide for prescribers of the precautionary wording from the SPC about high creatinine clearance, despite there being discussion of patients

with low creatinine clearance. The justification that Daiichi-Sankyo had given for the Initiation Information Guide also applied to this material. Additionally, in the Practical Guide, the discussion of patients with renal impairment was within a section discussing groups at increased risk of bleeding on page 15. The wording on page 15 indicated:

‘Several groups of patients are at increased risk of bleeding and should be carefully monitored for signs and symptoms of bleeding complications. Any treatment decision must be based on careful assessment of the treatment benefit against risk of bleeding.’

Patients with high creatinine clearance were not at increased risk of bleeding with Lixiana, and therefore discussion of this group would not be suitable within this section. Patients with high creatinine clearance were referred to in the prescribing information on page 20.

The front page of the Practical Guide also had the clear statement:

‘Prescribing information can be found on the back cover.’

The following page which was an overview of the material stated:

‘Please consult the Summary of Product Characteristics (SmPC) for full prescribing information.’

Thus, health professionals were expressly and clearly instructed to consult the prescribing information and SPC for full information.

Given health professionals’ responsibility to familiarise themselves with product information if not already so familiar, Daiichi-Sankyo stated that it would expect all health professionals reviewing the above materials to follow the clear instruction to refer to the prescribing information or SPC if they needed to, in order to become properly acquainted with the product. Daiichi-Sankyo disagreed with the inference made by the Alliance that the prescribing information was not sufficiently prominent to come to the prescriber’s attention and/or that prescribers would not refer to it because it was ‘usually placed at a distance at the back of the material’. The prescribing information in both documents was easy to locate on the last page, so very accessible for anyone seeking to review it. Prescribers would recognise the importance of the clear instructions to refer to it for more detailed information.

Daiichi-Sankyo stated that Lixiana had been evaluated by NICE in Technology Appraisal 355 (TA355). The Alliance had stated in its letter of complaint that Daiichi-Sankyo UK had selectively quoted aspects of TA355 as part of its defence. Daiichi-Sankyo noted that the passage from TA355 in question was not quoted in any promotional materials; rather it was quoted by Daiichi-Sankyo UK during inter-company dialogue. In the initial written response to the Alliance on 14 November 2017, Daiichi-Sankyo UK stated:

‘I will draw your attention to the National Institute for Health and Care Excellence (NICE) Technology Appraisal 355 (TA355), titled “Edoxaban for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation”. Section 4.6 of this document discusses patients with high creatinine clearance, and states, “The Committee concluded that if edoxaban is used in accordance with the summary of product characteristics, there is no reason to make differential recommendations based on creatinine clearance.”’

Daiichi-Sankyo did not view this as a selective quote, as it was, in fact, the concluding statement of Section 4.6 of TA355, and adequately summarised the decision made by the Committee on that topic. It was clear that in the context of patients with high creatinine clearance and NVAf, NICE did not believe that differential recommendations were required. While Daiichi-Sankyo UK drew on NICE recommendations when developing promotional materials, it stressed that it had never advocated any use of Lixiana that was inconsistent with the SPC.

Daiichi-Sankyo noted that the Alliance had referred to the American FDA label for Lixiana in its complaint. However, as the Alliance had also noted, the FDA label wording was not relevant to UK regulatory guidance, and it was therefore irrelevant to this discussion about compliance with the Code. The SPC did not include any contraindication for Lixiana in patients with NVAf and high creatinine clearance.

The Alliance had alleged that the Initiation Information Guide and the Practical Guide, as well as other Lixiana promotional materials in general were unbalanced, misleading and potentially dangerous. For the reasons given above, Daiichi-Sankyo refuted those allegations.

The Alliance had alleged a breach of Clause 7.2. Daiichi-Sankyo did not agree that the materials were misleading; they were sufficiently complete to enable prescribers to form their own opinions on the therapeutic value of Lixiana. Indeed, the prescribing information encouraged prescribers to carry out a careful benefit risk evaluation in this group of patients, consistent with the SPC. On this basis, Daiichi-Sankyo denied a breach of Clause 7.2.

The Alliance had alleged a breach of Clause 7.10 but did not clearly explain why. Lixiana promotional materials encouraged the rational use of the medicine, as evidenced by the inclusion of precautionary wording in the prescribing information. There were no exaggerated or all-embracing claims in the materials and all claims about Lixiana’s properties could be substantiated. Daiichi-Sankyo denied a breach of Clause 7.10.

Further, Daiichi-Sankyo did not believe that high standards had not been maintained, or that it had brought discredit to or reduced confidence in the pharmaceutical industry, therefore it denied breaches of Clauses 9.1 and 2.

Daiichi-Sankyo stated that EDX/16/0171 was certified by two people – a registered medical practitioner

(Qualification MBBS), and a non-medical signatory who was a senior official of Daiichi-Sankyo UK. The certificate was provided. This material was disseminated as hard copy by representatives to health professionals. The audience were junior doctors, pharmacists, cardiologists, haematologists, geriatricians, stroke physicians, respiratory physicians and general medical physicians.

Daiichi-Sankyo stated that EDX/15/0091(4) was certified by a registered medical practitioner (Qualifications BMedSci(Hons), BM BS, DRCOG, MRCGP). The certificate was provided. This material was disseminated as hard copy and by email to health professionals. In responding to this complaint, Daiichi-Sankyo UK had learned that an administrative error had regrettably led to the registered medical practitioner’s name not being notified to the PMCPA and MHRA in advance. Corrective actions had been put in place and Daiichi-Sankyo would separately contact the Authority with further details of a voluntary disclosure in this regard.

PANEL RULING

The Panel noted that Lixiana was indicated for the prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation (NVAf) with one or more risk factors, such as congestive heart failure, hypertension, age \geq 75 years, diabetes mellitus, prior stroke or transient ischaemic attack (TIA). The Panel noted that the Alliance was concerned that there was a misleading omission of precautionary SPC wording with regard to Lixiana (edoxaban) use in patients with NVAf and high creatinine clearance in all Lixiana materials and referred to two items, the Lixiana ‘Initiation Information Guide’ (ref EDX/16/0171) and the Lixiana ‘Practical Guide’ (ref EDX/15/0091(4)).

The Panel noted Daiichi-Sankyo’s submission that during inter-company dialogue it had informed the Alliance in a letter dated 14 November that the Lixiana ‘Initiation Information Guide’ (ref EDX/16/0171) had already been withdrawn and thus considered that the complaint was resolved in relation to this item. In the Panel’s view that material had been withdrawn prior to and wholly independently of matters raised in subsequent inter-company dialogue did not mean that such intercompany dialogue had been successful. In addition, the Panel noted that in its letter dated 14 November Daiichi-Sankyo stated that it reserved the right to use substantially similar materials. The Panel noted that the Alliance minutes of the face to face meeting held on 8 December referred to promotional materials including, *inter alia*, EDX/16/0171 in relation to the subject matter of the present complaint. The Panel further noted that Daiichi-Sankyo’s minutes of the meeting stated that this matter was not agreed. The Panel therefore considered that intercompany dialogue had not resolved the matter with regard to the Lixiana ‘Initiation Information Guide’ and the item would therefore be considered by the Panel.

The Panel considered that whether a special warning or precaution needed to be referred to in material depended on a consideration of all of the

circumstances including the nature of the warning/precaution, the therapy area and the content and intended use of the material.

The Panel noted that Section 4.4 of the Lixiana SPC, Special warnings and precautions for use, stated under the sub heading Renal function in NVAF:

'A trend towards decreasing efficacy with increasing creatinine clearance was observed for edoxaban compared to well-managed warfarin (see section 5.1). Therefore, edoxaban should only be used in patients with NVAF and high creatinine clearance after a careful evaluation of the individual thromboembolic and bleeding risk. Assessment of renal function: CrCL should be monitored at the beginning of the treatment in all patients and afterwards when clinically indicated (see section 4.2).'

The Panel noted that a subgroup analysis based on renal function which used 3 categories of creatinine clearance (CrCl) was discussed in the NICE technology appraisal guidance on edoxaban for preventing stroke and systemic embolism in people with NVAF which stated that the subgroup analysis across three categories (normal renal function, mild renal impairment and moderate renal impairment) 'suggested that renal function had a significant impact on the efficacy of edoxaban compared to warfarin ($p=0.0042$)'. The hazard ratios for the primary efficacy endpoint (prevention of stroke or systemic embolic event) were 0.68 (95% CI 0.54-0.85) and 0.86 (95% CI 0.63-1.17) for patients with mild to moderate renal impairment. In contrast the relative risk of stroke or systemic embolic event was higher with edoxaban than with warfarin in patients with normal renal function (HR 1.31, 95% CI 0.96-1.79). The guidance noted the company's view that these results should be treated with caution because a variety of factors including an unusually low event rate in the warfarin group and the lack of randomisation within the sub-groups could have contributed towards the result. Section 4.6 of the guidance (Consideration of the evidence, Clinical effectiveness) noted evidence that the trend towards decreasing efficacy of edoxaban with increasing creatinine clearance was likely to be because with better renal function edoxaban was removed by the kidneys more quickly leading to a reduction in treatment effect. Evidence was also submitted that this might apply to all newer anticoagulants but data needed to be re-evaluated to confirm this. Evidence was provided to NICE that the proportion of people with good renal function measured by creatinine clearance who would be eligible for treatment with edoxaban was in the region of 5-10% and that these were often younger people. The NICE committee noted the relevant warning at Section 4.4 of the SPC before concluding that if edoxaban was used in accordance with that SPC there was no reason to make differential recommendations based on creatinine clearance. The Panel noted that the relevant clinical data was also discussed at Section 5.1 Pharmacodynamic properties, of the Lixiana SPC which showed event rate data for 6 creatinine clearance sub-groups. The Panel noted that the Lixiana SPC stated in a Section 4.2 under the sub-heading Special populations, assessment of renal

function, that renal function should be assessed in all patients by calculating creatinine clearance prior to initiation of treatment with Lixiana, *inter alia*, when deciding on the use of Lixiana in patients with increased creatinine clearance.

The Panel noted that the Lixiana Initiation Information Guide was a 6 page booklet containing important summary information designed to help prescribers initiate Lixiana appropriately including under the following headings: switching, contraindications, cautions, pregnancy and breast feeding, hepatic impairment, renal impairment and monitoring. The Panel noted that a section on page 2 headed 'CAUTIONS' stated that the use of Lixiana was not recommended in patients with end stage renal disease (ESRD) (CrCl <15ml/min or on dialysis). On the following page in a section headed renal impairment it stated that in patients with mild renal impairment the recommended Lixiana dose was 60mg once daily, in patients with moderate or severe renal impairment the recommended dose was 30mg once daily and repeated that in patients with ESRD or on dialysis Lixiana was not recommended. It further stated in a subsequent section headed 'Monitoring that renal function should be monitored before treatment and when clinically indicated during treatment'. There was no reference in the body of the booklet to the SPC warning at issue. The Panel noted Daiichi-Sankyo's submission that the warning was not included within the renal impairment section as there was no recommendation for dose alteration in patients with high creatinine clearance. The Panel noted the comments about the nature of the relevant subgroup analysis in the NICE guidance. The Panel noted that based on this data the regulators had decided to include a special warning about decreased efficacy in patients with high creatinine clearance in the SPC. The SPC clearly stated that edoxaban should only be used in those patients after a careful evaluation of the individual thromboembolic and bleeding risk. The Panel considered that the warning in question did more than 'encourage' prescribers to undertake a careful evaluation, as stated by Daiichi-Sankyo; the warning stated that edoxaban **should only** be used after a careful evaluation of the individual's thromboembolic and bleeding risk (emphasis added), thereby implying in the Panel's view that such an evaluation was a requirement in this patient population. The Panel noted the stated purpose of the booklet in question to help prescribers initiate Lixiana appropriately and considered that failure to include the special warning was misleading and did not encourage the rational use of the medicine. In the Panel's view it was not sufficient to rely on the prescribing information at the back of the guide to provide the warning about the use of Lixiana and the trend towards the decreasing efficacy in patients with NVAF and high creatinine clearance. Material had to be capable of standing alone with regard to the requirements of the Code and could not rely on qualification in either prescribing information or a footnote. The Panel noted the Alliance's submission about the potential life-changing or even fatal consequences of failing to undertake such an evaluation in the relevant patient population. A breach of Clauses 7.2 and 7.10 was ruled. The Panel considered that Daiichi-Sankyo had failed to

maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted that the second item at issue was a 19 page booklet entitled Lixiana 'Practical Guide' for prescribers in relation to the use of Lixiana. It included information on, *inter alia*, indications, summary of efficacy and safety, dosing recommendations, dose reductions, populations at potentially higher risk of bleeding, and special patient populations.

The Panel noted its general comments above about the warning at Section 4.4 of the SPC, Section 4.2 of the SPC, including comments about the relevant data in the NICE guidance and the prescribing information and considered that they applied here. The Panel noted that based on the data discussed in the NICE guidance the regulators had decided to include a special warning about decreased efficacy in patients with high creatinine clearance in the SPC. The Panel considered that the warning in question did more than 'encourage' prescribers to undertake a careful evaluation, as stated by Daiichi-Sankyo; the warning stated that edoxaban **should only** be used after a careful evaluation of the individual's thromboembolic and bleeding risk (emphasis added), thereby implying in the Panel's view that such an evaluation was a requirement. The Panel noted that the Practical Guide covered more matters than the Initiation Information Guide considered above and included discussion of efficacy and safety issues including patients at higher risk of bleeding and special patient populations. The Panel noted the Alliance's submission about the potential life-changing or even fatal consequences of failing to undertake such an evaluation in the relevant patient population. The Panel considered that failure to include the special warning at issue, particularly considering there was a page dedicated to special patient populations, was misleading and did not encourage the rational use of the medicine. A breach of Clauses 7.2 and 7.10 were ruled. The Panel considered that Daiichi-Sankyo had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted the comments in the NICE guidance about the size of the patient population with good renal function (measured by creatinine clearance) who would be eligible for treatment with edoxaban was in the region of 5-10%. The Panel further noted the trend towards decreasing efficacy of edoxaban with increasing creatinine clearance and the consequences of such and considered that Daiichi-Sankyo's failure to include the warning meant that it had potentially put those patients' safety at risk. The Panel considered that patient safety was of the utmost importance and Daiichi-Sankyo's failure in this regard brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled in relation to each item.

APPEAL BY DAIICHI-SANKYO

Daiichi-Sankyo stated that it remained committed to the ethical promotion of medicines and to adhering to the Code. Patient safety was a primary concern for all staff. Daiichi-Sankyo appealed all the rulings

of breaches of the Code in relation to the Lixiana Initiation Information Guide and the Practical Guide.

Daiichi-Sankyo submitted that the Initiation Information Guide had already been withdrawn from circulation prior to the Alliance's initial complaint and the Alliance had been made aware of this during intercompany dialogue on 14 November 2017. The notification from Daiichi-Sankyo head office to the field to withdraw all promotional materials as a result of an update to the prescribing information was made in August 2017. The item was not discussed during a face-to-face meeting between the Alliance and Daiichi-Sankyo as it was considered to have been resolved.

Daiichi-Sankyo submitted that it was not appropriate for the Panel to rule upon this historic and withdrawn material. Withdrawn materials had not been considered when complaints had been made in other cases and therefore Daiichi-Sankyo did not understand the basis for considering them in this case. Daiichi-Sankyo appealed breaches of Clauses 7.2, 7.10, 9.1 and 2 in relation to this material, on the basis that it was withdrawn prior to the initial complaint. It was unclear the basis upon which the Panel could consider material which was withdrawn prior to the initial complaint being made.

Notwithstanding the above, Daiichi-Sankyo submitted that if the Appeal Board decided that the Initiation Information Guide was appropriately considered as part of the complaint, all breaches related to this material were appealed in any event for the reasons set out below.

Daiichi-Sankyo submitted that the omitted wording from the material at issue did not cause patient safety issues. In Section 4.4 of the edoxaban SPC, under the subheading 'Renal function in NVAf [Nonvalvular atrial fibrillation]' it stated that 'A trend towards decreasing efficacy with increasing creatinine clearance [CrCl] was observed for edoxaban **compared to well-managed warfarin** (see section 5.1). Therefore, edoxaban should only be used in patients with NVAf and high creatinine clearance after a careful evaluation of the individual thromboembolic and bleeding risk,' (emphasis added).

Daiichi-Sankyo submitted that the decreasing efficacy trend described in the first sentence was for edoxaban compared to well-managed warfarin. It did not describe a trend in edoxaban's absolute efficacy. The second sentence began with the word 'Therefore ...' indicating that the second sentence directly related to the description of the comparison in the previous sentence. The statement that edoxaban should only be used in patients with NVAf and high creatinine clearance after a careful evaluation of the individual thromboembolic and bleeding risk, was linked to a description of the efficacy trend when edoxaban and well-managed warfarin were compared, not to the absolute efficacy of edoxaban when viewed in isolation.

Daiichi-Sankyo submitted that Table 5 of the edoxaban SPC showed that in the ENGAGE AF-TIMI 48 study, there was a trend to a decreasing annual

rate of ischaemic stroke/systemic embolic events (SEE) associated with a rise in creatinine clearance in NVAF patients taking edoxaban. The absolute event rate decreased from 1.89%/year in NVAF patients with CrCl ≥ 30 to ≤ 50 ml/min to 0.78%/year in NVAF patients with CrCl >130 ml/min. As described above, the trend towards a decreasing efficacy with edoxaban in patients with NVAF was relative to well managed warfarin, where the hazard ratio for edoxaban vs warfarin showed a rising trend as the creatinine clearance rose. Importantly, this trend was not statistically significant. Table 5 showed that the 95% confidence intervals for the hazard ratio were increasingly wide as creatinine clearance increased, corresponding to fewer absolute numbers of patients experiencing ischaemic stroke/SEE in both edoxaban and warfarin groups.

Daiichi-Sankyo submitted that an exploratory sub-analysis of the ENGAGE AF-TIMI 48 study, looking at the impact of renal function on outcomes with edoxaban (Bohula *et al* 2016) had been published. This noted that the 'Thromboembolic and bleeding event rates were lowest in those with the highest CrCl in all 3 treatment arms (warfarin, [high dose edoxaban regimen] HDER, and [low dose edoxaban regimen] LDER)'. HDER was the licensed dosing regimen of edoxaban which was discussed in the materials at issue.

Daiichi-Sankyo submitted that Bohula *et al* stated: 'The primary net clinical outcome of [stroke/SEE], major bleeding, and all-cause death was more favourable for HDER compared with warfarin across the range of renal function subgroups (CrCl 30–50 mL/min; HR, 0.86; 95% CI, 0.75–0.98; CrCl >50–95 mL/min: HR, 0.91; 95% CI, 0.82–1.00; CrCl >95 mL/min: HR, 0.93; 95% CI, 0.77–1.13; P for interaction=0.73... On the basis of a **nonsignificant interaction across renal subgroups**, findings were consistent with the overall trials results in which HDER was more favourable to warfarin for the secondary net clinical outcome of disabling stroke, life-threatening bleeding, or death (P for interaction=0.19) and tertiary exploratory net clinical end points comprising severe or irreversible events. However, **nonsignificant numerically higher rates** were observed with HDER versus warfarin in those with a CrCl >95 mL/min for these secondary and tertiary net clinical end points' (emphasis added).

Bohula *et al* went on to state 'exploratory analyses in patients with a CrCl >95 mL/min suggested lower **relative** efficacy for the prevention of thromboembolic events with HDER compared with warfarin. As a result of persistently lower rates of major bleeding in patients with a CrCl >95 mL/min, **the primary net clinical outcome remained favourable for HDER compared with warfarin**' (emphasis added).

Daiichi-Sankyo submitted that here again it was made clear that any decrease in efficacy for edoxaban in NVAF patients with high creatinine clearance was found only when compared to warfarin, and this was not statistically significant. It was also important to note that in relation to overall patient safety, when efficacy and safety were analysed together in the primary net clinical outcome

analysis (a composite of stroke, SEE, major bleeding and all-cause death), edoxaban was favourable compared to warfarin. Daiichi-Sankyo therefore did not agree that the omission of the warning at issue from the body of promotional materials posed a risk to patient safety and this was evidenced above by the clinical data.

Prescribing practice

Daiichi-Sankyo submitted that both efficacy and safety of a medicine were considered when prescribers were deciding on the suitability of a medicine for a particular patient. The overall benefit/risk ratio was taken into account. For overall patient safety, the net clinical outcome (which combined efficacy and safety measures) was a more relevant measure than efficacy alone. A careful evaluation of the risks and benefits of a medicine should always be undertaken by any prescriber. The high creatinine clearance statement in the edoxaban SPC did not alter this obligation on prescribers.

Daiichi-Sankyo submitted that in order to have an adequate knowledge of a patient's health when considering prescribing any anticoagulant for a patient with NVAF, a doctor would have undertaken a careful evaluation of the patient's thromboembolic and bleeding risk. The high creatinine clearance statement in the edoxaban SPC therefore **did not require that doctors should do anything additional to what they would already do when evaluating the risks and benefits of a medicine**. The presence or omission of the high creatinine clearance statement from the body of promotional materials did not impact on what a doctor would be required to do in any prescribing situation. The omission of the wording from the body of promotional materials did not pose a risk to patient safety.

Relationship of high creatinine clearance to renal impairment

Daiichi-Sankyo submitted that it was relevant to note that patients with high creatinine clearance did not have renal impairment. High creatinine clearance was not a disease process (unlike renal impairment), and therefore people with high creatinine clearance were not regarded in clinical practice as having any problems with their kidney function, or as being a part of a special population. A patient with high creatinine clearance would not be flagged as having an abnormal result in blood test reporting systems. Indeed, in Bohula *et al*, people with CrCl > 95ml/min were described as having normal renal function. The authors noted that the European Medicines Agency '...did not place any restrictions on the use of edoxaban in patients with normal renal function'.

Lixiana Initiation Information Guide

Daiichi-Sankyo noted that 'The Panel noted that the stated purpose of the booklet in question to help prescribers initiate Lixiana appropriately and considered that failure to include the special warning was misleading and did not encourage the rational use of the medicine. In the Panel's view it was not sufficient to rely on the prescribing information at the back of the guide to provide the warning

about **the use of Lixiana and the trend towards the decreasing efficacy in patients with NVAF and high creatinine clearance**' (emphasis added).

Daiichi-Sankyo submitted that it appeared that the Panel considered that the absolute rate of ischaemic stroke and SEE increased in patients with NVAF as the creatinine clearance increased and made a judgement on that basis. However, as described above, this was not so. The trend towards decreasing efficacy with increasing creatinine clearance in patients on edoxaban with NVAF, was only when compared to well-managed warfarin. The absolute rate of ischaemic stroke and SEE actually fell with edoxaban in NVAF patients as creatinine clearance rose. The net clinical outcome also remained favourable for edoxaban compared to warfarin in NVAF patients as creatinine clearance rose.

Daiichi-Sankyo submitted that the Panel had also emphasised in its ruling the fact that there were sections in the material related to renal impairment and edoxaban dose modification. It appeared that the Panel considered that if there was discussion of renal impairment, there should also be discussion of high creatinine clearance. However, Daiichi-Sankyo disagreed that this should be the case. As described above, renal impairment was due to a disease process, whereas high creatinine clearance was not. Patients with high creatinine clearance had normal renal function. Therefore, discussion of high creatinine clearance would not logically fit into sections discussing renal impairment. The edoxaban SPC mandated reduction of the edoxaban dose in patients with renal impairment, which was why it was important that this was emphasised in all materials, to ensure patients were not over-dosed. However, there was no change of edoxaban dose recommended for patients with high creatinine clearance, which was why this was not given the same level of emphasis. The high creatinine clearance statement was instead given in the prescribing information. The reader was referred on page 1 of the material to the SPC for full prescribing information. The recommendations given in the body of the material were entirely consistent with the SPC and the material was not misleading, and therefore not in breach of Clause 7.2.

Daiichi-Sankyo noted that as discussed above, in carrying out their prescribing duties, doctors were expected to have an adequate knowledge of a patient's health, which would include a careful evaluation of their thromboembolic and bleeding risk. There was nothing in the material that recommended that doctors should not carry out their usual obligations to assess a patient's health before prescribing edoxaban or recommended use of edoxaban in a manner that was not rational, and therefore the material was not in breach of Clause 7.10.

Consequently, high standards had been maintained, and Daiichi-Sankyo did not agree that omitting the wording was a risk to patient safety. Therefore, Daiichi-Sankyo submitted that this material was not in breach of Clauses 9.1 or 2.

Lixiana Practical Guide

Daiichi-Sankyo noted the Panel's view that the '... failure to include the special warning at issue, particularly considering there was a page dedicated to special patient populations was misleading and did not encourage the rational use of a medicine'.

Daiichi-Sankyo submitted that directly below the Special Patient Populations heading on page 15 the Practical Guide stated 'Several groups of patients are at increased risk of bleeding and should be carefully monitored for signs and symptoms of bleeding complications'. It was clear to the reader that this page was specifically talking about special patient populations at increased risk of bleeding. The material also contained sections on 'Patients at Potentially Higher Risk of Bleeding', and 'Management of Bleeding Complications'. Bleeding was the primary safety concern when considering the use of any anticoagulant, as it could have devastating consequences for a patient, which was why this particular topic was strongly emphasised. Patients with high creatinine clearance **were not at increased risk of bleeding**, and therefore the statement from the edoxaban SPC regarding high creatinine clearance would not logically fit into these sections. Furthermore, these patients would not be regarded by doctors as being part of a special patient population, as they had normal renal function. Therefore, this material was not misleading or in breach of Clause 7.2.

Daiichi-Sankyo submitted that as above, in carrying out their prescribing duties, doctors were expected to have an adequate knowledge of a patient's health, which would include a careful evaluation of their thromboembolic and bleeding risk. There was nothing in the material that recommended that doctors should not carry out their usual obligations to assess a patient's health before prescribing edoxaban or recommend use of edoxaban in a manner that was not rational, and therefore the material was not in breach of Clause 7.10.

Consequently, Daiichi-Sankyo submitted that high standards had been maintained, and it did not agree that omitting the wording was a risk to patient safety. Therefore, Daiichi-Sankyo submitted that this material was not in breach of Clauses 9.1 or 2.

Summary

Daiichi-Sankyo submitted that the materials were not misleading in that the materials did encourage the rational use of edoxaban. Consequently, high standards had been maintained. Patient safety had not been put at risk and therefore Daiichi-Sankyo appealed the Panel's ruling of a breach of Clause 2 for the materials.

Daiichi-Sankyo submitted that as stated previously, all doctors were expected to have an adequate knowledge of a patient's health prior to any prescribing decision. Thromboembolic risk and bleeding risk were integral factors of an NVAF patient's health that a doctor would evaluate when considering the appropriate anticoagulant to prescribe, whether that was edoxaban or another

product (such as warfarin). There was no evidence that the omission of the high creatinine clearance statement from the body of promotional materials had led to patient harm or could potentially lead to patient harm. On this basis Daiichi-Sankyo did not agree with the Panel that the omission of the high creatinine clearance statement from the body of promotional materials had put patients' safety at risk. Therefore, Daiichi-Sankyo did not agree with the Panel that Daiichi-Sankyo had brought discredit upon, and reduced confidence in the pharmaceutical industry, in breach of Clause 2.

Daiichi-Sankyo submitted that patient safety was central to its work and this was reflected in promotional materials. The materials pointed to situations where the dosage of edoxaban should be modified in line with the SPC in order to ensure patients were not over-dosed and not put at unnecessary risk of bleeding. There was also a strong emphasis on communicating data on bleeding which was the main safety concern of edoxaban and indeed all anticoagulants.

COMMENTS ON THE APPEAL BY THE ALLIANCE

The Alliance stated that it was notable that in Daiichi-Sankyo's response to its initial complaint to the PMCPA, a principal part of its defence was that the information relating to the precautionary wording was indeed included in the materials as part of the prescribing information and that this was sufficient. Daiichi-Sankyo's case now appeared to have shifted to one based on a general assertion that the precautionary wording did not need to be included at all.

The Alliance alleged that the rationale provided by Daiichi-Sankyo for its appeal relating to the omission of precautionary wording about the use of edoxaban in patients with a high creatinine clearance was long and complex but it could be distilled into a number of core points which it addressed below.

1 Daiichi-Sankyo's submission that the Panel was wrong to review the Lixiana Initiation Information Guide

The Alliance stated that this assertion demonstrated a lack of understanding of both the letter and principles of both the Code and the PMCPA Constitution and Procedure. The intercompany dialogue clearly demonstrated that Daiichi-Sankyo did not accept that the content of this material was in breach of the Code and that it had reserved the right to use similar content in the future, continuing to omit the essential precautionary statement relating to the use of edoxaban in patients with high creatinine clearance and therefore continuing to expose patients to unnecessary risk.

The Alliance noted Daiichi-Sankyo specifically stated in its appeal that 'The item the [Initiation Information Guide] was not discussed during a face-to-face meeting between the Alliance and DSUK'. Daiichi-Sankyo stated that the Alliance stated on 5 January 2018 that it considered 'all other matters raised in previous correspondence but not discussed at this [face-to-face] meeting to have been resolved'. The

Alliance referred to its minutes for this meeting. In paragraph 8 of this document, entitled 'Addition of high creatinine clearance warning & precaution statement as per SPC on all promotional materials', the minutes clearly stated the following:

'Alliance expressed the concerns that there have been multiple promotional materials including EDX/17/0087(1), EDX/16/0171, EDX/15/0091(4), EDX/17/0032(1), EDX/15/0088(4), EDX/15/0070(2) without a clear cautionary statement with regards to the edoxaban use in patients with high creatinine clearance as mentioned in edoxaban SPC section 4.4.'

Thus, the Alliance alleged that it was clear that this item was discussed during intercompany dialogue as a specific example of the ubiquitous omission of this important warning statement. The Alliance therefore did not understand why Daiichi-Sankyo would state that this item was not discussed during this meeting.

Furthermore, the Alliance referred to Daiichi-Sankyo's letter to the Alliance, 22 December 2017. The final sentence of a paragraph entitled 'Patients with high creatinine clearance' stated that:

'DSUK does not make any specific claims about patients with high creatinine clearance in its materials so does not believe there is any requirement to make further mention of the precaution statement from Section 4.4 of the SmPC, beyond that which is already mentioned in the Prescribing Information'.

The Alliance noted that Daiichi-Sankyo's appeal referred to the Alliance correspondence dated 5 January 2018. This was a letter concluding the intercompany dialogue and stating how the Alliance intended to proceed. In this letter, a paragraph entitled 'Patients with high creatinine clearance, stated:

'I note that DSUK continues to assert that omission of information relating to this precautionary statement from the body text of any edoxaban materials does not constitute a breach of the Code as this information is contained within the prescribing information. However, the Alliance continues to interpret this considered and ubiquitous omission to be a clear and serious breach of clauses 7.2, 7.10, 9.1 and 2 of the Code. Unfortunately, as we have been unable to resolve this matter through inter-company dialogue, we will now be placing this matter before the PMCPA for their consideration.'

Thus, the Alliance alleged that the Daiichi-Sankyo claim that the Alliance could have, in any way, considered this to be a satisfactory outcome for the intercompany dialogue relating to this item was disingenuous and not supported by the records. In these circumstances the Panel was clearly entitled to consider whether this material was in breach of the Code.

2 Daiichi-Sankyo's submission that the precautionary statement related only to edoxaban when compared to well-controlled

warfarin and not to the 'absolute efficacy of edoxaban when viewed in isolation'

The Alliance alleged that this assertion was difficult to comprehend as it appeared to be based on a complete misunderstanding of the role of controlled clinical trials in the investigation of a medicine's efficacy and safety, and the regulatory approval process. All the Non-Valvular Atrial Fibrillation pivotal regulatory trials for all the NOACs were conducted with warfarin as the comparator medicine. Therefore, all the efficacy and safety information relating to the NOACs, upon which the EMA licensing decisions were made and which was reflected in the wording of their SPCs, were derived from comparisons with warfarin. Similarly, an expressed concern of the regulatory authorities about decreased efficacy in patients with high creatinine clearance was derived from the comparative data. This issue was only highlighted in the edoxaban registration trials and not the other NOACs. Therefore, it was only the edoxaban SPC (and not the other NOAC SPCs) that contained the precautionary wording in patients with high creatinine clearance.

3 Daiichi-Sankyo appeared to be asserting that the available data did not support the precautionary statement

The Alliance noted that Daiichi-Sankyo had provided a detailed discussion of data derived from its pivotal ENGAGE study and its exploratory sub-analysis of these data. All of these data would have been made available to the regulatory authorities for consideration and would have been the basis of the decision by the EMA to include their precautionary wording about the use of this medicine, and by the FDA to contraindicate its use in this group of patients by the addition of a black box warning. It was not appropriate to attempt to undermine the decisions of the regulatory authorities simply because a company disagreed with their interpretation of its data. It was certainly not acceptable to simply ignore them for the same reason. Similarly, if there were new data or analyses which Daiichi-Sankyo considered could lead the regulatory authorities to change their opinion then it should submit them for appropriate regulatory consideration. Daiichi-Sankyo was not in a position to make decisions about the validity, or otherwise, of its SPC wording without the appropriate discussions with the regulatory authorities. The precautionary wording within the edoxaban SPC was clear and Daiichi-Sankyo had an obligation to ensure that all UK health professionals were properly informed about it when they were making their prescribing decision.

4 Daiichi-Sankyo stated that it was not necessary to include the precautionary wording in promotional material because it did not impact on what a doctor would be required to do in any prescribing situation

The Alliance alleged that when decisions were made about the clinical management of atrial fibrillation which might entail the use of anticoagulation there were usually two steps involved:

- a) Is anticoagulation needed?
- b) If so, which anticoagulant should be used?

The Alliance alleged that it was the second of these decisions which could be influenced by awareness of the precautionary wording under discussion here. Section 1.5 of the current NICE guidance on the management of atrial fibrillation (Clinical guideline [CG180] Published June 2014 Last updated: August 2014) stated the following:

'Discuss the options for anticoagulation with the person and base the choice on their clinical features and preferences.'

Section 1.2 of the NICE Technology Appraisal: Edoxaban for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation, Technology appraisal guidance [TA355] Published, 23 September 2015, stated the following:

'The decision about whether to start treatment with edoxaban should be made after an informed discussion between the clinician and the person about the risks and benefits of edoxaban compared with warfarin, apixaban, dabigatran etexilate and rivaroxaban. For people considering switching from warfarin, edoxaban's potential benefits should be considered against its potential risks, taking into account the person's level of international normalised ratio (INR) control.'

The Alliance alleged that there was now a choice for clinicians and patients when it came to choosing which oral anticoagulant to select for the prevention of stroke and systemic embolism in non-valvular AF. There were four NOACs and vitamin K antagonists. The clinical profiles of patients differed, as did the profiles and characteristics of the available oral anticoagulants. This was acknowledged and encompassed in the NICE recommendations quoted above. In order for the discussions and decisions recommended by NICE to take place, both clinicians and patients must be fully informed about the risks and benefits of all the options. The precautionary wording regarding high creatinine clearance was unique to edoxaban and both clinicians and patients were entitled to be made fully aware of it.

5 Daiichi-Sankyo stated that high creatinine clearance was not a disease state and also appeared to consider that therefore these patients were not at-risk and were also therefore not worthy of inclusion as a special patient population in their promotional material.

The Alliance alleged that the fact that a particular patient characteristic was not a disease state did not preclude its inclusion in an SPC as requiring precautionary wording. Pregnancy, low weight and advanced age were examples of special populations that were not disease states but required special attention to minimise risk. Similarly, patients with high creatinine clearance were a special population that the regulators had identified as requiring special attention to minimise risk if edoxaban was being considered. Indeed, the precaution was not a dosing modification but a determination as to whether to

use edoxaban at all in this population based on a benefit-risk evaluation. Bleeding was indeed an important risk for consideration when prescribing anticoagulants and it was true that patients particularly at risk from such bleeding were a special population. However, they were not the only special patient population and they were not the only population at risk. To state that a particular patient group was excluded from a risk discussion because they did not fit the description of the headings Daiichi-Sankyo had chosen to include in, or exclude from, its own material appeared an unconvincing explanation.

Daiichi-Sankyo actually stated in its appeal that these patients would not be regarded by doctors as being part of a special population, as they had normal renal function. The Alliance alleged that the consequences of lack of efficacy could be every bit as serious as those of bleeding. The purpose of the precautionary wording was to reduce the risk that patients with high creatinine clearance might experience a reduction in efficacy on edoxaban and as a consequence be at increased risk of stroke, disability and even death. It was uncommon to have such strong precautionary wording for patients with high creatinine clearance and it would be usual for clinicians to assume that, in the absence of any information to the contrary, patients with what they considered to be normal renal function would not be at any increased risk. If doctors were unaware that these patients should perhaps be on another anticoagulant other than edoxaban, because they did not consider them to be at risk, then surely this was the strongest reason possible why they needed to be made aware of the precautionary wording. It was worth remembering that mention of the precautionary wording relating to this at-risk special patient population was omitted from every single piece of promotional material, both electronic and hard copy, used by Daiichi-Sankyo to promote edoxaban in the UK. As the Alliance indicated, the NHS had been adopting guidelines relating to the use of edoxaban and these commonly did not make any reference to this warning and precaution in patients with high creatinine clearance. This suggested there was widespread failure by Daiichi-Sankyo to inform prescribers and payors of this warning and precaution. This comprehensive omission of important information from all promotional material was potentially putting at risk a significant proportion of patients who were receiving, or might be prescribed, edoxaban. Hence the request by the Alliance that Daiichi-Sankyo take immediate action to withdraw these promotional materials, and urgently inform the healthcare community of this important warning. Recent evidence suggested up to 15% of patients with AF had high creatinine clearance, illustrating the magnitude of this potential patient safety issue.

6 Daiichi-Sankyo's submission that there was no evidence that the omission of the precautionary statement from the body of its promotional materials had led to patient harm or could potentially lead to patient harm

The Alliance stated that the enforcement of compliance with the Code was designed to

prevent anyone coming to harm as a result of non-compliance. It was not a requirement that, before a breach could be judged, it must be demonstrated that the breach had actually resulted in harm to patients or the general public. Similarly, the wording of any medicine's licence was based on a review of all the clinical and preclinical data by the regulatory authority and was designed to ensure that the potential risks to a patient from use of the medicine were minimised whilst at the same time increasing the chances that the patient would obtain benefit. Daiichi-Sankyo might consider that there was no evidence that concealing the important precautionary wording from prescribers could potentially lead to patient harm but by their inclusion of this wording in the edoxaban SPC and label information, uniquely for this medicine within the NOAC class, both the EMA and the FDA had demonstrated that their review of the evidence had led them to a different conclusion.

In summary:

- The PMCPA was entitled to review all the materials currently under discussion
- The precautionary wording was a general warning about the potential for decreased efficacy of edoxaban in a specific population. Daiichi-Sankyo's use of terms such as 'absolute efficacy' or efficacy 'viewed in isolation' was meaningless in the context of SPC recommendations based on controlled clinical trials.
- The precautionary SPC wording in patients with high creatinine clearance was the result of an in-depth consideration of all the available data by the regulatory authorities. Daiichi-Sankyo had a responsibility to make it clear in its promotional material that these patients required particular consideration. The fact that Daiichi-Sankyo disagreed with the regulatory authority's interpretation of these data did not give it the right to pretend that this precautionary wording did not exist. Similarly, if Daiichi-Sankyo had new data or analyses which it thought might change the situation then it should discuss it with the regulatory authorities and not try and use it as a defence for its disregard of the requirements of the Code.
- The Alliance alleged that clinicians and patients with non-valvular AF now had a choice about which anticoagulant they wished to use. NICE recommended an informed discussion to decide amongst all the different options. All the available options had different profiles. These differences, positive and negative, should be transparently available to clinicians to enable them to have an intelligent, informed discussion with their patients. The precautionary wording relating to patients with high creatinine clearance was unique to edoxaban and was therefore potentially an important consideration for these prescribing decisions. The ubiquitous omission of any mention of this precaution from any Daiichi-Sankyo promotional material was a serious breach of the Code which had the potential to put a significant proportion of patients with non-valvular AF at risk of stroke, disability or death.
- High creatinine clearance, whilst not a disease state, might have a potential for increased risk

in such patients (a significant proportion of all patients with non-valvular AF) if edoxaban was used. These patients therefore should be considered as a special patient population. Excluding them from promotional material merely because they did not fall into the categories of risk which Daiichi-Sankyo had chosen (principally renal disease and bleeding) was highly misleading, and potentially impacted the safety of patients.

- It was not necessary to demonstrate that any patient had suffered harm before a breach of the Code could be ruled. Furthermore, it was the opinion of the regulatory authorities that there was sufficient evidence of a potential for a reduction in efficacy with edoxaban in patients with a raised creatinine clearance, hence the precautionary wording, which therefore also needed to be included in promotional material. The contrary opinion of Daiichi-Sankyo regarding the lack of evidence of potential for patient harm was irrelevant.

After receipt of the outcome in this case and prior to being notified of Daiichi-Sankyo's appeal the Alliance requested, *inter alia*, that Daiichi-Sankyo suspend use of the material at issue pending the outcome of any appeal. The Alliance provided three guidance documents from the NHS on the use of direct oral anticoagulants (DOACs) in NVAF where there was quite detailed information on prescribing more medicines where there was no reference to the consideration for high creatinine clearance with edoxaban. The Alliance separately requested that due to potential safety issues that Daiichi-Sankyo be required to take reparative action.

The Alliance's view was that Daiichi-Sankyo should be required to proactively communicate to all relevant UK prescribers and other relevant decision makers to include those NHS organisations which had issued guidance on the use of edoxaban in NVAF. The Alliance also provided data which showed that the proportion of patients with good renal function eligible for treatment with edoxaban was in the order of 14%. Daiichi-Sankyo proposed in its NICE submission that the proportion was 5-10%.

The Alliance's submission was provided to Daiichi-Sankyo for comment and in response it stated, *inter alia*, that the Lixiana Initiation Information Guide was withdrawn prior to intercompany dialogue and that the Lixiana Practical Guide was recalled on 20 August due to an update to the prescribing information. Daiichi-Sankyo submitted that it had suspended use all Lixiana promotional materials pending the outcome of the appeal.

APPEAL BOARD RULING

The Appeal Board noted the warning about decreased efficacy in patients with high creatinine clearance in the Lixiana SPC. Section 4.4 of the Lixiana SPC, Special warnings and precautions for use, stated under the sub heading, Renal function in NVAF:

'A trend towards decreasing efficacy with increasing creatinine clearance was observed for

edoxaban compared to well-managed warfarin (see section 5.1). Therefore, edoxaban should only be used in patients with NVAF and high creatinine clearance after a careful evaluation of the individual thromboembolic and bleeding risk.

Assessment of renal function: CrCL should be monitored at the beginning of the treatment in all patients and afterwards when clinically indicated (see section 4.2).'

The Appeal Board noted that the warning referred to a 'trend towards decreasing efficacy'. It also noted the comments in the NICE guidance about the size of the patient population with good renal function (measured by creatinine clearance) who would be eligible for treatment with edoxaban was in the region of 5-10%. The Appeal Board also noted the data submitted by the Alliance in this regard.

The Appeal Board noted that the FDA had contraindicated the use of Lixiana in this group of patients and noted Daiichi-Sankyo's submission that the EMA had assessed the data differently. Nevertheless, there was a warning about use in a patient population with normal kidney function which the Appeal Board considered was unusual. Both items at issue referred readers to the SPC for full prescribing information. In answer to a question at the appeal, the Daiichi-Sankyo representatives referred to an ongoing relevant study, the results of which were not yet available.

The Appeal Board noted that the Lixiana 'Initiation Information Guide' was a 6 page booklet containing important summary information designed to help prescribers initiate Lixiana appropriately including under the following headings: switching, contraindications, cautions, pregnancy and breast feeding, hepatic impairment, renal impairment and monitoring. There was no reference in the body of the booklet to the SPC warning at issue. The Appeal Board considered that prescribers would not necessarily expect patients with high creatinine clearance and thus normal kidney function to be at risk when prescribing a NOAC for NVAF; it was counter intuitive. It was therefore even more important that the SPC warning in question was drawn to their attention, particularly as Lixiana was the only NOAC that had this specific warning. The Appeal Board considered that it was wholly inadequate for Daiichi-Sankyo to only rely on the inclusion of the warning at issue in the prescribing information. Material had to be capable of standing alone with regard to the requirements of the Code and could not rely on qualification in either the prescribing information or a footnote. Other warnings from the SPC were included in the main body of the Initiation Information Guide, including in the Appeal Board's view special warnings and precautions with less strong wording and to omit the warning at issue downplayed its relative importance. The Appeal Board noted the position with the FDA. The Appeal Board considered that given the nature of the warning it was paramount that it appeared prominently in the body of the item at issue.

The Appeal Board thought it odd that, according to the company representatives, its field force had been trained on the warning at issue yet the company had omitted the warning from the body of the materials.

The Appeal Board considered that the failure to include the special warning in the body of the Initiation Information Guide was misleading and did not encourage the rational use of the medicine. The Appeal Board noted the Alliance's submission about the potential life-changing or even fatal consequences of failing to undertake such an evaluation in the relevant patient population. The Appeal Board upheld the Panel's rulings of a breach of Clauses 7.2 and 7.10. The Appeal Board considered that Daiichi-Sankyo had failed to maintain high standards and it upheld the Panel's ruling of a breach of Clause 9.1. The appeal on these points was unsuccessful.

The Appeal Board noted that the Lixiana Practical Guide was a 19 page booklet for prescribers. It included information on, *inter alia*, indications, summary of efficacy and safety, dosing recommendations, dose reductions, populations at potentially higher risk of bleeding, and special patient populations.

The Appeal Board considered that comments above applied equally to this item. The Appeal Board noted that the Practical Guide covered more matters than the Initiation Information Guide and included discussion of efficacy and safety issues including patients at higher risk of bleeding and special patient populations. The Appeal Board considered that the failure to include the special warning at issue in the body of the item, particularly considering there was a page dedicated to special patient populations and the missing information appeared in SPC under the heading special populations, was misleading and did not encourage the rational use of the medicine. The Appeal Board upheld the Panel's rulings of a breach of Clauses 7.2 and 7.10. The Appeal Board considered that Daiichi-Sankyo had failed to maintain high standards and it upheld the Panel's rulings of a breach of Clause 9.1. The appeal on these points was unsuccessful.

The Appeal Board noted the comments in the NICE guidance about the size of the patient population with good renal function. The Appeal Board further noted the trend towards decreasing efficacy of edoxaban with increasing creatinine clearance and the consequences of such and considered that Daiichi-Sankyo's failure to include the warning meant that it had potentially put those patients' safety at risk. Daiichi-Sankyo had not submitted any adequate explanation for this omission and it appeared had not treated patient safety as a priority. The Appeal Board considered that patient safety was of the utmost importance and Daiichi-Sankyo's failure in this regard brought discredit upon and reduced confidence in the pharmaceutical industry. The Appeal Board upheld the Panel's ruling of a breach of Clause 2 in relation to each item. The appeal on this point was unsuccessful.

The Appeal Board noted its comments and rulings of breaches of the Code in the above including a breach

of Clause 2. The Appeal Board considered that Daiichi-Sankyo's actions had meant that prescribers had been provided with material that failed to highlight an important patient safety consideration and consequently patients might have been put at risk. This was totally unacceptable. The Appeal Board noted that the NHS guidance on the use of DOACs in NVAF provided by the Alliance made no reference to the warning at issue. Consequently, the Appeal Board decided, in accordance with Paragraph 10.6 of the Constitution and Procedure, to require Daiichi-Sankyo to issue a hard copy corrective statement to all recipients of the material at issue. In addition, the Appeal Board considered that given the items broad dissemination including that in the Appeal Board's view it was more likely than not that this material would have been shared by prescribers with colleagues, the Appeal Board considered that the corrective statement should also be sent to relevant UK prescribers. The corrective statement should refer to the case report. Under Paragraph 10.6 details of the proposed content and mode and timing of dissemination of the corrective statement must be provided to the Appeal Board for approval prior to use.

In addition, the Appeal Board decided, in accordance with Paragraph 10.3, to require Daiichi-Sankyo to take steps to recover the material from those who had received it; written details of the action taken must be provided to the Appeal Board. This should be included in the corrective statement.

2 – TWITTER

COMPLAINT

The Alliance was concerned about the use of the Twitter campaign by Daiichi-Sankyo and its agencies to promote Lixiana which used the hashtag '#safeplicity' - clearly derived from combining the words 'safe' or 'safety' and 'simplicity'. In this regard, the Alliance noted that Clause 7.9 prohibited use of the word 'safe' without qualification. This prohibition applied equally to 'grammatical derivatives of the word such as 'safety'. (The Alliance also noted Article 3, Section 3.07 of the EFPIA Health Professional Code stated that 'The word "safe" must never be used to describe a medicinal product without proper qualification').

The Alliance noted that it was an established principle under the Code that companies were responsible under the Code for external persons or groups acting on their behalf or with their authority including advertising agencies, PR agencies and meeting organisers. If a breach of the Code occurred in relation to an activity carried out on a pharmaceutical company's behalf, then that company would be held responsible.

The Alliance noted particular Twitter posts (copies provided) which could be found on Twitter at #safeplicity. It was clear from these posts that:

- 1 The #safeplicity had been used to promote Lixiana. In the screenshots provided of the Twitter feed, there were a number of posts which consisted of photographs which prominently

included both the hashtag claim '#safeplicity' and the brand name and branding colours of Lixiana. A number of these had apparently been posted by employees of the UK agency engaged by Daiichi-Sankyo to develop its congress stand and promotional activities. During inter-company dialogue, Daiichi-Sankyo UK had stated that its parent company, Daiichi-Sankyo Europe GmbH based in Germany, had used this hashtag and instructed UK-based agencies to use it as well. The hashtag was also used frequently on the Twitter feed for Daiichi-Sankyo Europe and when readers clicked on this hashtag they were transferred to the hashtag page which contained promotional photographs. However, it was not made clear in any of the posts by these agencies that the activity was sponsored by Daiichi-Sankyo. Neither was it clear from the Daiichi-Sankyo posts that by clicking on the #safeplicity readers would access Lixiana promotional material. This constituted disguised promotion. Furthermore, as Twitter was very widely used by the public, this promotional activity was also accessible by the public.

- 2 This promotion was carried out by Daiichi-Sankyo and its UK based agencies. The term safeplicity and the #safeplicity were developed by these agencies and therefore originated in the UK. (The Alliance referred to the highlighted sections of the screenshots provided of these agencies showing their location and that the scope of their work for Lixiana was promotional).
- 3 Since the Alliance initiated inter-company dialogue with Daiichi-Sankyo on the matter, this hashtag had continued to be used on Twitter, including on the Daiichi-Sankyo Europe twitter feed – the latest example of which was 29 December 2017.

During inter-company dialogue The Alliance had asked Daiichi-Sankyo to immediately stop using the #safeplicity or the term safeplicity in any of its materials or activities and remove it from any search engine optimisation systems in which it might have been included.

The Alliance also asked Daiichi-Sankyo to explain in detail what it proposed to do to ensure no further use of this term or hashtag. Daiichi-Sankyo UK, however, had stated that it was unable to give any undertakings about the further or continued use of the hashtag. Daiichi-Sankyo had stated that its parent company, Daiichi-Sankyo Europe GmbH based in Germany, had, however, used this hashtag and instructed UK agencies to use this hashtag. The hashtag was displayed at the Daiichi-Sankyo Europe stand at the European Society of Cardiology (ESC) congress 2017 in Barcelona, and UK health professionals were sponsored by Daiichi-Sankyo UK to attend the ESC. Daiichi-Sankyo UK was asked during the inter-company dialogue whether any Daiichi-Sankyo UK personnel manned this stand but was unable to provide that information. Daiichi-Sankyo UK had apparently informed Daiichi-Sankyo Europe GmbH of its strong concerns regarding the appropriateness of this hashtag and advised that it was no longer used. However, the

hashtag continued to be used. Daiichi-Sankyo UK had asserted that as it was not involved with the commissioning of this hashtag, and did not encourage health professionals, patients or the public to view any messages containing this hashtag, it did not believe this fell within the scope of the Code.

The Alliance's view was that this was a very serious matter. The promotional use of the term safeplicity and the hashtag on Twitter, originating in the UK, was in breach of both the ABPI and EFPIA Codes. In the Alliance's view, this activity brought the pharmaceutical industry into disrepute and therefore needed to be stopped immediately. The Alliance alleged breaches of Clauses 7.9, 12.1, 26.1, 26.2, 9.1 and 2.

RESPONSE

Daiichi-Sankyo UK stated that it had never and did not intend to use the #safeplicity or any term similar to 'safeplicity' in any materials or activities targeted at UK health professionals or members of the public; it had not commissioned any external party (UK based or otherwise) to use the #safeplicity or 'safeplicity' as a term.

Daiichi-Sankyo noted that its parent company, Daiichi-Sankyo Europe GmbH was based in Germany. The Twitter posts submitted by the Alliance showed pictures of Daiichi-Sankyo Europe's stand at the ESC congress in Barcelona. Daiichi-Sankyo Europe was responsible for the set-up and design of the stand. Daiichi-Sankyo UK had no input into the design. Daiichi-Sankyo UK did not send any tweets or commission any external party to send any tweets regarding the ESC congress. An agency was commissioned directly by Daiichi-Sankyo Europe to develop the #safeplicity concept. Another agency was commissioned directly by Daiichi-Sankyo Europe to design the stand at ESC which displayed the #safeplicity wording. Although both agencies had offices in the UK, they were not contracted by and had not acted on behalf of Daiichi-Sankyo UK, and the #safeplicity messaging and ESC activities took place outside the UK.

During the course of inter-company dialogue the Alliance had alleged that another agency also had a role in the use of #safeplicity. Due to a lack of relevant contract information from Daiichi-Sankyo Europe available to Daiichi-Sankyo UK at the time, this allegation was not then contested or disputed by Daiichi-Sankyo UK. Having now received the correct information, Daiichi-Sankyo confirmed that neither Daiichi-Sankyo UK nor Daiichi-Sankyo Europe had commissioned this agency to use the term 'safeplicity' in any form. Indeed, Daiichi-Sankyo could find no evidence on Twitter that the agency had used this hashtag. The Alliance had not provided evidence to show that the agency had used this hashtag and it was unclear why the Alliance initially thought that the agency was involved with the #safeplicity concept.

The Alliance had asked Daiichi-Sankyo UK to remove the term 'safeplicity' from search engine optimisation systems. Daiichi-Sankyo UK had not

carried this out and had no knowledge of any search engine optimisation activities relating to the term 'safeplicity'. The Lixiana.co.uk website had never contained any metadata which would link an internet search for 'safeplicity' to the UK site.

Daiichi-Sankyo UK sponsored UK health professionals to attend the ESC in Barcelona in August 2017. The Daiichi-Sankyo Europe stand was in an area of the congress venue clearly demarcated for promotional stands from various companies. The UK health professionals were never briefed or invited by Daiichi-Sankyo UK or Daiichi-Sankyo Europe to attend the Daiichi-Sankyo Europe promotional stand.

At the time of a meeting between Daiichi-Sankyo UK and the Alliance, Daiichi-Sankyo UK did not have details to hand of any Daiichi-Sankyo UK staff who had worked on the ESC stand and was unable to answer the Alliance's question in this regard. Two UK representatives worked on the stand but they were not briefed to specifically target UK health professionals. The two staff members received stand briefings directly organised by Daiichi-Sankyo Europe in Barcelona prior to the start of the ESC. Daiichi-Sankyo UK did not have previous sight of the briefing presentation. Daiichi-Sankyo provided the full briefing deck (ESC 2017 – Booth Staff Training), although as explained below, neither representative saw the full deck.

Daiichi-Sankyo stated that one of the representatives was an hour late for the main briefing session, the day before ESC started, so did not see the beginning of the deck. According to the agenda timings on slide 8 of the deck, the representative would have seen from slide 65 onwards. This was consistent with the representative's recollection of the briefing given below.

The representative logged interactions with two UK health professionals during ESC on Daiichi-Sankyo UK's contact recording system. According to the statement provided by the representative below, those interactions did not take place on the Daiichi-Sankyo Europe stand. The representative confirmed that Daiichi-Sankyo UK told him/her that the ABPI Code must apply in all interactions with health professionals.

The statement provided by the representative was:

'Just to confirm that my time allocated manning the stand at ESC I did not see any UK customers, customers recorded in ... were from interaction in the evening or off of the Daiichi stand.

I attended part of the briefing meeting, where logistics around how the stand was built and the different zone areas of the stand were discussed, this was an opportunity to get to know my colleagues and to discuss good practice when manning a stand i.e. not eating on stand, not talking or texting on phone etc. At no time was clinical data discussed.

Marketing from the UK had already briefed the UK team that this is a different environment from the UK around various messages that other

countries may use myself and my UK colleagues were always to follow UK ABPI rules in any interaction with customers.'

The other representative also did not attend the main briefing session as he/she arrived in Barcelona on the opening morning of the ESC, and so had a shortened briefing. The Daiichi-Sankyo Europe trainer had stated:

'I did not create a bespoke presentation for the catch-up briefing the next day. I used the same deck but obviously focused on the main booth expectation points from the main briefing from the previous day. I'm confident that the focus was on logistics and rota management rather than safeplicity or other marketing messages simply because of the time limitation.'

The other representative logged interactions with six UK health professionals during ESC. According to a statement provided by him/her, those interactions did not take place on the Daiichi-Sankyo Europe stand. The representative also confirmed that Daiichi-Sankyo UK told him/her that the ABPI Code must apply in all his/her interactions with health professionals.

The statement provided by the second representative was:

'Contacts recorded in ... were based on conversations at evening meetings on the days of the conference.

... [Daiichi-Sankyo UK Marketing] told me to adhere to the UK code, which superseded any other guidance.

The briefing I attended on the Saturday was not the full briefing held the previous day. The key messages I recall were ensuring we used only authorised ipads and all additional enquiries were directed to the medical team.'

Although two UK staff worked on the Daiichi-Sankyo Europe stand, there was no evidence that they interacted with UK health professionals on the stand, and they both recalled being instructed by Daiichi-Sankyo UK to follow the ABPI Code, regardless of any briefing they received from Daiichi-Sankyo Europe.

UK health professionals were not specifically targeted either by Daiichi-Sankyo UK or Daiichi-Sankyo Europe to view the Daiichi-Sankyo Europe stand or to be exposed to any #safeplicity messaging which was on the stand.

Daiichi-Sankyo UK had made very clear to Daiichi-Sankyo Europe that it was very concerned about the use of the term 'safeplicity' or the associated hashtag in any scenario. It was certainly not a term Daiichi-Sankyo UK intended to use in the UK. However, Daiichi-Sankyo could not give an undertaking that Daiichi-Sankyo Europe would not continue to use this term in promotional campaigns on the internet or at European congress stands outside the UK. Daiichi-Sankyo stressed, however, that UK health

professionals and members of the public were not specifically targeted by this campaign.

Daiichi-Sankyo UK stated it had not commissioned any party to use the #safeplicity. Furthermore, no Daiichi-Sankyo affiliate had specifically targeted UK health professionals, other relevant decision makers or members of the public with messaging containing this hashtag or similar terminology. Therefore Daiichi-Sankyo denied a breach of Clause 7.9.

Daiichi-Sankyo UK stated it had had no involvement in the use of the #safeplicity on the internet and UK health professionals had not been specifically targeted. Any promotion that occurred on the Daiichi-Sankyo Europe stand at ESC 2017 was organised by Daiichi-Sankyo Europe, not Daiichi-Sankyo UK, and was in an area clearly demarcated for promotion. Daiichi-Sankyo therefore denied that there had been any disguised promotion or any breach of Clause 12.1.

Daiichi-Sankyo UK stated it had had no involvement in the use of the #safeplicity on the internet, there had been no advertising of medicines to the public by Daiichi-Sankyo UK, so it denied any breach of Clause 26.1. Daiichi-Sankyo denied that unfounded hopes of successful treatment had been raised, or that any misleading statements had been made about the safety of medicines. Daiichi-Sankyo therefore denied a breach of Clause 26.2.

Further to the above, Daiichi-Sankyo did not believe that high standards had not been maintained, or that Daiichi-Sankyo UK had brought discredit to, or reduced confidence in, the pharmaceutical industry. Therefore, Daiichi-Sankyo denied breaches of Clauses 9.1 and 2.

In response to a request for further information Daiichi-Sankyo submitted that a master services agreement with one of the agencies was signed in 2014 was in place at the time of ESC 2017, although the agreement did not specifically mention ESC 2017. This agency carried out work related to ESC 2017 as well as other projects as part of the master services agreement.

According to Daiichi-Sankyo briefings between Daiichi-Sankyo Europe and the agency were conducted verbally through teleconferences and meetings, as part of the master services agreement. There were no written arrangements in place between Daiichi-Sankyo Europe and the agency that specifically related to ESC 2017 or #safeplicity. The agency was verbally briefed on the use of the #safeplicity during these meetings and designed the ESC stand according.

Daiichi-Sankyo Europe's social media policy and social media procedure applied in the UK; the UK did not have a separate policy in that regard.

Daiichi-Sankyo submitted that Daiichi-Sankyo Europe wrote 25 tweets relating to ESC 2017 from its Twitter account @EUdaiichisankyo in the lead up to and during ESC 2017. Only four members of staff were able to write tweets from this account, all worked

in corporate communications and were subject to Daiichi-Sankyo Europe's social media policy and social media procedure. At the time of ESC 2017, the Twitter account @EUdaiichisankyo had 5519 followers. Daiichi-Sankyo submitted that it was not possible to obtain information on the nationality of the followers as this information was not available, they might be individuals or organisations. Daiichi-Sankyo submitted that there was no specific intended audience for the Daiichi-Sankyo Europe Twitter feed. The wording associated with the account, which was visible to all visitors to the page was: 'This channel is provided by the pharmaceutical company Daiichi-Sankyo Europe GmbH' which was followed by a link to the community guidelines. Daiichi-Sankyo submitted that there was no intended specific audience for the agency's Twitter feed. The wording associated with the account, which was visible to all visitors to the page was: 'Award winning strategy, design and management for conferences, exhibitions and events'.

Daiichi-Sankyo submitted that whilst an account had been created (@DaiichiSankyoUK), this had only been to reserve the username and ensure nobody else could use it. The account was protected and the profile was not accessible to the public. The only tweet ever sent from the account was for testing purposes and was not visible to the public. There was no intention that this account would ever be used to disseminate any information.

The UK health professionals sponsored by Daiichi-Sankyo UK to attend ESC 2017 received an invitation from Daiichi-Sankyo UK and subsequently a welcome letter from Daiichi-Sankyo Europe which referred to a 'welcome pack' to be picked up from the hotel. The welcome pack was the standard ESC pack available to all registered attendees plus the individual confirmation of registration and name badge. Daiichi-Sankyo did not have access to the materials in the welcome pack.

Daiichi-Sankyo submitted that the two UK account managers on stand duty spent 8.5 and 9 hours respectively manning the stand over the course of the congress.

Daiichi-Sankyo explained that the UK team had been briefed prior to ESC. As part of this briefing it was made clear that they must adhere 'to all UK SOPs and ABPI requirements'. After the UK team were briefed in Barcelona by Daiichi-Sankyo Europe, a named Daiichi-Sankyo UK employee verbally briefed them that they should 'adhere to the UK Code, which superseded any other guidance'.

PANEL RULING

The Panel noted that it could not make any rulings regarding the EFPIA Code as it had no locus to do so. National associations such as the ABPI were obliged as members of EFPIA to incorporate the requirements of the EFPIA Code into their local codes as far as national law permitted. The Panel noted that even if the UK Code did not apply Daiichi-Sankyo was an affiliate member of EFPIA.

The Panel noted that the complainant had provided twelve tweets, ten of which included the hashtags #ESCCongress, referring to the 2017 Congress in Barcelona, and #safeplicity and two of which included only #safeplicity. Two of the tweets were from employees of the agency, three were from another company and five were from Daiichi-Sankyo Europe (@EUdaiichisankyo). The Panel was unsure of the status of the senders of the remaining two tweets, they did not appear to be from Daiichi-Sankyo or from its employees or agents.

Firstly, the Panel had to decide whether the tweets in question were subject to the Code. The Panel noted that Clause 28.2 stated that information or promotional material about prescription only medicines which was placed on the Internet outside the UK would be regarded as coming within the scope of the Code if it was placed there by a UK company or an affiliate of a UK company or at the instigation or with the authority of such a company and it made specific reference to the availability or use of the medicine in the UK.

With regard to the tweets sent by Daiichi-Sankyo Europe, the Panel noted it was an established principle under the Code that UK companies were responsible for the acts or omissions of their overseas affiliates that came within the scope of the Code. Daiichi-Sankyo UK was thus responsible for any acts or omissions of Daiichi-Sankyo Europe and/or its agencies that came within the scope of the Code.

The Panel noted Daiichi-Sankyo UK's submission that the Twitter account in question belonged to Daiichi-Sankyo Europe based in Germany and the tweets' authors all worked in Daiichi-Sankyo Europe's corporate communications department. Daiichi-Sankyo UK further submitted that it had had no involvement in the use of the #safeplicity on the internet and that Daiichi-Sankyo UK did not send any tweets or commission any external party to send any tweets regarding the ESC congress. The Panel also noted Daiichi-Sankyo's submission that no affiliate had specifically targeted UK health professionals, other relevant decision makers or members of the public with messaging containing this hashtag or similar terminology. Daiichi-Sankyo was unable to provide information on the nationality of the followers of the Twitter account in question. The corporate tweets all contained the hashtag #safeplicity, one also contained the hashtag '#MakeYourHeartFeelGood' and another referred to avoiding heart problems during the holidays. The Panel was concerned about these tweets. The Panel noted that the tweets did not specifically refer to the use of medicines in the UK. The Panel noted that the UK company did not have its own active Twitter account and there was no evidence before the Panel that the UK company, its agents or affiliates, had directly or indirectly pointed UK health professionals or others to the Twitter account in question. The Panel thus considered that for all the reasons set out above the five tweets sent by Daiichi-Sankyo Europe were not within the scope of the Code and the Panel therefore ruled no breach of Clauses 7.9, 12.1, 26.1, 26.2, 9.1 and 2.

The Panel noted that the tweets would be covered by a code of practice and it was simply a question of which applied. As the tweets had been issued by Daiichi-Sankyo Europe based in Germany, the German Code might apply.

With regard to the tweets sent by employees at the agency, the Panel noted Daiichi-Sankyo's submission that the agency was a UK based agency commissioned directly by Daiichi-Sankyo Europe to design the stand at ESC, which displayed the #safeplicity wording. The safeplicity concept had been designed by another agency engaged by Daiichi-Sankyo Europe. The Panel noted that it was an established principle under the Code that pharmaceutical companies are responsible for work undertaken by third parties on their behalf which came within the scope of the Code. Thus, in the Panel's view if the agency's tweets came within the scope of the Code Daiichi-Sankyo Europe would be responsible for them and therefore the UK company would be responsible as it was responsible for its affiliates act/omissions which fell within the scope of the UK Code.

The Panel noted that Clause 28.1 stated that promotional material about prescription only medicines directed to a UK audience which was provided on the internet must comply with the Code. The Panel also noted the scope of the Code at Clause 1.1 which covered promotional and certain non-promotional activities. The Panel considered that the tweets sent by the employees of a UK based agency were placed on the internet in the UK and published on a UK agency's Twitter account and were therefore within the scope of the Code.

The Panel considered that it was entirely foreseeable that a communications agency would use digital media to highlight its work with a pharmaceutical company. In the Panel's view it was good governance to discuss and agree such use at the outset. Daiichi-Sankyo Europe should have been aware that the agency in question had previously published photographs of its Lixiana stand at the 2016 ESC congress on its website and corporate Twitter account.

The Panel noted that one of the tweets dated 29 August was a picture of two of the agency's staff with the exhibition stand robot beneath the #safeplicity. The tweet included the hashtags #ESCCongress and #safeplicity, there was no direct reference to product. The second tweet was also dated 29 August but was sent by a different employee and featured a picture of a column which formed part of the exhibition stand and which bore the prominent #safeplicity above fire extinguishers. The author stated 'Oh how ironic' and in the left hand side of the photograph the brand name, Lixiana, in logo format was clearly visible. The tweet bore the hashtags safeplicity, esccongress and Barcelona. The Panel noted the Alliance's submission that the #safeplicity had been used to promote Lixiana and when readers clicked on this hashtag they were transferred to the hashtag page which it considered contained promotional photographs. Daiichi-Sankyo made no comment in this regard. The Panel considered that the hashtag

page was part of the complaint and noted that it contained references to Lixiana, including pictures of the exhibition stand robot which bore a screen which, on some tweets, clearly referred to Lixiana. Some tweets on the hashtag page referred to preventing stroke.

The Panel noted that the #safeplicity concept was commissioned by Daiichi-Sankyo Europe and in the Panel's view the content of the hashtag page which was linked to directly from the #safeplicity on the tweets in question was thus relevant when considering the acceptability of the tweets. In the Panel's view, the #safeplicity would generate open access social media activity in relation to Lixiana and the ESC and in this regard, was promotional. The Panel noted that Lixiana was a direct oral anticoagulant and considered that safeplicity was a strong unqualified claim. On one tweet, the Panel noted that the product name in logo format was clearly visible in the background of one photograph and its design and colour clearly linked it to the prominent safeplicity hashtag on the exhibition column in the foreground. The tweets had been published on the agency's open access Twitter accounts. Clicking on the #safeplicity took the reader to the safeplicity hashtag page described above which appeared to be, in part, a promotional vehicle for the product and where some tweets clearly referred to Lixiana. The Panel considered that the two tweets in question bearing the #safeplicity one of which referred to Lixiana and both linked to the hashtag page which referred to the product were promotional and promoted Lixiana to the general public. A breach of Clause 26.1 was ruled in relation to each tweet. These rulings were appealed.

The Panel considered that the hashtag safeplicity as used in the tweets in question and on the hashtag page would be clearly associated with Lixiana. The Panel noted that Clause 7.9 stated, *inter alia*, that the word 'safe' must not be used without qualification. The relevant supplementary information stated that these restrictions applied equally to all grammatical derivatives of the word safe such as safety. The Panel noted a slide from the Daiichi-Sankyo Europe's ESC 2017 briefing document stated 'How to summarize Lixiana in one single word? #safeplicity'. Below this it read 'Safety, efficacy and convenience of a once-daily NOAC for all of your NVAF and VTE patients'. In the Panel's view, the addition of 'plicity', which readers would associate with the word 'simplicity' to the word 'safe', compounded the already unacceptable impression given and implied that there was something straightforward or simple about the product's adverse event profile and, in the Panel's view, that was not so. The Panel noted the adverse effects of Lixiana as stated in Section 4.8 of the SPC and the special warnings and precautions for use in Section 4.4 of the SPC. The Panel considered that the term safeplicity used to describe Lixiana was inconsistent with the requirements of Clause 7.9 and a breach of that clause was ruled with regard to each of the agency's tweets. These rulings were appealed.

The Panel noted that Clause 26.2 stated that information about prescription only medicines available to the public, directly or indirectly must

be factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading about the safety of the product. The Panel noted its ruling of a breach of Clause 7.9 above and considered that the unqualified use of the term safeplicity was misleading about the safety of Lixiana. A breach of Clause 26.2 was ruled with regard to each of the agency's tweets. These rulings were appealed.

The Panel noted that Clause 12.1 stated that promotional material and activities must not be disguised. The supplementary information stated, *inter alia*, in addition that the identity of the responsible pharmaceutical company must be obvious. The Panel considered that this requirement was to ensure that promotional material was not disguised. The Panel considered that the tweets in question which linked to the hashtag page were, however, clearly promotional. No breach of Clause 12.1 was ruled.

The Panel considered that Daiichi-Sankyo had apparently been let down by its parent company. Nonetheless, noting the UK company's responsibility for its affiliate, the Panel noted its rulings above and considered that high standards had not been maintained in relation to the tweets in question. A breach of Clause 9.1 was ruled. The Panel noted that the supplementary information to Clause 2 gave prejudicing patient safety and/or public health as an example of activity likely to be in breach of the Code. Noting its comments and rulings above the Panel considered that Daiichi-Sankyo had brought discredit to and reduced confidence in the industry and ruled a breach of Clause 2. These rulings were appealed.

The Panel noted that the Alliance had referred to use of the hashtag by another UK agency. Daiichi-Sankyo submitted that neither it nor its European affiliate had commissioned the agency to use the hashtag in any form and could find no evidence that the agency had used the hashtag as alleged. The Panel noted that the Alliance bore the burden of proof and considered that it had not established that the hashtag had been used by that agency as alleged. No breach of Clauses 26.1, 26.2, 9.1, 7.2 and 2 were ruled.

The Panel noted that the Alliance had also provided tweets from another non-UK based agency which appeared to have created the robot used at the exhibition stand but made no specific allegations about that agency. Similarly, neither the complainant nor the respondent had identified the senders of the remaining two tweets, nor were specific allegations made about their content. Although the Alliance provided copies of these tweets, it had not made out its complaint including any UK link and the Panel therefore made no rulings in this regard.

The Panel then considered whether the use of the #safeplicity on the exhibition stand at the ESC 2017 Congress in Barcelona came within the scope of the Code. The Panel noted its comments above about the UK company's responsibility for the acts and omissions of its parent company that came within the scope of the Code.

Clause 1.1 stated that the Code applied to the promotion of medicines to members of the UK health professions and to other relevant decision makers. Furthermore, the supplementary information to Clause 1.1, Scope of the Code, stated that it also included 'promotion to UK health professionals and other relevant decision makers at international meetings held outside the UK, except that the promotional material distributed at such meetings will need to comply with local requirements'.

The Panel noted that the supplementary information to Clause 22.1, Meetings organised by Affiliates outside the UK, stated 'Companies should remind their affiliates outside the UK that the ABPI Code of Practice must be complied with if UK health professionals attend meetings which they organise regardless of whether such meetings occur in the UK or abroad'.

The Panel noted Daiichi-Sankyo UK's submission that it had sponsored UK health professionals to attend the ESC in Barcelona in August 2017 but these UK health professionals were not briefed or invited by Daiichi-Sankyo UK or Daiichi-Sankyo Europe to attend the Daiichi-Sankyo Europe promotional stand. The Panel noted Daiichi-Sankyo's submission that two UK employees manned the stand for 8.5 and 9 hours respectively over the course of the congress but were not specifically briefed to target UK health professionals. The Panel noted that one representative manning the stand logged interactions with two UK health professionals during ESC but these interactions did not take place at the Daiichi-Sankyo Europe stand. Similarly, the other representative logged interactions with six UK health professionals during ESC but also stated that these interactions did not take place on the Daiichi-Sankyo Europe stand. The Panel considered that although it was possible that a UK sponsored health professional attending the stand might prefer to speak to UK staff and/or might be directed towards UK staff there was no evidence before the Panel that this had occurred.

The Panel noted that the exhibition stand would be covered by a code, or codes it was a question of whether the UK Code applied. The Panel considered that there was no evidence to show that either Daiichi-Sankyo UK or Daiichi-Sankyo Europe had invited UK health professionals to visit the stand nor was there any evidence to show that Daiichi-Sankyo had any role in relation to the exhibition stand. On balance, the Panel thus did not consider that in the particular circumstances of this case the requirements of the UK Code applied and it ruled no breach of Clauses 2, 9.1, 7.9, 26.1 and 26.2 of the Code because it considered that the matter of complaint did not fall within the scope of the Code.

During its consideration of this case the Panel was very concerned about the use of the #safeplicity and that the German affiliate had apparently continued to use it after the UK affiliate and the Alliance had raised concerns. The Panel noted its comments and rulings of a breach of Clauses 7.9 and 2 above.

The Panel was also very concerned at what it considered to be wholly inadequate training of UK staff manning the exhibition stand. The Panel noted Daiichi-Sankyo's response in this regard. Reminding staff that they had to be Code compliant was wholly insufficient given that UK staff were on an exhibition stand which bore the prominent #safeplicity. The exhibition stand, in the Panel's view, invited questions about safety and Lixiana and made an unqualified claim about the safety of the product. In the Panel's view, staff should have been trained on how to address such queries compliantly given the Panel's view above about the #safeplicity. The Panel was very concerned to note that the ESC 2017 booth staff briefing included extensive use of the words 'safety' and #safeplicity in relation to Lixiana. Whilst noting that such briefing to non-UK staff might not be within the scope of the UK Code the Panel queried whether such claims were consistent with the requirements of Clauses 7.9 and 2. Nonetheless, in the absence of any briefing to UK staff on how to respond to safety questions within the context of the stand the Panel was concerned that the stand environment including non-UK staff discussing safety as briefed and use of the #safeplicity on the stand might have influenced UK staff. There was no complaint in this regard.

The Panel queried whether it was likely that UK health professionals, particularly those invited to attend by the UK affiliate, would talk to neither of the UK representatives manning the stand particularly considering the length of time spent on the stand by each of them. Further, the Panel could not understand how the UK representatives could be expected to man the stand without referring to or being seen to use the promotional messages on it.

The Panel asked that Daiichi-Sankyo be advised of its concerns.

APPEAL BY DAIICHI-SANKYO

With regard to the use of #safeplicity, Daiichi-Sankyo UK submitted that it had never and would never make use of this hashtag or any similar messaging.

Daiichi-Sankyo understood the established principle that UK pharmaceutical companies were responsible for the acts and omissions of overseas affiliates that came within the scope of the Code. Daiichi-Sankyo understood that the agency was commissioned by Daiichi-Sankyo Europe and therefore acts and omissions by this agency which fell under the scope of the ABPI Code were also the responsibility of Daiichi-Sankyo UK. However, Daiichi-Sankyo did not believe that the agency's tweets fell under the scope of the ABPI Code for the reasons set out below.

Daiichi-Sankyo noted that Clause 28.1 stated that 'Promotional material about prescription only medicines **directed to a UK audience** which is provided on the Internet must comply with all relevant requirements of the Code' (emphasis added).

Daiichi-Sankyo noted that the Panel had considered that the two tweets sent by employees of the agency

were within the scope of the Code because it was a UK based agency, the tweets were placed on the internet in the UK and published on a UK agency's Twitter account. Daiichi-Sankyo did not agree with the Panel's assessment in this regard. There was no evidence that the agency's tweets were directed to a UK audience. In addition, there was no evidence that the tweets were placed on the internet in the UK. It was highly likely that the tweets were placed on the internet in Spain at the ESC 2017 conference.

Daiichi-Sankyo noted that Twitter was an international platform. The agency's Twitter page showed its location as 'Worldwide' and it described its business as 'strategy, design and management for conferences, exhibitions and events'. A screenshot of the Twitter page was provided and this indicated that it considered itself to be a worldwide events organisation and its activities spanned non-UK countries, as evidenced in this case where it operated at the ESC 2017 congress in Spain. There was no evidence and nothing within the tweets to suggest, that a UK Twitter user would be more likely than any non-UK Twitter user to see a tweet by the agency. On the Twitter platform, users had to actively choose to follow another user in order to automatically see that other user's tweets on their own feed. As the agency was advertised as a worldwide agency, there was no evidence that it was more likely to have active UK followers than active non-UK followers. There was also no evidence that UK Twitter users would be more likely than non-UK Twitter users to manually search for the agency's tweets.

Furthermore, Daiichi-Sankyo submitted that the two tweets were clearly posted from the conference in Spain and further the hashtags from the conference in Barcelona were used (#Barcelona and #ESCCongress). There was nothing contained within the tweets to suggest that a UK audience was targeted.

Furthermore, Daiichi-Sankyo submitted that the Panel's analysis that because a tweet came from an employee of a UK company, it was by default directed at a UK audience, was an incorrect interpretation. On this analysis, any UK third party company working with or for an international affiliate of a UK pharmaceutical company could not post material on the internet without it being deemed to be directed to a UK audience. This was surely not what was envisaged by Clause 28.1 of the Code which stated 'directed to a UK audience'. Just because the author of the tweet worked for a UK company could not infer or mean that the tweet was 'directed to a UK audience'. For this reason, Daiichi-Sankyo submitted that the tweets did not fall under the scope of the ABPI Code.

Summary of Appeal

Daiichi-Sankyo submitted that on the basis that the two tweets were not directed to a UK audience, they did not fall within the scope of the Code. Therefore Daiichi-Sankyo appealed all breaches (Clauses 7.9, 26.1, 26.2, 9.1 and 2) stemming from the tweets on the grounds that they were not within the scope of the ABPI Code.

Daiichi-Sankyo emphasised that it considered the seriousness of advertising medicines to the public and misleading the public about the safety of medicines. Daiichi-Sankyo did not engage in any of these activities, nor did it encourage any affiliate or agency to do so. Patient safety was at the forefront of Daiichi-Sankyo's activities. The agency tweets were sent without the knowledge of Daiichi-Sankyo's staff.

Clause 2

In relation to the tweets, Daiichi-Sankyo immediately brought the reported concerns to the attention of Daiichi-Sankyo Europe. Daiichi-Sankyo had, at all times, acted appropriately and responsibly to the concerns raised. In the circumstances, Daiichi-Sankyo's conduct did not amount to a breach of Clause 2.

Concerns of the Panel

Daiichi-Sankyo noted that the Panel was concerned about the continued use of #safeplicity by Daiichi-Sankyo Europe after Daiichi-Sankyo UK and the Alliance had raised concerns. Daiichi-Sankyo agreed that this was concerning. Daiichi-Sankyo UK now worked more closely with Daiichi-Sankyo Europe on the development of marketing campaigns and this increased collaboration would help to ensure messaging and materials were developed to a high ethical standard.

Daiichi-Sankyo noted that the Panel was concerned about the inadequate training given to UK staff manning the Daiichi-Sankyo Europe stand at ESC 2017. This concern had been taken on board by Daiichi-Sankyo, including the medical, compliance and marketing departments. In future, specific certified UK briefings would be given to any UK promotional staff attending international congress, specifying their obligations to adhere to the Code, and detailing any activities they should not be involved in.

In closing, Daiichi-Sankyo took patient safety very seriously and was committed to promoting the rational use of medicines and adhering to the Code.

COMMENTS FROM THE ALLIANCE

The Alliance agreed entirely with the decision of the Panel that pharmaceutical promotional material developed by a UK based agency, placed on the internet in the UK and published on the UK agency's Twitter account was intended for a UK audience and therefore fell within the scope of the Code. The ESC congress had a significant proportion of UK delegates and hence #safeplicity had a high likely exposure to a UK audience at the ESC as well as exposure to a UK audience in the UK.

The Alliance alleged that the fact that the hashtag #safeplicity was clearly designed to promote Lixiana despite the prohibited use of the word 'safe' which had not been disputed by Daiichi-Sankyo. The fact that it was used for this purpose had also been clearly demonstrated as had the fact that it was also used to promote a prescription medicine to

the general public in the UK. Thus, the findings of numerous Code breaches, and the sanctions associated with them, were correct, appropriate and necessary.

APPEAL BOARD RULING

The Appeal Board noted that it first needed to assess whether the tweets at issue were subject to the Code. The Appeal Board noted the requirements of Clause 28.2 and the role of Daiichi-Sankyo Europe which had employed the agency sending the tweets.

The Appeal Board did not consider that the two tweets at issue made specific reference to the availability or use of Lixiana in the UK. Taking all the circumstances into account, the Appeal Board considered that Clause 28.2 did not apply to the tweets, thus the ABPI Code did not apply. The Appeal Board ruled no breaches of Clauses 2, 7.9, 9.1, 26.1 and 26.2 because it considered that the matter of complaint did not fall within the scope of the Code. The appeal on this point was successful.

During its consideration the Appeal Board noted that the representatives from Daiichi-Sankyo UK agreed

that the use of #safeplicity was unacceptable and that it had never and would never make use of this hashtag or any similar messaging. The safeplicity concept had been designed by an agency engaged by Daiichi-Sankyo Europe. The Appeal Board was very concerned about the use of #safeplicity by Daiichi-Sankyo Europe which continued after Daiichi-Sankyo UK and the Alliance had raised concerns. The Appeal Board considered that the use of #safeplicity would be unacceptable under the ABPI Code. Another code of practice would apply to the tweets. This was likely to be the German Code which, like the ABPI Code, was required to reflect the EFPIA Code.

Complaint received	12 January 2018
Undertaking received	3 October 2018
Appeal Board Consideration	13 September, 17 October 2018
Corrective Statement issued	14 December 2018

Daiichi-Sankyo sent the following Corrective Statement to recipients of the material at issue and relevant UK prescribers:

‘Corrective statement

Between July 2016 and 20 August 2018, a Lixiana (edoxaban) Initiation Information Guide (ref EDX/16/0171) and/or a Lixiana Practical Guide (ref EDX/15/0091(4)) might have been provided to you by Daiichi-Sankyo UK Limited.

Section 4.4 of the Lixiana SPC, Special warnings and precautions for use, states under the sub heading ‘Renal function in [nonvalvular atrial fibrillation] NVAf’:

‘A trend towards decreasing efficacy with increasing creatinine clearance was observed for edoxaban compared to well-managed warfarin (see section 5.1). Therefore, edoxaban should only be used in patients with NVAf and high creatinine clearance after a careful evaluation of the individual thromboembolic and bleeding risk.

Assessment of renal function: CrCL should be monitored at the beginning of the treatment in all patients and afterwards when clinically indicated (see section 4.2).’

Daiichi-Sankyo apologises for the fact that the items at issue failed to include this warning other than in the prescribing information. Daiichi-Sankyo takes its responsibilities under the ABPI Code of Practice for the Pharmaceutical Industry and patient safety seriously and is disappointed at these failings. As an organisation we will take all possible steps to ensure that this is not repeated.

Following a complaint under the ABPI Code of Practice for the Pharmaceutical Industry, the Code of Practice Appeal Board ruled that the omission rendered the materials misleading and therefore the materials did not encourage the rational use of the medicine. The Appeal Board also ruled that Daiichi-Sankyo had failed to maintain high standards and had brought discredit upon and reduced confidence in the pharmaceutical industry. As a result of the above Daiichi-Sankyo has been required to issue this corrective statement and to refer to the published report for the case which contains full details. In addition Daiichi-Sankyo has been required to recover the material at issue. If you still have the material at issue please return it in the attached prepaid envelope as soon as possible.

Details of this case (Case AUTH/3010/1/18) are also available on the PMCPA website (www.pmcpa.org.uk).’

ANONYMOUS, NON-CONTACTABLE HEALTH PROFESSIONAL v GW PHARMACEUTICALS

Promotion of Epidiolex

An anonymous, non-contactable complainant, who described him/herself as a health professional, alleged that GW Pharmaceuticals had promoted Epidiolex (cannabidiol) at a meeting in January 2018 before the medicine had been granted a marketing authorization.

The complainant alleged that the GW Pharmaceuticals exhibition stand displayed Epidiolex material and that a named employee introduced the medicine as a new treatment for paediatric patients with Dravet Syndrome and patients with Lennox-Gastaut Syndrome and stated that the medicine had been licensed by the European Medicines Agency (EMA) and would soon be available in the UK. The complainant had since found out that Epidiolex had not been approved by the EMA; the information from GW Pharmaceuticals was misleading.

The detailed response from GW Pharmaceuticals is given below.

The Panel noted that when the meeting was held, Epidiolex did not have a marketing authorization although licences had been applied for in the EU and US. GW Pharmaceuticals had submitted that it expected a decision from the European Commission for Epidiolex in mid-2019.

The Panel noted that the named GW Pharmaceuticals employee stated that the company's presence at the meeting comprised a small medical booth staffed by him/her and another member of the UK medical team. The booth was intended to provide a non-promotional presence to demonstrate the company's commitment to research and development, its corporate awareness as a pharmaceutical development company, non-product specific disease awareness, and information on GW Pharmaceuticals' main research activities including cannabinoid medicines. Copies of the materials available at the booth were provided; none mentioned Epidiolex by name. The Panel noted that it was an accepted principle under the Code that a product could be promoted without its name ever being mentioned.

Photographs of the exhibition stand showed material including the infographics that were striking and very prominently placed and thus highly visible to delegates visiting the stand. The material discussed various aspects of Dravet Syndrome and Lennox-Gastaut Syndrome and highlighted that current therapeutic options were inadequate. Material for Lennox-Gastaut Syndrome stated 'Up to 80% of patients are refractory to anti-epileptic drug therapy' and that for Dravet Syndrome stated 'Only

16% of patients experience complete resolution in their seizures. All seizure types extremely resistant to treatment'. In the Panel's view, these statements would, on the balance of probabilities, solicit questions about the company's pipeline products. A leaflet entitled 'A World leader in the development of cannabinoid medicines' discussed GW Pharmaceuticals' commitment to cannabinoid treatments. The final page gave more details describing the cannabinoid development pipeline by indication under investigation and phase of clinical study. Seven neuroscience pipeline indications were listed and it was stated that Dravet Syndrome and Lennox-Gastaut Syndrome had completed Phase 3 trials. It was further stated that the company's 'lead cannabinoid' had received orphan drug designation in these indications. The Panel noted that whilst Epidiolex was not named, sufficient information about it was given such that it was indirectly identified and on the balance of probabilities the material would solicit questions about the company's 'lead cannabinoid'.

In the Panel's view, the cumulative effect of the material, including the reference to the company's 'lead cannabinoid', meant that the exhibition stand promoted a medicine prior to the grant of its marketing authorization. Breaches of the Code were ruled including a breach of Clause 2.

The Panel noted that the materials had a promotional appearance and considered that they went beyond disease awareness information and/or non-promotional information about the company and its research interests.

The Panel noted the complainant's comments about statements allegedly made by the named employee ie that Epidiolex was a new treatment for paediatric patients with Dravet Syndrome and patients with Lennox-Gastaut Syndrome and that it had been licensed by the EMA and would soon be available in the UK. GW Pharmaceuticals denied that such comments had been made. The Panel noted that it was often impossible in complaints based on one party's word against the other to determine precisely what had happened. The complainant had the burden of proving his/her complaint on the balance of probabilities. The complainant was non-contactable and it was not possible to ask him/her for further information. The Panel had to make a ruling on the evidence before it.

The Panel noted its comments above about responses to unsolicited enquiries and also the statement of the company employee manning the booth in relation to training, the nature of queries received at the exhibition stand, and whether he/

she would have responded as alleged. The Panel also noted the detailed briefing for staff to use at conferences in response to unsolicited requests advising that discussions with health professionals must be reactive and in response to the requested information. Staff were advised to narrowly tailor the response to the level of the question posed. The company's report on interactions at the conference did not closely mirror the complainant's allegation. In relation to the alleged comments made at the exhibition stand, it was impossible to determine where the truth lay and the Panel accordingly ruled no breach of the Code.

An anonymous, non-contactable complainant who described him/herself as a health professional alleged that GW Pharmaceuticals had promoted Epidiolex (cannabidiol) before the grant of its marketing authorization.

COMPLAINT

The complainant explained that he/she had attended the British Paediatric Neurology Association (BPNA) meeting on 5 January 2018 where GW Pharmaceuticals had had an exhibition stand with Epidiolex materials. A named medical representative introduced Epidiolex as a new treatment for paediatric patients with Dravet Syndrome and patients with Lennox-Gastaut Syndrome. The representative stated that Epidiolex had been licensed by the European Medicines Agency (EMA) and would soon be available for UK prescribers.

The complainant stated that he/she had since found out that Epidiolex had not been approved by the EMA, the application was only submitted in December 2017, and the medicine would not be available until the application process had been completed.

The complainant considered that the information from GW Pharmaceuticals was misleading and promoted an unlicensed medicine.

The complainant provided photographs of some of the material available on the exhibition stand, cited a press release about the submission of the marketing authorization published on GW Pharmaceuticals' website and provided a website address for the conference in question.

When writing to GW Pharmaceuticals, the Authority asked it to consider the requirements of Clauses 2, 3, 7.2, 9.1 and 15.2.

RESPONSE

GW Pharmaceuticals submitted that the complainant's allegations were entirely unfounded; the company flatly denied any wrong-doing or impropriety on its part or that of its representatives. GW Pharmaceuticals understood the difficulty in investigating and responding to this type of anonymous complaint, but it was comfortable that the complaint had no basis. The named individual, was a highly experienced, qualified, eminently sensible and conscientious medical affairs professional and had satisfied the company that he/

she had not made the alleged statement. He/she was fully aware of the Code and his/her responsibilities under it. His/her account was also backed by contemporaneous records of interactions with health professionals with whom he/she interacted at the BPNA conference and his/her summary of that meeting, as well as briefing materials on which he/she was well-trained. A number of factual issues and inconsistencies in language in the complaint led the company to suspect that it was unfounded or fabricated, that the complainant might have been mistaken or that the complaint had resulted from a misunderstanding.

GW Pharmaceuticals provided a detailed statement from the named individual in question and after careful enquiry it was satisfied that, along with his/her professional background and experience, he/she had through the company and its third party partner, received appropriate and comprehensive briefing and training in order to enable him/her to represent GW Pharmaceuticals to high standards of ethical conduct in compliance with the Code.

The named individual had provided a rigorous and detailed account of the events which occurred at the BPNA conference over 3-5 January 2018, backed by robust supporting materials, including a number of contemporaneous records of his/her interactions with health professionals. GW Pharmaceuticals had complete trust in his/her account of events and thus supported him/her in refuting the allegations. GW Pharmaceuticals noted in particular that the named individual recorded instances where health professionals requested information on the development status of products. As indicated in the statement, he/she responded appropriately and provided detailed accounts of having done so. GW Pharmaceuticals noted in particular that in a summary of the meeting he/she made shortly afterwards which indicated that '[health professionals] still thinking [Epidiolex] available in mid 2018. We are disappointing customers' expectations'. This clearly indicated that he/she and GW Pharmaceuticals were consistently telling health professionals that Epidiolex would be available later than many of them expected. The named individual also recalled an earlier incident in which a third-party health professional stated that Epidiolex would be available in 2018 to which he/she took prompt action to correct this mistaken position.

GW Pharmaceuticals stated that it had also taken particular care to re-assess and review, in the context of the complaint, all relevant material, procedures, processes, instructions, briefing and training which might pertain to the alleged events, including anything which might have resulted in a representative making the alleged statement in error. The company had also reviewed the employee's account of events and of any instructions he/she received. Further, the company had reviewed all the materials which were available or displayed on the stand, including photographic evidence of the same. All of this material, where relevant, was provided.

GW Pharmaceuticals submitted that it had never, implicitly or directly, promoted or encouraged the promotion of any unlicensed medicine, including

Epidiolex. Indeed, it went to particular lengths to ensure that the alleged claims would not happen even by reason of genuine error; in that regard it referred to its standard responses to enquiries on cannabidiol.

GW Pharmaceuticals submitted that the materials displayed on the stand were disease awareness information and/or genuine non-promotional information about the company and its research interests.

Finally, GW Pharmaceuticals outlined significant concerns about the language used in the complaint, which it considered questioned its credibility. The named individual had identified a number of elements in what he/she was alleged to have said that made little sense and that an experienced medical affairs professional would never state, including that the product was authorized, that the EMA had authorized it and that it would be available to patients soon. The named individual explained that he/she knew that the product was not authorized and that a determination on whether to authorize would not be made until 2019 and that as reflected in the briefing and stand materials, the Commission, not the EMA, approved medicines, and there would be a delay between approval and access by patients in the UK. Indeed, the National Institute for Health and Care Excellence (NICE) intended to subject cannabidiol to its standard single technology appraisal (STA) process, which would most likely extend the date for routine access by patients in England and Wales well beyond its likely approval in 2019.

GW Pharmaceuticals noted the complainant's allegation that the company had a manned exhibition stand with Epidiolex materials. The materials, however, only referred to cannabidiol by its non-proprietary name; the brand name was not used at all. This was reflected in the company's briefing and training materials.

GW Pharmaceuticals noted that the complainant provided a direct quotation of what the named individual was alleged to have stated but did so in a seemingly implausible manner. The allegation was that he/she introduced Epidiolex as a new treatment, yet there was no introduction to, or presentation on, cannabidiol. Those manning the booth reacted to requests and questions from health professionals. The named individual would simply not have stated this in conversation with a health professional, because it was not a natural expression when responding to an unsolicited request.

Finally, GW Pharmaceuticals stated that the complainant seemed to have used extensive knowledge of medicines advertising law and the Code to construct a complaint covering all the elements that the PMCPA would look for when seeking to identify inappropriate pre-approval promotion of a medicine, ie:

- Involvement of sales representatives in medical information activities – by suggesting that the named individual was a representative, the complainant had implied that GW Pharmaceuticals

had manned a medical stand with sales staff. The named individual was not a representative. GW Pharmaceuticals noted that the complainant had referred to a 'medical representative', a term typically used by those with extensive familiarity with the Code eg the supplementary information to Clause 16.3.

GW Pharmaceuticals doubted whether a genuine health professional would be aware of this terminology, or indeed the distinction between a medical representative and a generic representative.

- Use of a product's brand name pre-approval – the complainant alleged that the stand materials and statements referred to cannabidiol by its brand name, Epidiolex. That was clearly incorrect to the extent it related to the stand materials, and GW Pharmaceuticals denied that the named individual ever stated that.
- Alleged pre-authorization and misleading advertising – the complaint also seemed carefully constructed to suggest that GW Pharmaceuticals had engaged in both illegal pre-approval *and* misleading advertising of Epidiolex, which again suggested familiarity with medicines advertising law and the manner in which the Panel considered cases.

The above led GW Pharmaceuticals to query whether the complainant was genuinely a health professional attendee at the stand.

GW Pharmaceuticals stated that it considered that the complaint was unmerited and implausible and that the Panel should dismiss it. However, the company also appreciated that the anonymity of the complainant and paucity of evidence in support of what was in effect one person's word, presented the Panel particular difficulties in adjudicating this matter. In this regard, GW Pharmaceuticals noted that when adjudicating complaints involving conflicting claims, the appropriate standard to be used was the 'balance of probabilities'. In that regard, GW Pharmaceuticals referred to cases in UK law and to two previous cases under the Code (Case AUTH/2572/1/13 and Case AUTH/2824/2/16).

GW Pharmaceuticals submitted that its version of events was more probable than that put forward by the complainant. Indeed, given the substantial evidence provided and careful assessment of the materials at issue and relevant events, GW Pharmaceuticals did not consider that the complainant had discharged the burden of proof on the balance or probabilities assessment. In conclusion, GW Pharmaceuticals submitted that it was impossible on a common sense view to find against the company on the basis of the simple statement put forward by the complainant, given its flaws and the weight of contradictory evidence and material submitted by the company.

With regard to approval certificates for the materials in question, GW Pharmaceuticals submitted that as it was non promotional it did not require certification. The supplementary information to

Clause 14.3 required that other material which was not promotional *per se*, such as corporate advertising should be examined to ensure that it did not contravene the Code. GW Pharmaceuticals confirmed that it had undertaken such examination and found all applicable material at issue was compliant.

GW Pharmaceuticals therefore denied any breaches of the Code, including of Clauses 3, 7.2, 9.1, 15.2 and 2.

FURTHER INFORMATION FROM GW PHARMACEUTICALS

GW Pharmaceuticals had continued to investigate the matter beyond the submission date of the response above. When GW Pharmaceuticals was advised of the second complaint (Case AUTH/3024/3/18) it again immediately investigated the matter independently of the ongoing investigation in this case. GW Pharmaceuticals considered that rather than two unrelated incidents, leading to separate complaints by unrelated complainants, the complaints were entirely fabricated by the same individual. GW Pharmaceuticals gave further, confidential background information about the suspected complainant and the events which led to the submission of his/her complaints.

PANEL RULING

The Panel noted that the anonymous complainant had, as set out in the introduction to the Constitution and Procedure, the burden of proving his/her complaint on the balance of probabilities. Anonymous complaints were accepted and, like all complaints, judged on the evidence provided by the parties. The Panel also noted that as the complainant was non-contactable it was not possible to ask him/her for further information.

The Panel noted the complainant's concern that GW Pharmaceuticals had promoted Epidiolex at the 2018 BPNA prior to the grant of its marketing authorization. The complainant's concerns covered both the materials on the exhibition stand and what he/she alleged was said by a company representative at the exhibition stand.

The Panel noted that when the meeting was held on 3-5 January 2018, Epidiolex did not have a marketing authorization although a licence had been applied for in the EU and US. The Panel noted GW Pharmaceuticals' submission that it currently expected a decision from the European Commission for Epidiolex in mid-2019. The company briefing on its standard responses for enquiries about Epidiolex (EU version 1.0, June 2017) stated that it was difficult to anticipate if, or when Epidiolex would be approved although the Panel noted that this document pre-dated the submission of the application for a marketing authorization.

The Panel noted that according to a press release dated 29 December 2017, the proposed indications in the EMA marketing authorization application for Epidiolex were as adjunctive treatment for seizures

associated with Lennox-Gastaut Syndrome and Dravet Syndrome, each forms of childhood onset epilepsy. Orphan designation had been granted for these proposed indications. In addition, the press release stated that orphan designations had been granted for West Syndrome and Tuberous Sclerosis Complex.

The Panel noted that although Clause 3 prohibited the promotion of a medicine prior to the grant of its marketing authorization, the Code permitted companies to undertake certain limited activities with regard to unlicensed medicines. GW Pharmaceuticals had not argued that any of the material and activities at issue constituted the legitimate exchange of medical and scientific information during the development of a medicine. The Panel noted that Clause 1.2 and its supplementary information permitted companies to respond in certain circumstances to unsolicited enquiries about a medicine including those without a marketing authorization; such responses should, *inter alia*, not go beyond the orbit of the original enquiry and the company should be satisfied that the enquiry was truly unsolicited.

The Panel noted that in a signed statement, the named GW Pharmaceuticals employee at the exhibition stand stated that the company's presence at the BPNA conference comprised a small medical booth staffed by him/her and another member of the UK medical team. According to GW Pharmaceuticals, the exhibition booth was intended to provide a non-promotional presence that demonstrated the company's commitment to research and development, its corporate awareness as a pharmaceutical development company, non-product specific disease awareness, and information on GW Pharmaceuticals' main research activities including cannabinoid medicinal products. GW Pharmaceuticals provided copies of the materials available at the booth; none mentioned Epidiolex by name. The Panel noted that it was an accepted principle under the Code that a product could be promoted without its name ever being mentioned.

An annotated photograph of the exhibition stand provided by GW Pharmaceuticals showed a table on which two infographics and five stacks of three leaflets were clearly displayed. An exhibition panel to the left of the table, headed 'GW Pharmaceuticals' depicted a photograph of a parent and child and referred the reader to the corporate website.

Two A3 infographics on Dravet Syndrome and Lennox-Gastaut Syndrome were each placed at the front of the table on the right-hand side. In the Panel's view, their location and striking design was such that they would have been highly visible to delegates visiting the stand. Each discussed age of onset of disease, prevalence, diagnosis, seizure types, aetiology, mortality rate and costs/economic burden. Each highlighted that current therapeutic options were inadequate. That for Lennox-Gastaut Syndrome stated 'Up to **80%** of patients are **refractory to anti-epileptic drug therapy**'. That for Dravet Syndrome stated 'Only **16%** of patients experience complete resolution in their seizures. All

seizure types **extremely resistant to treatment**'. In the Panel's view, these statements on materials at a pharmaceutical company exhibition stand would, on the balance of probabilities, solicit questions about the company's pipeline/other products.

A leaflet entitled 'Early-Onset Epilepsy Syndromes: Facts and Figures' reproduced the two aforementioned infographics on Lennox-Gastaut Syndrome and Dravet Syndrome. It also included two further infographics on Infantile Spasms and Tuberous Sclerosis Syndrome. These further infographics also implied that current therapy was inadequate; 'Most cases are **resistant** to anti-epileptic medications **45%** have intractable seizures after 3 years follow-up' (Infantile Spasms) and '63% of patients have refractory seizures' (Tuberous Sclerosis Complex). The Panel considered that its comments above in relation to the A3 infographics applied to this leaflet.

A leaflet entitled 'A World leader in the development of cannabinoid medicines' discussed GW Pharmaceuticals' commitment to cannabinoid treatments. The final page gave more details describing the cannabinoid development pipeline by indication under investigation and phase of clinical study. Seven neuroscience pipeline indications were listed. Dravet Syndrome and Lennox-Gastaut Syndrome had completed Phase 3 trials. Tuberous Sclerosis was shown as halfway through Phase 3 trials and infantile spasm halfway through Phase 2. A highlighted box beneath discussed the scale of the Phase 3 clinical development programmes with Dravet Syndrome and Lennox-Gastaut Syndrome and noted that the company's 'lead cannabinoid' had received orphan drug designation in these indications. The Panel noted that whilst Epidiolex was not named, sufficient information about its proposed indications, clinical development and orphan status was given such that it was indirectly identified and on the balance of probabilities the material would solicit questions about the company's 'lead cannabinoid'.

A fifth item was a glossary of cannabinoid terms. The Panel noted its concerns about the materials set out above. The Panel also noted that the materials had a promotional appearance. The Panel considered that the materials went beyond disease awareness information and/or non-promotional information about the company and its research interests as asserted by GW Pharmaceuticals.

In the Panel's view, the cumulative effect of highlighting the specific conditions for which it was anticipated the product would be licensed (as opposed to a more general discussion of paediatric epilepsy), deficiencies of current therapeutic options for the proposed indications in the infographics and discussing the Phase 3 clinical development program including referring to the company's 'lead cannabinoid', meant that the exhibition stand

promoted a medicine prior to the grant of its marketing authorization. A breach of Clause 3.1 was ruled. High standards had not been maintained; a breach of Clause 9.1 was ruled.

The Panel noted that promoting a product prior to the grant of its marketing authorization was listed in the supplementary information to Clause 2 as an activity likely to give rise to a breach of that Clause. The Panel noted its comments and rulings above and considered that GW Pharmaceuticals had brought discredit upon and reduced confidence in the pharmaceutical industry and a breach of Clause 2 was ruled.

The Panel noted the complainant's further allegation about comments that he/she alleged were made by a named company representative at the stand, namely that Epidiolex was introduced as a new treatment for paediatric patients with Dravet Syndrome and patients with Lennox-Gastaut Syndrome and that it had been licensed by the EMA and would soon be available in the UK. GW Pharmaceuticals denied that such comments had been made. The Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was often impossible in such circumstances to determine precisely what had happened. The introduction to the Constitution and Procedure stated that a complainant had the burden of proving their complaint on the balance of probabilities. The complainant was non-contactable and it was not possible to ask him/her for further information. The Panel had to make a ruling on the evidence before it.

The Panel noted its comments above about responses to unsolicited enquiries and Clause 1.2 of the Code and its supplementary information. The Panel also noted the signed statement of the company employee manning the booth in relation to training, the nature of queries received at the exhibition stand, and whether he/she would have responded as alleged. The Panel also noted the detailed briefing to medical affairs staff to use at conferences in response to unsolicited requests. The briefing pre-dated the submission of the company's marketing authorization application to the EMA and advised that discussions with health professionals must be reactive and in response to the requested information. Staff were advised to narrowly tailor the response to the level of the question posed. The company's report on interactions at the conference did not closely mirror the complainant's allegation. In relation to the alleged comments made at the exhibition stand, it was impossible to determine where the truth lay and the Panel accordingly ruled no breach of Clauses 15.2, 9.1, 7.2, 3.1 and 2.

Complaint received **24 January 2018**

Case completed **22 November 2018**

ANONYMOUS, NON CONTACTABLE HOSPITAL CONSULTANT v GW PHARMACEUTICALS

Alleged promotion of Epidiolex

An anonymous, non-contactable complainant, who described themselves as a consultant neurologist, complained about the pre-licence promotion of Epidiolex (cannabidiol) by GW Pharmaceuticals at a hospital meeting in February 2018. An application for a marketing authorization had been submitted to the European Medicines Agency (EMA) for its use as an adjunctive treatment for seizures associated with Lennox-Gastaut Syndrome and Dravet Syndrome.

The complainant had attended the multi-disciplinary team meeting at which GW Pharmaceuticals hosted a presentation on Epidiolex treatment. The complainant stated that after the presentation, he/she was informed that Epidiolex was unavailable to prescribe as it was not currently licensed in the UK or Europe.

The detailed response from GW Pharmaceuticals is given below.

The Panel noted that GW Pharmaceuticals referred to a third party organisation that employed managers to represent GW Pharmaceuticals. The Panel noted that it was an established principle under the Code that companies were responsible for the acts/omissions of third parties acting on their behalf.

The Panel noted that an application for a marketing authorization for Epidiolex was submitted to the EMA on 29 December 2017; its proposed indications were as adjunctive treatment for seizures associated with Lennox-Gastaut Syndrome and Dravet Syndrome, each forms of child onset epilepsy.

The Panel noted that the slides provided by the parties in relation to the meeting in February differed. The complainant provided photographs of nine slides, some of which were such that the full slide could not be seen, whilst GW Pharmaceuticals provided thirty-two slides. The Panel noted GW Pharmaceuticals' detailed submission about the slides including that those provided by the complainant were not those used at the meeting. It was difficult in such circumstances to establish which set of slides was used. The complainant could not be contacted for more information. The Panel however noted that a photograph taken by GW Pharmaceuticals at the meeting of a particular slide appeared to be consistent with that slide as provided by the company as part of its response; both appeared to contain the header 'Cannabidiol is an investigational product and is not licensed in the EU'.

The Panel examined the slides provided by both parties and noted that while most of the 32

slides provided by GW Pharmaceuticals stated that cannabidiol was not EMA approved, the nine slides provided by the complainant did not. The Panel noted that the slides provided by GW Pharmaceuticals discussed cannabidiol, Phase III trial data including Dravet Syndrome and Lennox-Gastaut Syndrome and GW Pharmaceuticals' cannabidiol pharmaceutical production.

The Panel noted GW Pharmaceuticals' submission that the meeting in question was the legitimate exchange of medical and scientific information in response to an unsolicited enquiry about the development of cannabidiol. The Panel noted that the Code prohibited the promotion of a medicine prior to the grant of its marketing authorization; supplementary information stated that the legitimate exchange of medical and scientific information during the development of a medicine was not prohibited provided that this did not constitute promotion which was prohibited by the Code. The Panel queried whether a product subject to Phase III trials, and for which licence applications had been submitted, would be considered an investigational molecule or otherwise in development. The Panel noted that the GW Pharmaceuticals' slides included the proposed indications, usage and dosage. In the Panel's view and given the content of the presentations provided by each party, health professionals were likely to view Epidiolex as a pre-licence product. The Panel considered that its view was supported by the list of questions asked by those present which included questions about cost, shelf life, storage and others relevant to the product's use. There did not, on the information before the Panel, appear to be an exchange of medical and scientific information about the development of the product. In the Panel's view, the presentation could not take the benefit of the supplementary information in the Code.

With regard to GW Pharmaceuticals' submission that the presentation was provided in response to an unsolicited enquiry, the Panel noted that the Code provided an exemption to the definition of promotion stating that replies made in response to individual enquiries from members of the health professions or other relevant decision makers or in response to specific communications from them whether of enquiry or comment, were excluded from the definition of promotion, but only if they related solely to the subject matter of the letter or enquiry, were accurate and did not mislead and were not promotional in nature. The Panel noted that the exemption only applied to unsolicited enquiries, an enquiry made without any prompting from the company. If an enquirer subsequently

requested further information this could be provided and would be exempt from the Code provided the additional information met the requirements of this exemption. The Panel noted that when relying on this limited exemption in relation to a meeting about an unlicensed product, documentation was very important.

The Panel noted GW Pharmaceuticals' submission that the presentation was provided in response to an unsolicited verbal request from health professionals for a medical presentation on updated clinical data and properties of cannabidiol in December 2017 during a meeting between two managers representing GW Pharmaceuticals and two doctors from the hospital in question. The Panel noted that GW Pharmaceuticals provided some evidence in support of its position. The general points covered in the presentation provided by GW Pharmaceuticals appeared to be consistent with the points raised by the health professionals. When asked if the presentation was scientific or promotional in nature, one of the doctors stated that it was scientific in nature, as new scientific data which he/she had not seen before was shared. The doctor stated that he/she was particularly interested to hear more about study results, safety information, side-effects, efficacy and also to get an update on recent trial data, when market approval might be expected and whether prescriptions on a named patient basis might be a possibility. The Panel noted the list of 12 attendees. From the evidence before the Panel, it appeared that in requesting the meeting the two health professionals, rather than GW Pharmaceuticals, had decided that the content was appropriate for the small specialized departmental group.

Whilst the Panel had some concerns about the meeting, including the lack of formal documentation, it noted that based on the company's account there was no evidence that the meeting went beyond the original information requested by the two doctors. The Panel noted that the complainant bore the burden of proof and had not established that the meeting was promotional and not in response to an unsolicited request. On the evidence before it, the Panel considered that, on balance, GW Pharmaceuticals could take the benefit of the exemption of the definition of promotion in the Code in relation to unsolicited requests and therefore did not consider on the particular facts of this case, that the meeting promoted Epidiolex prior to the grant of its license as alleged. The Panel therefore ruled no breaches of the Code.

An anonymous non-contactable complainant who described him/herself as a consultant neurologist complained about the pre-licence promotion of Epidiolex (cannabidiol) by GW Pharmaceuticals at a hospital meeting in February 2018. An application for a marketing authorization had been submitted for its use as an adjunctive treatment for seizures associated with Lennox-Gastaut Syndrome and Dravet Syndrome.

COMPLAINT

The complainant submitted that he had attended a multi-disciplinary team meeting at a named hospital at which GW Pharmaceuticals hosted a presentation on Epidiolex treatment. Pictures of some of the slides were provided. The complainant stated that after the presentation, he/she was informed that Epidiolex was unavailable to prescribe as it was not currently licensed in the UK or Europe.

When writing to GW Pharmaceuticals it was asked to bear in mind the requirements of Clauses 3.1, 9.1 and 2 of the Code. The case preparation manager stated that Clause 15.2 might also be relevant.

RESPONSE

GW Pharmaceuticals noted that the anonymous complainant had provided little detail and while it was thus difficult to respond, it had nonetheless investigated the issues raised and was comfortable that the complaint had no basis. It trusted that the level of diligence was reflected in its detailed response.

GW Pharmaceuticals explained that in response to an unsolicited request and invitation by health professionals in December 2017, managers representing GW Pharmaceuticals' attended the named hospital in February 2018 to exchange scientific and medical information about the development of cannabidiol. There was no formal agenda but the intention of what would be addressed at the meeting was set out in emails between one of the managers (A) and health professionals at the hospital (copy provided) and contemporaneous notes. The purpose of the meeting was to present tailored and appropriate data on cannabidiol in response to the unsolicited request. There was no promotional intent. A full list of attendees was provided.

As part of its investigation, GW Pharmaceuticals had obtained statements (copies provided) from manager A, who arranged the meeting/presentation in question, and manager B who attended the presentation. The company also provided a signed summary/record of a telephone call on 23 March 2018 between the health professional who requested and attended the presentation in February, and two other senior employees from the third party organisation.

GW Pharmaceuticals submitted that manager (A) who had arranged the meeting, in particular had provided a rigorous and detailed account of the presentation, backed by robust supporting materials, including a number of records of his/her interactions with health professionals at, and prior to, the presentation. The manager had satisfied GW Pharmaceuticals that the presentation at issue was not promotional. The manager was highly experienced and qualified and, in GW Pharmaceuticals' view, an eminently sensible and conscientious medical affairs professional. He/she was fully aware of the Code and his/her responsibilities under it. His/her account was backed by: (i) contemporaneous

records of his/her communications with health professionals with whom he/she interacted as a result of unsolicited requests at a meeting with named health professionals in December 2017, and at the presentation in question; (ii) his/her contemporaneous photograph of the presentation slides used at the February meeting; (iii) the slides themselves; and (iv) briefing materials on which he/she was well-trained. Manager B's statement corroborated entirely manager A's detailed account. The summary/record signed by one of the health professionals further corroborated these accounts. Together these statements and the accounts and supporting materials provided a clear, comprehensive and credible account of the meeting on 7 February 2018 and the background to it.

GW Pharmaceuticals stated that it had re-assessed in the context of the complaint, all relevant material, procedures, processes and instructions which might pertain to the alleged events, including anything which might have prompted promotional statements to be made or promotional material to be presented in error. The briefing and training materials given to manager A, along with his/her account of any instructions he/she received, was also reviewed. Similarly, GW Pharmaceuticals had considered manager B's professional background, experience and training records provided in his/her statement. The slides which were presented at the February 2018 meeting had been reviewed, including photographic evidence of the same, along with manager A's detailed account and the corroborative accounts of manager B and a health professional. Any material, where relevant, was provided as exhibits to manager A's statement.

Having thoroughly investigated the complaint, GW Pharmaceuticals considered that the allegations were entirely unfounded; the company denied any wrongdoing or impropriety on its part or by its managers. A number of factual issues and inconsistencies in the complaint, as set out below, led the company to suspect that the complaint was unfounded and/or fabricated.

GW Pharmaceuticals submitted that it had never implicitly, or directly, promoted or encouraged the promotion of any unlicensed medicine, including Epidiolex. Indeed, the company considered that it went to particular lengths to ensure that the alleged claims would not happen even by reason of genuine error. In that regard GW Pharmaceuticals referred to statements by manager A which constituted the company's standard responses to enquiries on cannabidiol.

GW Pharmaceuticals stated that, unprompted, health professionals had requested a medical presentation on updated clinical data and properties of cannabidiol which was what was provided at the presentation. The request was corroborated by the email exchange between manager A and the requesting health professionals which stated: 'Thanks for your request to present an update on cannabidiol data and progress'.

According to GW Pharmaceuticals, the basis and nature of the presentation was clear from the email

exchange and the disclaimer on slide 2 which stated; 'This slide deck is being presented following an unsolicited request from a healthcare professional'. One health professional also clearly confirmed that he/she and another health professional had invited GW Pharmaceuticals to make a presentation, the first health professional being 'particularly interested to hear more about study results, safety information, side effects, efficacy and also to get an update on recent trial data, when market approval might be expected and whether prescriptions on a named patient basis might be a possibility'.

Manager A stated 'Great care was taken to ensure that the presentation was balanced, noting trial design and balancing any efficacy data with safety data including laboratory findings, common adverse events and serious treatment emergent adverse events. In my view, the information presented was balanced, fair, objective and unambiguous, and was as stated, based on an up-to-date evaluation of the evidence available'. GW Pharmaceuticals stated that in its view the slides comprised scientific and medical information, genuine non-promotional information about GW Pharmaceuticals and its research interests and disease awareness information. One of the health professionals also agreed and stated that in his/her opinion 'The presentation and meeting were of a scientific nature as new scientific data was shared which he/she had not seen before'.

Following the presentation, manager A's contemporaneous notes from the meeting showed that there followed, from the health professionals, a series of specific and unsolicited queries about the data and properties of cannabidiol. GW Pharmaceuticals was satisfied from this material and accounts of attendees that the discussion/Q&A was non-promotional and that the presentation and any interactions around it were part of an entirely appropriate response to an unsolicited request aimed to legitimately exchange medical and scientific information.

GW Pharmaceuticals noted that although it was not expressed the complainant implied that he/she only became aware that Epidiolex was not licensed after the presentation. Although not stating exactly when he/she received the correct information, the complainant implied that during the presentation, and perhaps for some time after, he/she understood that cannabidiol was available to prescribe and licensed in the UK and Europe. GW Pharmaceuticals assumed either that the complainant alleged that he/she misunderstood the presentation and/or was misled by it.

GW Pharmaceuticals noted that manager A addressed this issue in depth in his/her statement. The company was comfortable from his/her and other attendees' accounts, and its review of supporting material, that it was simply implausible that anyone who had attended the presentation, even if only part of it, could have misunderstood, or worse, been misled, as to the licensing status of Epidiolex.

GW Pharmaceuticals noted that on slide 2 there was a large and prominent disclaimer which stated ‘Cannabidiol is an investigational product and is not FDA or EMA approved, for any indication’; the licensing status could thus not be clearer. GW Pharmaceuticals understood that a third employee who presented the data spent quite some time bringing this message to the attention of attendees. Even if the complainant had arrived late and missed this slide, 21 out of 33 of the slides prominently displayed in clear and large font: ‘Cannabidiol is an investigational product and is not licensed in the EU’. This warning was featured throughout the slides including on the first and concluding slides. The contemporaneous photograph which manager A took of the presentation showed that the wording was prominent and legible even at a distance. Thus, anyone who attended the presentation at least had the opportunity to see this warning.

GW Pharmaceuticals submitted that it had no reason to believe, on the basis of the employees’ professional background, experience and training, that they would have orally provided incorrect information on the licensing status or introduced uncertainty. Indeed, it would have been problematic to introduce such uncertainty given the clarity of the words on the slides, and it would have required significant departure and contradiction which would have prompted queries from the attendees, especially as at least two of the health professionals had been expressly informed of the licensing status and availability at the meeting in December 2017 and again by email. From his/her signed statement, one of the health professionals was apparently in no doubt before and at the presentation that the product was not approved. GW Pharmaceuticals thus rejected entirely that misleading information about the status and availability of cannabidiol was presented at the meeting in February.

GW Pharmaceuticals stated that it was satisfied that it and its third party had discharged their duties to provide appropriate and comprehensive briefing and training in order to enable managers A and B and the speaker to represent GW Pharmaceuticals in their respective roles to high standards of ethical conduct fully in compliance with the Code.

Finally, GW Pharmaceuticals submitted that it had significant concerns with aspects of the complaint itself, which it considered went to its credibility.

GW Pharmaceuticals noted that the complainant’s allegation that GW Pharmaceuticals or its representatives hosted the meeting, was inaccurate. From the statements and supporting information, and in particular the email exchange leading up to the meeting, it was clear that:

- the presentation was in response to an unsolicited request from two health professionals;
- the two health professionals invited the GW Pharmaceuticals representatives and not the other way around;
- the health professionals invited GW Pharmaceuticals to their premises, and no GW Pharmaceuticals or any other premises arranged by GW Pharmaceuticals or its representatives

were offered and

- the health professionals provided the facilities whereas the representatives only took an electronic copy of the slide deck on their devices.

GW Pharmaceuticals further noted that although the complainant alleged that GW Pharmaceuticals hosted a presentation on Epidiolex, that brand name was not used in the presentation or contemporaneous notes; these all referred to cannabidiol or CBD only by its non-proprietary name. That was reflected in the company’s briefing and training materials.

For the reasons stated above, GW Pharmaceuticals considered that it was implausible that the complainant, if he/she attended the presentation, could have been confused as to the licensing status of Epidiolex or informed of the correct status only after the event.

GW Pharmaceuticals alleged that the complainant was either not at the presentation or had made fraudulent allegations, because:

- The slide deck presented contained a licensing warning/header on most of the slides. However, the photographs of the slides which were attached to the complaint did not contain that wording. Although a number of the slides had been cropped, if these were true contemporaneous photographs of the presented deck, at least five were extended enough to have shown this wording (namely photographs of slides 3, 4, 6, 21 and 27) but they did not.
- In addition, the presenter’s name and role were clearly located below the title on slide 1 of what was presented but were obviously missing from the photograph which purported to be of this slide.
- The photographs therefore could not be contemporaneous.
- The selective nature of the photographs both in terms of excluding the disclaimer slide and by possibly doctoring the slides to remove the warning, undermined the credibility of the complaint and the complainant.
- GW Pharmaceuticals stated that neither it nor its third party had found a slide deck which matched the photographs. The company understood that the slides were not provided in electronic or hard copy to attendees in advance, during or at the presentation. There was no evidence that the slides or any related decks were shared beyond GW Pharmaceuticals and its third party. GW Pharmaceuticals stated that it was still investigating but could state at this stage that the photographs were not of the slides which were presented and must have been obtained and/or doctored improperly, if not illegally.
- The photographs were poor quality and contained the type of glare which would normally appear when taking photographs of an electronic device such as tablet or laptop screen at close range, and not a large presentation screen. In that regard, GW Pharmaceuticals compared managers A’s contemporaneous photograph and statement. Also the usual tablet/laptop black surround could be seen in a number of the photographs whereas

the presentation surround was clearly grey/white and irrespective of the quality of the images, it was highly unlikely that there would be such a stark change or that such contrast difference would not have caused the slides to also be blacked out. As well as further supporting the company's submission that the photographs were not of the presented slides, GW Pharmaceuticals stated that these factors also caused it to believe that the photographs were taken of a set of slides on a laptop or tablet device and not at the presentation.

GW Pharmaceuticals stated that, in its view, the only conclusion must be that the complainant did not attend the presentation, and/or had improperly or illegally obtained copies of the slides or created or doctored them to appear like those presented, and/or had fraudulently presented these as contemporaneous or true copies of the slides which were presented. GW Pharmaceuticals did not currently know the motivation for this series of illicit acts but was deeply troubled by them.

GW Pharmaceuticals stated that in its view the complaint was without merit and implausible, if not fraudulent, and that it should be dismissed by the Panel. However, it also appreciated that the anonymity of the complainant and paucity of evidence in support of what was in effect one person's word, presented the Panel particular difficulties in adjudicating this matter. With this in mind, GW Pharmaceuticals referred the Panel to the summary provided in its response to Case AUTH/3014/1/18 on the appropriate standard when adjudicating complaints involving conflicting claims, namely the 'balance of probabilities'.

Considering the points raised in this summary and applicable case law, GW Pharmaceuticals submitted that its version of events was more probable than that of the complainant. GW Pharmaceuticals had provided substantial evidence and careful assessment of the materials at issue and relevant events. Conversely, the complainant's allegations and account of events were simply not plausible. GW Pharmaceuticals stated that to its knowledge the complainant had provided no credible evidence to discharge the burden of proof on the balance of probabilities assessment. Indeed, for the reasons set out above, GW Pharmaceuticals considered that the material attached to the complaint should be viewed at best with caution, if not as misrepresentative or even fraudulent. Therefore this 'evidence', rather than supporting the complainant's allegations, entirely undermined his/her credibility.

To conclude, GW Pharmaceuticals submitted that it was impossible on a common sense view to find against the company on the basis of the simple, brief complaint, given its flaws and the weight of contradictory evidence submitted by GW Pharmaceuticals. GW Pharmaceuticals thus denied any breach of the Code, including Clauses 3.1, 9.1 and 2 and also 15.2 and 15.9 if these are considered by the Panel.

GW Pharmaceuticals noted that the Authority had asked for certificates approving the material

in question but as it was non-promotional it did not require certification under the Code. The supplementary information to Clause 14.3 required that 'other material...which is not promotional *per se*, such as corporate advertising...should be examined to ensure that it does not contravene the Code or the relevant statutory requirements'. GW Pharmaceuticals confirmed that it and/or its third party had examined all applicable materials at issue and found them to be compliant. In particular, manager A, who was a highly experienced medical affairs professional and qualified Code signatory, arranged the content of the presentation, examined the presentation material, supervised the presentation, and participated in post-presentation discussions, and did not consider there had been any breach of the Code.

GW Pharmaceuticals stated that a marketing authorization application for Epidiolex was submitted on 29 December 2017 and as and until the European Commission issued its marketing authorization, it remained unlicensed in the EU.

FURTHER INFORMATION FROM GW PHARMACEUTICALS

GW Pharmaceuticals stated that when first advised of Case AUTH/3014/1/18, it and its third party immediately investigated the circumstances and merits of the complaint; both companies had serious misgivings about the legitimacy of the complaint, as well as concerns over the inaccuracies and inconsistencies in the complainant's brief account. GW Pharmaceuticals had continued to investigate the matter beyond the submission date of the response set for Case AUTH/3014/1/18. When GW Pharmaceuticals was advised of the second complaint, (Case AUTH/3024/3/18) it again immediately investigated the matter, independently of the ongoing investigation in Case AUTH/3014/1/18. Although investigations were still ongoing, GW Pharmaceuticals provided its outline finding below.

GW Pharmaceuticals submitted that rather than two unrelated incidents, leading to separate complaints by individual and unrelated complainants, the complaints were entirely fabricated by the same individual. GW Pharmaceuticals suspected, but was investigating, the position of the complainant and details were provided including that the complaints were made anonymously and without the possibility for follow-up because they were disingenuous. The complaints were also each entirely implausible for the reasons set out above and were made some time after the alleged events.

In relation to this case, GW Pharmaceuticals was especially concerned that the photographs provided by the complainant were not of the slides presented in February 2018, as he/she claimed. In particular, the slides provided by the complainant did not match any slide deck found so far and so must have been doctored without consent, possibly on a personal device. GW Pharmaceuticals considered that the omission of the licensing status of cannabidiol from all of the slides and the selective presentation were intended to present a particularly egregious impression of the company and its representatives.

With this in mind, GW Pharmaceuticals had hoped to be able to provide the Panel with a signed statement from the person who presented the slides. That person prepared a statement (copy enclosed) in March 2018 and indicated that he/she was happy to sign it; he/she also provided a copy of the slides presented. However, he/she then declined to sign it or any statement or to attest to the authenticity of the slide deck which he/she stated he/she presented in February 2018. Manager A stated, to the best of his/her knowledge and belief, that the slide deck provided by GW Pharmaceuticals was the slide deck which was presented. GW Pharmaceuticals stated that it did not yet know with certainty why the presenter appeared troubled when confronted by inconsistencies between the slides presented and those in the complaint, but the Panel could draw whatever inferences it wished.

GW Pharmaceuticals noted that Case AUTH/3029/4/18 had the same troubling inconsistencies in the slide deck as seen in Case AUTH/3024/3/18. GW Pharmaceuticals referred to its response to Case AUTH/3029/4/18 and noted that the Panel should be aware that the complainant was aware that the slides which he/she attached to an email in February 2018 were not those presented and were in fact created by the complainant in February 2018.

Bearing in mind the above, and from the company's knowledge of the circumstances and individuals involved, GW Pharmaceuticals was satisfied that the three complaints were without merit and were fraudulent.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable and that, as set out in the introduction to the Constitution and Procedure, complainants had the burden of proving their complaint on the balance of probabilities. Anonymous complaints were accepted and, like all complaints, judged on the evidence provided by the parties. The Panel noted that as the complainant was non-contactable it was not possible to ask him/her for further information.

The Panel noted that the company's response implied that it was aware of the complainant's identity. The Panel noted that from the PMCPA's perspective, the complainant was anonymous and non-contactable.

The Panel noted a third party organisation employed manager A and B to represent GW Pharmaceuticals. The Panel noted that it was an established principle under the Code that companies were responsible for the acts/omissions of third parties acting on their behalf.

The Panel noted the complainant's allegation that Epidiolex was promoted prior to the grant of its marketing authorization at a hospital meeting on 7 February 2018. The Panel noted that an application for a marketing authorization was submitted to the European Medicines Agency (EMA) on the 29 December 2017; its proposed indications were as adjunctive treatment for seizures associated with

Lennox-Gastaut Syndrome and Dravet Syndrome, each forms of child onset epilepsy.

The Panel noted that the content of the slides provided by the parties in relation to the meeting on 7 February differed. The complainant provided photographs of nine slides, some of which had been cropped such that the full slide could not be seen, whilst GW Pharmaceuticals provided thirty-two slides (ref VV-MED-01262). The Panel noted GW Pharmaceuticals' detailed submission about the slides provided by the complainant including that they were not those used at the meeting in question. It was difficult in such circumstances to establish which set of slides was used. The complainant could not be contacted for more information. The Panel noted its comments above about the burden of proof. The complainant had not provided any additional evidence on this point. The Panel however noted that a photograph taken by GW Pharmaceuticals at the meeting in question of a particular slide appeared to be consistent with slide 10 in the presentation provided by GW Pharmaceuticals as part of its response; both appeared to contain the header 'Cannabidiol is an investigational product and is not licensed in the EU'. The Panel noted the company's submission that the employee who presented the material at issue had prepared but ultimately declined to sign a statement.

The Panel examined the slides provided by both parties. The Panel noted that the second slide of the presentation 'GW Pharmaceuticals and Cannabidiol Oral Solution' provided by GW Pharmaceuticals stated that 'Cannabidiol was an investigational product and was not FDA or EMA approved, for any indication. All labelling language was subject to change'. This slide was not included in those provided by the complainant. The Panel noted that the header referred to above 'Cannabidiol is an investigational product and is not licensed in the EU' appeared on 21 of the 32 slides provided by GW Pharmaceuticals. However, those provided by the complainant did not contain such wording including five slides which showed that part of the slide where the header appeared in the equivalent GW Pharmaceuticals' version. The Panel noted that the slides provided by GW Pharmaceuticals discussed cannabidiol, Phase III trial data including Dravet Syndrome and Lennox-Gastaut Syndrome and GW Pharmaceuticals' cannabidiol pharmaceutical production.

The Panel noted that GW Pharmaceuticals submitted that the meeting in question in February 2018 was the legitimate exchange of medical and scientific information in response to an unsolicited enquiry about the development of cannabidiol. The Panel noted that Clause 3.1 prohibited the promotion of a medicine prior to the grant of its marketing authorization; supplementary information stated that the legitimate exchange of medical and scientific information during the development of a medicine was not prohibited provided that this did not constitute promotion which was prohibited by Clause 3 or any other clause. The Panel queried whether a product subject to Phase III trials and for which a licence had been applied for in the US and Europe would be considered an investigational

molecule or otherwise in development. The Panel noted that the GW Pharmaceuticals' version of the slides presented included the proposed indications, usage and dosage. In the Panel's view and given the content of the presentations provided by each party, health professionals were likely to view Epidiolex as a pre-licence product. The Panel considered that its view was supported by the list of questions asked by those present which included questions about cost, shelf life, storage and others relevant to the product's use. There did not, on the information before the Panel, appear to be an exchange of medical and scientific information about the development of the product. In the Panel's view the presentation could not take the benefit of the supplementary information to Clause 3.1.

The Panel noted that GW Pharmaceuticals also submitted that the presentation was provided in response to an unsolicited enquiry. The Panel noted that Clause 1.2 provided an exemption to the definition of promotion stating that replies made in response to individual enquiries from members of the health professions or other relevant decision makers or in response to specific communications from them whether of enquiry or comment, were excluded from the definition of promotion, but only if they related solely to the subject matter of the letter or enquiry, were accurate and did not mislead and were not promotional in nature. The Panel noted that the exemption only applied to unsolicited enquiries, an enquiry made without any prompting from the company. If an enquirer subsequently requested further information this could be provided and would be exempt from the Code provided the additional information met the requirements of this exemption. The Panel noted that when relying on this limited exemption in relation to a meeting about an unlicensed product, documentation was very important.

The Panel noted GW Pharmaceuticals' submission that the presentation was provided in response to an unsolicited verbal request from health professionals for a medical presentation on updated clinical data and properties of cannabidiol in December 2017 during a meeting between managers A and B and two doctors from the hospital. The Panel noted that GW Pharmaceuticals provided some evidence in support of its position. Manager A's statement and his/her notes of the meeting in December 2017 indicated that the health professionals had requested that GW Pharmaceuticals present at the departmental multi-disciplinary meeting on cannabidiol and clinical data. A follow-up email from manager A to the two doctors referred to their request to present an update on cannabidiol data and progress at the weekly department meeting and asked for specific questions around cannabidiol to ensure that the company presented the most pertinent information. The Panel queried whether it could be argued that this email was soliciting enquiries, however it did not appear that either doctor responded with any specific topics to be covered. The general points covered in the presentation provided by GW Pharmaceuticals

appeared to be consistent with the points raised by the health professionals at the earlier meeting in December. That the meeting in February resulted from an unsolicited request was also corroborated by a signed statement from manager B who attended the meetings in December 2017 and in February 2018. In addition, a signed transcript of a telephone conversation with one of the health professionals confirmed, in response to a question about whether GW Pharmaceuticals had suggested the meeting or whether it had been requested by him/herself and the other doctor, that he/she and the other doctor had asked GW Pharmaceuticals to arrange the presentation. One of the doctors noted that whilst he/she did not remember whether or not the presentation included any disclaimers that the product was not yet licensed, that would not be something he/she would have paid special attention to as he/she already knew that it was not. When asked if the presentation was scientific or promotional in nature, the doctor stated that it was scientific in nature, as new scientific data which he/she had not seen before was shared. The doctor stated that he/she was particularly interested to hear more about study results, safety information, side-effects, efficacy and also to get an update on recent trial data, when market approval might be expected and whether prescriptions on a named patient basis might be a possibility.

The Panel noted the list of 12 attendees. From the evidence before the Panel, it appeared that in requesting the meeting the two health professionals, rather than GW Pharmaceuticals, had decided that the content was appropriate for the small specialized departmental group.

Whilst the Panel had some concerns about the meeting, including the lack of formal documentation, it noted that based on the company's account there was no evidence that the meeting went beyond the original information requested by the two doctors. The Panel noted that the complainant bore the burden of proof and had not established that the meeting was promotional and not in response to an unsolicited request. On the evidence before it, the Panel considered that, on balance, GW Pharmaceuticals could take the benefit of the exemption of the definition of promotion at Clause 1.2 in relation to unsolicited requests and therefore did not consider on the particular facts of this case, that the meeting promoted Epidiolex prior to the grant of its license as alleged. The Panel therefore ruled no breach of Clause 3.1 and subsequently no breach of Clauses 15.2, 9.1 and 2.

The Panel noted that the case preparation manager had raised Clause 15.9. The Panel did not consider that the complainant's allegation raised a Clause 15.9 matter and therefore ruled no breach of Clause 15.9.

Complaint received **12 March 2018**

Case completed **18 October 2018**

ANONYMOUS EMPLOYEE v SANOFI

Promotion of Toujeo and Lantus

An anonymous, non-contactable complainant who described themselves as a Sanofi employee complained about a manager's briefing with regard to the promotion of Lantus (insulin glargine 100 units/mL) and Toujeo (insulin glargine 300 units/mL). Both medicines were used in diabetes mellitus.

The complainant provided a copy of an email sent from a manager to his/her team of representatives. The email chain included a regional head who responded and endorsed the email. The complainant alleged that Sanofi acknowledged the manager's success but turned a blind eye as to how it was achieved, as his/her results were significantly higher compared with other colleagues.

The complainant alleged that the manager actively encouraged representatives to have detailed discussions around patients with health professionals thereby resulting in audits and identification of patient groups. This was documented as best practice and included:

- 1 Patients to be identified and started on Toujeo via other ways and means of the agreed policy.
- 2 Several mentions of adverse reactions with Lantus.
- 3 Discussions around off-licence, twice daily Lantus.
- 4 The Toujeo coach service for patients was being used and tracked by the representative.

The detailed response from Sanofi is given below.

The Panel noted the complainant's allegation that the manager was encouraging identification of patients for Toujeo outside an agreed policy. (Sanofi submitted the policy was an NHS protocol provided by consultants to general practitioners). The Panel noted that within the email two representatives made reference to the agreed policy being a barrier in certain circumstances. The Code did not state that a medicine must be promoted within the terms of local, regional or national guidelines. However, the Code required information claims and comparisons to be, *inter alia*, accurate, balanced, fair and not inconsistent with the particulars in its summary of product characteristics (SPC). The Panel did not consider that the complainant had provided any evidence which demonstrated that any of Sanofi's representatives had promoted Toujeo outside the terms of its marketing authorisation or that the email in question advocated such use and therefore no breach of the Code was ruled.

The Panel noted the complainant's statement that 'Several mentions of adverse reactions with Lantus' were documented. The Panel noted that the email

in question referred to a Lantus patient experiencing recurrent hypoglycaemia. The Panel noted that it was of the utmost importance that such information about side-effects was processed by the company in accordance with, *inter alia*, the Code. However, the Panel noted that it was not for the Panel to infer detailed reasons to support the allegation. It was for the complainant to establish his/her case on the balance of probabilities. The Panel considered that the very general nature of the allegation was such that the subject matter of the allegation was unclear and the complainant had not discharged his/her burden of proof and thus ruled no breach of the Code including Clause 2.

With regard to the allegation that the email documented discussions around off-licence twice daily use of Lantus, the Panel noted that the email highlighted the field activities of named representatives in a given territory and was provided to representatives from another territory as an example of the types of Toujeo discussions being had with health professionals. The Panel noted Sanofi's submission that the intent was to share personal highlights to support teamwork and motivation and it was not intended to be directional. The Panel noted Sanofi's submission that the manager in question was currently managing the representatives from both territories. The Panel noted the manager's comment in the email provided to the second territory which stated 'It is abundantly clear that they [the first territory] are all having detailed conversations with HCPs and that this is translating to new patients for Toujeo'. In the Panel's view, the manager's email encouraged the second territory to learn from and adopt the activities of the first territory in terms of engagement with health professionals for the promotion of Toujeo. The Panel considered that the information therefore constituted briefing material.

The email in question mentioned conversations that three representatives had had with health professionals regarding patients on twice-daily Lantus who subsequently switched to Toujeo. The Panel noted Sanofi's submission that the references to twice-daily Lantus was not in any way directional in terms of how the product should be promoted. The Panel noted that the Code stated that briefing material must not advocate either directly or indirectly any course of action which would be likely to lead to a breach of the Code. The Panel further noted that slides from the Operational Plan and Segmentation Workshop held in 2018 referred to a segment of customers described as 'Comfortable with patients having to take BD [twice-daily] Lantus as part of their basal bolus regime' and that such customers needed to 'See benefit of switching to Toujeo from Lantus in T1D [type 1 diabetes] and T2D [type 2 diabetes]'.

In the Panel's view the references to twice-daily use of Lantus in the email in question, without any qualification that such use was off-label and should not be proactively discussed, could encourage representatives, within the context of promoting Toujeo, to initiate discussions about twice-daily Lantus use, which was not within Lantus' licence, and a breach of the Code was ruled in relation to this representatives briefing materials. The Panel considered that the complainant had not provided evidence to demonstrate that on the balance of probabilities representatives went on to promote Lantus to health professionals in such a manner that was inconsistent with its SPC and ruled no breach of the Code.

With regard to the complainant's allegation that the patient support programme, Toujeo Coach, was being 'used and tracked by the representative', the Panel noted Sanofi's submission that Toujeo Coach was a Sanofi patient support programme that offered diabetes nurse specialist, psychologist and dietician coaching as well as support and access to educational resource and advice. According to Sanofi, it would be offered to a health professional or healthcare organisation once they had made the decision to prescribe Toujeo. The Panel noted that it was not clear why the complainant considered that reference to the Toujeo Coach service, in particular, that it was being used and tracked by a representative, was in breach of the Code. The Panel noted Sanofi's submission that the sales team was briefed on how to share the Toujeo Coach service as part of the Toujeo sales aid and accompanying briefing. The Panel noted Sanofi's submission that the representatives received reports of the number of patients enrolled on the Toujeo Coach programme at a clinical commissioning group (CCG) level. The complainant bore the burden of proof and had provided no evidence that in using and tracking the Toujeo Coach programme the representative had not complied with the relevant requirements of the Code. No breach was ruled.

The Panel was concerned that Sanofi did not consider the email in question to be briefing material. In the Panel's view, the email was clearly giving guidance regarding how the manager would like the representatives to conduct promotional activity for Toujeo and encouraging them to adopt such practices. The Panel considered that the failure to recognise that the email in question was briefing material and required certification raised concerns about the company's governance of such matters and meant that Sanofi had not maintained high standards. A breach was ruled accordingly.

The Panel noted that a breach of Clause 2 was a sign of particular censure and should be reserved for such use. The Panel did not consider that in the particular circumstances of this case Sanofi had brought discredit upon or reduced confidence in the pharmaceutical industry and ruled no breach of Clause 2.

An anonymous, non-contactable complainant who described themselves as a Sanofi employee complained about a manager's briefing with regard to the promotion of Lantus (insulin glargine 100

units/mL) and Toujeo (insulin glargine 300 units/mL). Both medicines were used in diabetes mellitus.

COMPLAINT

The complainant provided a copy of an email sent from a manager to his/her team of representatives in March 2018. The email chain including a regional head who endorsed the email. The complainant alleged that Sanofi acknowledged the manager's success but turned a blind eye as to how it was achieved, as his/her Toujeo market share was significantly higher since the initial promotion of Toujeo compared with other colleagues.

The complainant alleged that the manager actively encouraged representatives to have detailed discussions around patients with health professionals thereby resulting in audits and identification of patient groups. This was documented as best practice and included:

- 1 Patients to be identified and started on Toujeo via other ways and means of the agreed set policy in place (Rationale for Initiation, Continuation and Discontinuation (RICaD)).
- 2 Several mentions of adverse reactions with Lantus.
- 3 Discussions around off-licence, twice daily Lantus.
- 4 The Toujeo coach service for patients was being used and tracked by the representative.

When writing to Sanofi, the Authority asked it to bear in mind the requirements of Clauses 2, 3.2, 9.1, 15.2 and 15.9 of the Code.

RESPONSE

Sanofi submitted that it took its obligation under the Code very seriously and was concerned to receive such a complaint which appeared to originate from a member of staff. Sanofi submitted that it had conducted a comprehensive internal investigation, which included interviewing relevant staff. A review with the human resources department was also performed. Sanofi believed that there were three elements to this case: (1) the cultural aspects within Sanofi regarding compliance reporting and investigating (2) the intent behind the email and (3) the perception of inappropriate information contained within the email.

Culture

Sanofi stated that it had a very open culture with a robust process in place that encouraged reporting and dialogue around any compliance concerns, wherever these occurred within the business. This provided a number of opportunities for anyone to raise concerns about compliance, either with their own manager or senior leader(s), any other senior leader in the organisation or with the compliance team directly. Sanofi treated all concerns seriously and confidentially, and took appropriate action, regardless of the status of the person(s) involved or commercial/company objectives.

With respect to the complainant's concerns about named employees, the investigation had not identified any concerns over their conduct, management skills or compliance with the Code.

Intent behind the email

Sanofi provided details of the named manager's role and territory and explained that he/she also managed a second territory. The email in question was sent to the team in the second territory on their request and summarised highlights of the first territory team's week.

The email was an initiative from the manager used to share the team's work to support teamwork and motivation. It was not intended to be directional or giving actions for the team to complete and so Sanofi did not believe this was a briefing that required certification; it confirmed that the email was not certified.

Information in the email

Sanofi stated that the information in the email was simply a summary of highlights of the week and examples of operationalising of the sales model of the diabetes team. It shared examples of discussions team members had had with health professionals once patients suitable for treatment with the products they promoted had been identified.

The sales force promotional materials were provided including the Toujeo and Lantus sales aids and accompanying briefings. In addition, the Toujeo sales aid included relevant information on 'Toujeo Coach'. The 2018 Diabetes Operational plan, which was provided, was presented to the field teams in January 2018 to provide structure on how it was to promote Toujeo and Lantus.

Sanofi stated that Lantus was not approved for use twice daily and was therefore not discussed proactively by representatives. However, Sanofi recognised that some health professionals made the decision to use Lantus twice daily and so this verbatim information from the health professionals was recorded in the email. This was not encouragement of twice daily use of Lantus. Representatives did not proactively raise the use of Lantus twice daily in their calls with health professionals but explored with them patients with unmet medical need who might benefit from treatment with Toujeo. If a health professional referred to twice daily Lantus use, the representative would understand that this indicated a patient who might require a high dose of Lantus or had difficulty with recurrent hypoglycaemia, both of which represented unmet medical need that might be addressed by Toujeo. A promotional discussion of the benefits of Toujeo could then be based on the value of the product in addressing those needs.

Sanofi explained that Toujeo Coach was a Sanofi patient support program that offered diabetes nurse specialist, psychologist and dietician coaching as well as support and access to educational resources and advice. It could be offered to a health professional or healthcare organisation once they

had decided to prescribe Toujeo. The sales team was briefed on how to share this offering as part of the Toujeo sales aid and accompanying briefing.

Sanofi explained that the agreed policy referred to was an NHS protocol that was external to Sanofi, which outlined the conditions that allowed initiation, continuation and discontinuation of the specific medicine to which it referred; it was provided by consultants to GPs with information to support their decision making. A copy was provided.

Sanofi submitted that it supported audits of diabetes care in the form of a programme provided as a medical and educational goods and services (MEGS) termed 'SDARs' – Sanofi Diabetes Analysis and Reporting Service. SDARs was a practice-based programme, delivered by a third-party provider, which identified sub-optimally controlled patients for review by practice staff. It was only introduced in brief by the sales team; if a health professional or healthcare organisation wanted more information on the service and subsequently used it, this was managed by Sanofi's NHS Outcome Managers (NOM) team in a non-promotional capacity and did not involve the sales teams (the representatives' briefing, the NOM briefing and the leavepiece for health professionals from NOM visit were provided). Sanofi noted that although some healthcare organisations in the region had had this MEGS support, none of the healthcare organisations referenced in the email in the complaint had received the service. The audits referred to in the complainant's email were all performed by the healthcare organisation directly and without Sanofi's involvement or support.

In conclusion Sanofi stated that based on its investigation it did not consider that the manager's or the senior manager's conduct had been inappropriate. Sanofi had found no evidence that any of its medicines had been promoted in a manner inconsistent with their marketing authorisations and it did not consider that any of the material provided or included in the email advocated any course of action which would breach the Code. Sanofi thus denied breaches of Clauses 2, 3.2, 9.1, 15.2 and 15.9.

Following a request for further information, Sanofi submitted that its pharmacovigilance department had no record of any adverse reaction reports or off label use reports that matched any of the detail in the email in question. Sanofi provided copies of training material for employees on reporting adverse reactions and events of special interest. Sanofi stated that personnel were trained during their onboarding and refresher training was conducted annually.

Sanofi submitted that a comment in the email by one of the representatives which stated 'track using enrolment data' referred to the representative checking whether there was an increase in the number of patients enrolled on to the Toujeo Coach programme in the locality. Sanofi explained that representatives received reports of the number of patients enrolled on to the Toujeo Coach programme at a clinical commissioning group (CCG) level.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable and therefore could not be contacted for further information. The Constitution and Procedure stated that anonymous complaints would be accepted but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities.

The Panel noted that Clause 15.9 of the Code required companies to prepare detailed briefing material for representatives on the technical aspects of each medicine which they would promote. Briefing material must comply with the relevant requirements of the Code and was subject to the certification requirements of Clause 14. The supplementary information to Clause 15.9 stated that the briefing material referred to in the Clause consisted of both the training material used to instruct representatives about a medicine and the instructions given to them as to how the product should be promoted.

The Panel noted the complainant's allegation that the manager was encouraging identification of patients for Toujeo outside of the agreed policy. The Panel noted Sanofi's submission that the agreed policy was an NHS protocol that was external to Sanofi and was provided by consultants to general practitioners. The Panel noted that two representatives made reference to the agreed policy being a barrier in certain circumstances. The Panel noted that Clause 3.2 of the Code required a medicine to be promoted in a manner that was not inconsistent with the particulars in its summary of product characteristics (SPC). The Code did not state that a medicine must be promoted within the terms of local, regional or national guidelines. However, the Code required information, claims and comparisons to be, *inter alia*, accurate, balanced, fair, based on an up-to-date evaluation of the evidence and not misleading either directly or by implication. The Panel did not consider that the complainant had provided any evidence which demonstrated that any of Sanofi's representatives had promoted Toujeo outside the terms of its marketing authorisation or that the email in question advocated such use and therefore no breach of Clauses 3.2, 15.2 and 15.9 were ruled on that point.

The Panel noted the complainant's statement that 'Several mentions of adverse reactions with Lantus' were documented in the email. It was not entirely clear from the complaint what he/she was alleging to be in breach of the Code in relation to adverse events. The complainant appeared to have made a general allegation but had not submitted any detailed reasons. The complainant was anonymous and could not be contacted for more information. The Panel noted that the email in question did refer to a Lantus patient experiencing recurrent hypoglycaemia. The Panel noted that it was of the utmost importance that such information about side-effects was processed by the company in accordance with, *inter alia*, the Code. However, the Panel noted that it was not for the Panel to infer detailed

reasons to support the allegation on behalf of the complainant. It was for the complainant to establish his/her case on the balance of probabilities. The Panel considered that the very general nature of the allegation was such that the complainant had not discharged his/her burden of proof and the subject matter of the allegation was unclear. The Panel on this narrow ground ruled no breach of Clauses 15.2, 15.9 and 9.1. The Panel consequently ruled no breach of Clause 2.

The Panel noted the complainant's allegation that the email documented discussions around off-licence twice daily use of Lantus. The Panel noted that the email highlighted the field activities of five named representatives in a given territory and was provided to representatives from another territory as an example of the types of Toujeo discussions that the first territory was having with health professionals. The Panel noted Sanofi's submission that the intent was to share personal highlights to support teamwork and motivation and it was not intended to be directional. The Panel noted Sanofi's submission that the manager in question was currently managing the representatives from both territories. The Panel noted the manager's comment in the email provided to the second territory which stated 'It is abundantly clear that they ... are all having detailed conversations with HCPs and that this is translating to new patients for Toujeo'. In the Panel's view, the manager's email encouraged the second territory to learn from and adopt the activities of the first territory in terms of engagement with health professionals for the promotion of Toujeo. The Panel considered that the information therefore constituted briefing material.

The email in question mentioned conversations that three representatives had had with health professionals regarding patients on twice-daily Lantus who subsequently switched to Toujeo. The Panel noted Sanofi's submission that the references to twice-daily Lantus was not in any way directional in terms of how the product should be promoted. The Panel noted that Clause 15.9 stated that briefing material must not advocate either directly or indirectly any course of action which would be likely to lead to a breach of the Code. The Panel further noted that slides from the Operational Plan and Segmentation Workshop held in 2018 referred to a segment of customers described as 'Comfortable with patients having to take BD [twice-daily] Lantus as part of their basal bolus regime' and that such customers needed to 'See benefit of switching to Toujeo from Lantus in T1D [type 1 diabetes] and T2D [type 2 diabetes]'.

In the Panel's view the references to twice-daily use of Lantus in the email in question, without any qualification that such use was off-label and should not be proactively discussed, could encourage representatives, within the context of promoting Toujeo, to initiate discussions about twice-daily Lantus use, which was not within Lantus' licence, and a breach of Clause 15.9 was ruled. The Panel considered that the complainant had not provided evidence to demonstrate that on the balance of probabilities representatives went on to promote

Lantus to health professionals in such a manner that was inconsistent with its SPC and ruled no breach of Clauses 3.2 and 15.2.

The Panel noted the complainant's allegation that the patient support programme, Toujeo Coach, was being 'used and tracked by the representative'. The Panel noted Sanofi's submission that Toujeo Coach was a Sanofi patient support programme that offered diabetes nurse specialist, psychologist and dietician coaching as well as support and access to educational resource and advice. According to Sanofi, it would be offered to a health professional or healthcare organisation once they had made the decision to prescribe Toujeo. The Panel noted that as above it was not clear why the complainant considered that reference to the Toujeo Coach service, in particular that it was being used and tracked by a representative, was in breach of the Code. The Panel noted Sanofi's submission that the sales team were briefed on how to share the Toujeo Coach service as part of the Toujeo sales aid and accompanying briefing. The Panel noted Sanofi's submission that the representatives received reports of the number of patients enrolled on the Toujeo Coach programme at a CCG level. The complainant bore the burden of proof and had provided no evidence that in using and tracking the Toujeo Coach programme the representative had not complied with the relevant requirements of the Code. No breach of Clause 15.2 was ruled.

The Panel noted Sanofi's submission that the email was not intended to be directional or to give actions for the team to complete and therefore Sanofi did not consider it to be briefing material that required certification. The Panel noted its comments and rulings above on this point. The Panel was concerned that Sanofi did not consider the email in question to be briefing material. The email was provided by a manager to a group of representatives to demonstrate how the activities of another group of representatives had translated into 'new patients for Toujeo'. In the Panel's view, the email was clearly

giving guidance regarding how the manager would like the representatives to conduct promotional activity for Toujeo and encouraging them to adopt such practices. The Panel considered that the failure to recognise that the email in question was briefing material and required certification raised concerns about the company's governance of such matters and meant that Sanofi had not maintained high standards. A breach of Clause 9.1 was ruled accordingly.

The Panel noted that a breach of Clause 2 was a sign of particular censure and should be reserved for such use. The Panel did not consider that in the particular circumstances of this case Sanofi had brought discredit upon or reduced confidence in the pharmaceutical industry and ruled no breach of Clause 2.

During the consideration of this Case, the Panel noted that the email in question referred to an adverse reaction in one patient and off-label use of Lantus in specific patients. The Panel noted Sanofi's submission that its pharmacovigilance department had no record of relevant reports. Both Sanofi's onboarding and annual pharmacovigilance training materials stated that employees must report such matters. The Panel was extremely concerned to note that the adverse event and reports of off-label use with Lantus had not been reported to its pharmacovigilance department. Given the email's circulation the Panel was extremely concerned that no-one had reported the events. The Panel asked that Sanofi be made aware of its concerns in this regard and considered it would be helpful if Sanofi reviewed its activities in this area to ensure that all such matters were reported in accordance with company procedures, the Code and relevant legislation.

Complaint received	16 March 2018
Case completed	19 December 2018

EX-EMPLOYEE v ABBVIE

Promotion of a poster and use of case studies

A contactable, ex-employee complained about the production of a poster by AbbVie and the use of case studies. The poster in question related to Synagis (palivizumab) which was indicated for the prevention of serious lower respiratory tract disease requiring hospitalisation caused by respiratory syncytial virus (RSV) in children at high risk for RSV disease. The complainant had previously complained to AbbVie about the matter.

The complainant explained that the national team was tasked with finding a trust that would participate in the Embrace Stars poster submission. The complainant joked with his/her line manager that the only way he/she would be able to achieve this after only a few months on territory would be to write a poster him/herself on behalf of a trust; he/she was shocked when the manager agreed. The manager's only concern was that the ideas suggested could not be 'too commercially written' but otherwise the manager fully agreed with the project and suggested multiple edits. The complainant stated that he/she made it very clear he/she would never write a poster on behalf of registered clinical nurses again; it was uncomfortable and stressful.

The complainant explained that the submission was forwarded to the nurses to approve and then forwarded to the agency. At one point the nurses told the agency that they did not recognise the work.

Eventually the poster was published and showcased around the country; ironically it was judged as 'outstanding' by the steering committee of nurse specialists. The complainant considered that they would be disappointed if they knew that the poster was written by the company that funded the process. To make matters worse, the statement 'This poster has been reviewed for compliance purposes by AbbVie with no influence on the content/opinions being presented' was printed on the bottom of the poster. This was not so. The poster was falsely portrayed as being written by health professionals and was written in such a way as to encourage health professionals to increase clinical capacity by up to 40%. It was wholly unethical. The conduct of the complainant's manager to support such an activity was detrimental to AbbVie's global reputation. This action and conduct brought shame upon, and reduced confidence in, not only AbbVie, but the whole industry.

The complainant added that team members were asked to present case studies at regional Embrace meetings. These case studies had not been put through the approval process and many in the team were extremely uncomfortable with the request

as the case studies have been presented by health professionals or by AbbVie's medical team.

The complainant noted that AbbVie partially upheld his/her complaint about the compliance issue and stated that it would take corrective action. The complainant considered that AbbVie had failed to properly investigate the poster submission; it had concluded that there was no breach of compliance. The complainant suggested motives behind the company's poor attempt at an investigation and also noted that the company had not referred to any contact with its communications agency to confirm or deny the suggestion that the nurses did not recognise the work – which would confirm that AbbVie was heavily involved in the writing of the health professional poster.

The complainant noted that AbbVie had partially upheld his/her complaint, however, he/she disputed this as he/she considered that AbbVie had failed to self-report this breach as required. AbbVie had stated in its response that the claim of account managers presenting the case studies was unsubstantiated, however, the complainant stated that he/she had a photograph that was posted by his/her manager to a WhatsApp group, of a named account manager presenting the said case studies; this clearly substantiated the original grievance which demonstrated that AbbVie was clearly misleading in its response 'unsubstantiated'. Either AbbVie never investigated or deliberately tried to withhold information.

The complainant listed some of the issues he/she had experienced with the internal complaints system and details were provided.

Subsequent to receipt of the complaint, the complainant provided additional evidence, a copy of a draft poster with track changes and comments which was provided to AbbVie.

The detailed response from AbbVie is given below.

The Panel noted that Case AUTH/2997/12/17 and Case AUTH/3028/3/18 contained similar allegations with regard to a named AbbVie representative presenting clinical case studies which had not been certified at a meeting in September 2017. In Case AUTH/2997/12/17, the Panel ruled a breach of the Code as a Pathways document which consisted of three different scenarios (case studies), which were discussed in a session facilitated by an AbbVie representative, had not been certified, as acknowledged by AbbVie. The Panel noted that the complainant bore the burden of proof and considered that there was no evidence to show that in facilitating a discussion on the three scenarios within the Pathways document, the representative

in question, or the company, had failed to maintain high standards on this narrow point. No breach of the Code was ruled. The Panel noted that it was not necessarily unacceptable under the Code for a representative to present case studies, as alleged, provided that the manner in which it was done complied with the Code.

Turning to the current case, Case AUTH/3028/3/18, the Panel noted the complainant's allegations regarding non-medical employees presenting uncertified case studies at regional Embrace meetings. The Panel noted that the complainant had referred broadly to all regional Embrace meetings and had only subsequently referred to the meeting at issue in Case AUTH/2997/12/17 as an example of a relevant meeting when commenting on AbbVie's findings during his/her grievance proceedings. The Panel considered that the rulings in Case AUTH/2997/12/17 set out above were relevant. The Panel similarly ruled a breach of the Code in the present case in relation to AbbVie's failure to certify the Pathways document (case studies) and no breach of the Code as the complainant in this case had not established that it was inappropriate for promotional staff to present case studies at promotional meetings as alleged.

The Panel noted that a further allegation in this case, Case AUTH/3028/3/18, concerned AbbVie's involvement in the production of an Embrace Stars poster and its failure to accurately declare such involvement. The poster at issue included the statement 'This poster has been reviewed for compliance purposes by AbbVie with no influence on the content/opinions being presented'. The Panel noted that the entry pack for the submission of the posters stated that the programme was organised and funded by AbbVie and would be certified as promotional material given that the posters were intended for display at a series of promotional educational meetings. It also stated that AbbVie would have ownership of the posters created and would use the material promotionally subject to approval for the wider sharing of best practice in the field of RSV prevention. The entry pack stated that AbbVie would provide support in developing posters through a communications agency. In the Panel's view, AbbVie's role went beyond reviewing for compliance purposes as stated on the poster. The role of its communications agency, whilst made clear to the participants at the outset and not necessarily unacceptable, went beyond matters of compliance and as shown by the track change comments on the completed template, at the very least influenced the content of the poster. In addition, the Panel noted that the initial completed template submitted for the poster in question stated within the methodology section 'working in conjunction with [named AbbVie representative] a simple spreadsheet was formulated to identify babies all year round ...'. In the Panel's view, this supported the complainant's assertion and it appeared that the named AbbVie representative was involved in the project that was the subject of the poster. The Panel was concerned to note that the reference to the representative's involvement did not appear on the published poster.

The Panel noted that whilst AbbVie's involvement might have been clear to those submitting posters, the Panel did not consider that the declaration 'This poster has been reviewed for compliance purposes by AbbVie with no influence on the content/opinions being presented' accurately reflected AbbVie's involvement to readers. In addition, the Panel considered that the prominence of the health professional authors' names and pictures of the hospital compounded the misleading impression given by the declaration and a breach was ruled.

The Panel noted its comments above in relation to the failure of AbbVie to accurately reflect its involvement in the production of the poster. High standards had not been maintained and a breach was ruled.

The Panel had some concerns about email communications between AbbVie staff and its communications agency and between the communications agency and the nurses said to be the authors of the poster, as well as concerns regarding AbbVie employees' involvement with regards to the Embrace Stars poster at issue. The Panel noted that the Code did not preclude the involvement of representatives in the creation of promotional material but companies should exercise caution in this regard. The Panel noted its rulings of breaches of the Code including its concerns about the role of the AbbVie representative. However, based on the narrow allegation, the Panel did not consider that the complainant had provided evidence to show that, on the balance of probabilities, the representative's role, and/or influence, was such that it could be stated that the representative had created the poster or that it was created at the express request of his/her manager and that the representative had not applied high standards in this regard. Based on the narrow allegation, the Panel ruled no breach of the Code.

Upon appeal by the complainant the Appeal Board considered that there was evidence to show that the complainant, the nurse(s) and AbbVie and its agency were involved with the production of the poster. In that regard the Appeal Board noted the Panel's ruling of a breach of the Code in relation to AbbVie's declaration of its involvement in the production of the poster. The Appeal Board considered that on the information available it did not have sufficient evidence to show on the balance of probabilities that the complainant had created the poster *de novo* at the direction of his/her manager, as alleged. Consequently, on the narrow allegation, the Appeal Board considered that there was no evidence that the representative had not applied high standards in this regard. The Appeal Board upheld the Panel's ruling of no breach of the Code. The appeal on this point was unsuccessful.

The Panel noted its comments and rulings above and did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was as a sign of particular censure and reserved for such use. No breach of Clause 2 was ruled which was upheld on appeal.

A contactable, ex-employee complained about the production of a poster by AbbVie Limited and the use of case studies. The poster in question related to Synagis (palivizumab) which was indicated for the prevention of serious lower respiratory tract disease requiring hospitalisation caused by respiratory syncytial virus (RSV) in children at high risk for RSV disease.

COMPLAINT

The complainant stated that in December 2017 he/she formally complained to AbbVie about an issue with which he/she had been very uncomfortable about for some time; it took a lot of soul searching to even bring the matter to the company's attention as it was so detrimental to its reputation.

The complainant explained that the national team was tasked with finding a trust that would participate in the Embrace Stars poster submission. Under immense pressure, the complainant joked with his/her line manager that the only way he/she would be able to achieve this after only a few months on territory would be to write a poster him/herself on behalf of a trust; he/she was shocked when the manager agreed and suggested topics for the poster and scheduled time to discuss the matter further. During this discussion, the manager's only concern was that the ideas suggested could not be 'too commercially written' but otherwise he/she fully agreed with the project and suggested multiple edits. The complainant stated that he/she made it very clear he/she would never do anything like that ever again; it was uncomfortable and stressful being involved in the writing of a poster on behalf of registered clinical nurses.

The complainant explained that the submission was forwarded to the nurses to approve and then forwarded to a communications agency. At one point the nurses told the agency that they did not recognise the work. This was extremely stressful to manage and there were multiple discussions with the nurses to ask them to agree to the content of the poster.

Eventually the poster was published and showcased around the country; ironically it won many votes and finally came a very close second to the winning poster which was judged by the steering committee of elite clinical reference group (CRG) and clinical nurse specialists. The complainant considered that the steering committee would be disappointed if it knew that it had judged a poster as outstanding that was written by the company that funded the process. To make matters worse, the statement 'This poster has been reviewed for compliance purposes by AbbVie with no influence on the content/opinions being presented' was printed on the bottom of the poster. This was not so, the poster made a mockery of the Embrace Stars format, as it was falsely portrayed as being written by health professionals and was written in such a way as to encourage health professionals to increase clinical capacity by up to 40%. It was wholly unethical. The conduct of the business unit manager to allow such insidious behaviour to go on, let alone support it and suggest edits, was reckless and detrimental to AbbVie's

global reputation. This action and conduct brought shame upon, and reduced confidence in, not only AbbVie, but the whole industry in breach of Clauses 9 and 2. Furthermore, it was common knowledge within the team and marketing that AbbVie wrote this poster on behalf of a trust.

The complainant added that team members were asked to present case studies at regional Embrace meetings. These case studies had not been put through the Zinc process and many in the team were extremely uncomfortable with the request as they should have been presented, at best, by health professionals or alternatively by AbbVie's medical team.

The complainant noted that AbbVie only partially upheld his/her complaint about the compliance issue and stated that it would take corrective action.

The complainant considered that AbbVie had failed to properly investigate the poster submission; it had concluded that there was no breach of compliance. The complainant confirmed that the poster was written by AbbVie and suggested that the company's poor attempt at an investigation proved, beyond doubt, that it was attempting to deflect as it had failed to mention or comment on whether it had contacted the nurses to confirm or deny. The complainant submitted that the nurses would confirm his/her version of events. The complainant also noted that the company had not referred to any contact with the communications agency to confirm or deny the suggestion that the nurses did not recognise the work – again, this would only confirm that AbbVie was heavily involved in the writing of the health professional poster. Further, the complainant noted that he/she had a document (copy provided) sent to him/her by AbbVie as part of a subject access request, albeit late and incomplete, a document that suggested changes/edits to the poster and comments from the manager as follows:

'could we elaborate on "time of eligibility"
'we will add in figures here once obtained firm figures requested above'
'we haven't really explained the changes in the service here'.

The complainant submitted that AbbVie's submission that it was not clear that the manager had directed or sanctioned guidance was ludicrous based on that one document alone. The manager, who held a very senior position within AbbVie, knew about the poster submission being written by AbbVie on behalf of the nurses and the complainant stated that he/she would stand in a court of law under oath to confirm this.

The complainant noted that AbbVie had partially upheld his/her complaint, however, he/she disputed this as he/she considered that AbbVie had failed to self-report this breach as required. AbbVie had stated in its response that the claim of account managers presenting the case studies was unsubstantiated, however, the complainant stated that he/she had a photograph that was posted by his/her line manager to a WhatsApp group, of an account manager presenting the said case studies with the caption '[account manager]

in action' (the time and date were provided); this evidence substantiated the original grievance which demonstrated that AbbVie was clearly misleading in its response 'unsubstantiated'. Either AbbVie never investigated or deliberately tried to withhold information.

The complainant explained some of the issues he/she had experienced with the internal complaints system and details including the outcome were provided.

The grievance complaint contained an allegation that medical case studies were used that were not Zinc certificated. Corrective action would be put in place to ensure that this did not happen again.

Outcome: Upheld in part. The action recommended to the business was to take corrective action to ensure that medical case studies were Zinc certificated.

The complainant did not feel that AbbVie had taken these very serious allegations seriously and that they needed to be fully investigated.

The complainant stated that he/she was prepared to be as cooperative as required and wished to remain an anonymous but contactable. As part of a subject access request, AbbVie provided him/her with the track changes document in relation to the poster submission, the complainant was happy to provide this if required.

Subsequent to receipt of the complaint, the complainant provided additional evidence, a copy of a draft poster with track changes and comments which was provided to AbbVie.

When writing to AbbVie, the Authority asked it to bear in mind the requirements of Clauses 2, 9.1, 9.10, 14.1 and 15.2.

RESPONSE

AbbVie submitted that the facts of this complaint were very similar to a complaint made by an anonymous health professional in December 2017 (Case AUTH/2997/12/17: Promotion of Synagis). AbbVie had responded in detail to that complaint and for completeness, a copy of that response was provided and would be referred to as the 'related complaint'. AbbVie noted that there was significant repetition in relation to the 'case studies' which it addressed below.

AbbVie believed that the complainant in both cases was the same person and the reasons for this were initially explained in the response to Case AUTH/2997/12/17. AbbVie noted that it had sought to clarify the complainant's interest, direct or indirect, in Case AUTH/2997/12/17 or in AbbVie but he/she had not responded to the Authority's request in that regard. This was a material consideration for the Panel in both cases and supported the position that the complainant was the same individual in both cases.

AbbVie stated that its response to Case AUTH/2997/12/17 it had addressed the case studies in detail which were the secondary focus of this complaint. In that response, AbbVie recognised that the case studies document (which it believed was the subject of Case AUTH/2997/12/17) was not certified. As explained, the document was not intended to promote Synagis, although it was used in the context of a promotional meeting. AbbVie submitted, therefore, that it had already taken appropriate remedial action about this element of the current complaint and it referred to its submission in Case AUTH/2997/12/17.

AbbVie stated that for the reasons set out below, it did not believe there was sufficient evidence to enable the complainant to discharge the burden of proof on the balance of probabilities.

AbbVie noted that the complainant was a 'contactable ex-employee' who had brought a series of internal grievances, largely about employment matters, in accordance with AbbVie's grievance process. AbbVie acknowledged that in order to maintain high standards, it was critical that individuals (whether employees or not) had the right to complain to the PMCPA.

The purpose of submitting posters to the Embrace Stars programme was to recognise best practice in the field of respiratory syncytial virus (RSV) protection, improvement in the RSV service for infants and their families and support best practice in the NHS. The submission process was intended to generate a poster (the content of which was non-promotional) by nurses involved in RSV prevention. AbbVie considered that the opportunity to author and display a poster would be a useful educational opportunity for nurses since this was not part of their normal practice. It was not intended that the poster would promote Synagis, although it was clear from the outset that it would be used in the context of a promotional meeting and reviewed for compliance.

All representatives were provided with a briefing pack or 'Meeting Alignment Toolkit' for the purpose of the Mini Embrace meeting series (copy provided). This material provided guidance to the team on the need to comply with the Code. While the guidance focussed on the meeting preparation, it also referred to the 'Embrace Stars' concept. This reinforced the aims of the project.

A member of the Synagis marketing team briefed the representatives about the programme and entry pack in late April 2017. The role of the representatives was to identify potential applicants to enter an idea for a poster and support the development of the posters (and the application form) in the entry pack. Successful posters would be displayed at the 'Mini Embrace' meeting series and on an AbbVie website for health professionals.

The Entry Pack for the submission of posters (copy provided) stated that the programme was 'Organised & Funded' by AbbVie and would be certified as promotional material given that the posters were intended for display at a series of promotional

educational meetings. It also stated on page two that 'AbbVie will have ownership of the posters created and will use the material promotionally (subject to approval) for the wider sharing of best practice in the field of RSV prevention'.

The Entry Pack also stated that 'AbbVie will provide support in developing posters through ... communications' agency and so AbbVie's involvement was transparent from the outset. All participants therefore knew that the posters they submitted would be used for promotional purposes. The process was managed primarily by AbbVie's communications agency, in conjunction with AbbVie.

The Entry Pack contained some examples of what an entry could cover and the assessment criteria – these were non-promotional. For example, 'Your entry could be a well-developed service delivery programme, on line training or be related to commissioning'.

Entries were judged by an independent steering committee of four health professionals. In January 2017, the steering committee for the Embrace 2017 Meeting series met to discuss the educational needs to be addressed in the meeting series and agreed to judge the Embrace Stars 2017 posters with objective assessment criteria that were also set out in the Entry Pack. It was proposed at that meeting that recognition for Embrace Stars 'could be an advertorial in a journal publication or editorial of their choice'. In particular, this would be for the best practice poster only and would be an AbbVie advertisement which contained an extract of the poster.

AbbVie received five poster applications which were all considered, by default, to be finalists. The posters were sent by the communications agency directly to the steering committee in early September 2017 for it to select a winner. The posters were not blinded as there was no conflict of interest with the steering committee. The authors of the poster, that was deemed to represent the best practice and to meet the assessment criteria, were notified in October. AbbVie noted that the best practice poster was not the one subject of the complaint.

The focus of the complaint initially suggested that AbbVie (the complainant) prepared the poster and that AbbVie was heavily involved in its preparation. AbbVie stated that it would address this further below although it noted that the complainant did not clearly articulate which of these two scenarios he/she was complaining about. AbbVie stated that it had tried to address both but there was insufficient evidence to draw any conclusions.

AbbVie noted that the complainant suggested that he/she wrote the subject poster application and then sent it to the nurses to approve. There was insufficient evidence to confirm the allegations based on discussions with the relevant business unit manager, the communications agency and the complainant's colleagues. AbbVie had also reviewed documents still in its possession which included documents that were retrieved during the grievance process, and collected in response to the

complainant's subject access request (referred to by the complaint above) which had been kept on file. However, the evidence did not show that the complainant was asked to prepare a poster for the nurses as alleged.

The key chronology appeared to be as follows:

- 26 May 2017 – The complainant sent his/her manager an email which attached an Embrace Stars Entry Pack for 2017. The complainant stated in the email, 'Sneak peak of [named trust] poster, feel free to suggest amendments I am seeing [nurse] next week to finalise'. There was no response to this email and the manager was not sure why the document was sent to him/her as opposed to the communications agency or a named AbbVie employee.
- June – At the bottom of an email chain (copy provided) was an email from a nurse from the named trust to the complainant which stated, 'Here is our poster'. AbbVie noted that there was no date on this email. The original email could not be located on AbbVie's system because the complainant had left the company and so the email had been deleted in accordance with the company's standard email retention procedure.
- 7 June – A second version of the email chain referred to above showed that the complainant sent what appeared to be the communications agency application to a named AbbVie employee who sent it to the communications agency.

In all of the five examples of poster review, the representatives were involved as a 'go between' to facilitate poster production. AbbVie noted that four out of the five poster submissions were made by nurses via representatives to the communications agency.

- 12 June – The next email (copy provided) was from AbbVie's communication agency to a named AbbVie employee. The attachment was a copy of the poster submitted from the NHS trust which included text mark up and comments from the communications agency. This was the same document that the complainant submitted to the PMCPA and was subsequently provided to AbbVie by the Authority.

The communication agency engaged medical writers and all the posters that were submitted required medical writing support. Initial questions following the medical writer review were communicated to authors via AbbVie or the named AbbVie employee. This ranged from clarifying information and requesting further details to requesting photographs and images for the poster.

- 12 June – A further email which the named AbbVie employee sent to the complainant's manager who sent the comments from the communications agency to the complainant, and complimented him/her for ensuring that his/her sales territory (which included the NHS trust) had already prepared a poster. This email clearly stated that

the agency comments were to 'strengthen the information', not to influence the content. This was an important distinction. The comments from the complainant's manager were directed at the nurses to improve the accuracy of the poster, not the complainant.

- 16 June – An email from a different AbbVie representative to the complainant explained that the word count had been checked and additional information had been included. The representative recalled that the complainant wanted help, mainly with grammatical issues and a 'sense check' of the NHS trust's application pack.
- 27 June – The complainant sent the named AbbVie employee the trusts poster.
- 27 July – The poster was sent from the communications agency back to Abbvie. This contained the graphics and artwork that the communications agency had added.
- 31 July – The communications agency sent the fully art worked poster to the nurses and an email showed that they sought confirmation from the nurses. There was no reply to this email and so the communications agency emailed the nurses again on 7 August as a reminder and asked for a photograph of the nurses and the hospital to be included in the final poster. AbbVie understood that no final written approval was sent by the nurses to the communications agency and verbal approval was received through the complainant.
- By 4 September – All posters certified (including the poster at issue) before being sent to the steering committee. A copy of the final version of the poster and certificate was provided.
- From 8 September – All posters were displayed at Mini Embrace meetings.

AbbVie noted that the two nurses who submitted a poster then presented at the complainant's 'Mini Embrace' meeting in September 2017. The agenda for this meeting was provided. All five posters were displayed at this meeting and none of the nurses expressed any concern about their poster or suggested that they had not written it. The complainant stated that 'the nurses at one point responded to [the communications agency] saying they did not recognise the work, this was extremely stressful to manage and I had to have multiple discussions with the nurses to ask them to agree to the contents for the submission'. There was no evidence of this and as referred to above, no nurses from the trust raised any concern with AbbVie or the communications agency about this.

The alternative reading of the complaint was the allegation that AbbVie inappropriately influenced the content or opinions expressed in the poster. There was insufficient evidence to support that. AbbVie acknowledged, however, that the complainant might have helped the nurses to prepare their application form, modifying it and helping them through the process. Comments from the communications

agency were then provided to correct factual inaccuracies, tighten drafting and request that certain other information be added, for example, references to the Joint Committee on Vaccination and Immunisation (JCVI) Guidelines. A comparison with the final version of the poster at issue showed that some comments were included, but not all. AbbVie noted the final version of the poster was certified given that it was intended to be displayed at a promotional educational meeting.

Contrary to the allegations, AbbVie was clear that all posters were to be owned by the company and it would use the material for promotional purposes. As such, the company was obliged to ensure that the information was accurate and balanced and reviewed for compliance with the Code. The original substance of the poster submitted by the nurses was retained.

The complainant particularly noted the statement on the bottom of the final version of the poster 'This poster has been reviewed for compliance purposes by AbbVie with no influence on the content/opinions being presented'. As set out above, AbbVie had to review the posters (as did the communications agency) but the evidence supported that no substantive changes were made to the content or opinion. Abbvie also knew that the events articulated in the poster were true.

AbbVie accepted that the disclaimer statement on the final poster could have been clearer so that it was stated 'with no influence on the opinions being presented'. However, this did not alter the fact that the content did not change substantively and AbbVie's involvement in the organisation and funding of the project (and its plans for the subsequent use of the posters) was transparent.

In view of the above, and based on its review of the available information, AbbVie stated that it did not have sufficient evidence to confirm an allegation that the poster was actually prepared by the complainant. In relation to allegations about the role of others within AbbVie, there was a differing version of events and the conduct as alleged by the complainant was not recognised. As stated above, the complainant no longer worked for AbbVie.

AbbVie denied any breach of the Code.

With regard to case studies, AbbVie reiterated that they formed part of Case AUTH/2997/12/17 and the background on the case studies (or 'scenarios') as set out in its response to Case AUTH/2997/12/17.

AbbVie noted that the complaint focussed on the fact that a representative presented the case studies. This was not factually accurate. The purpose of the scenarios was explained in the response to Case AUTH/2997/12/17. This was an AbbVie facilitated session and during the session the attendees were divided by tables; every table had to discuss the scenarios, ask questions and then each health professional would provide feedback. The scenarios were printed and left on tables during the session for discussion and were not formally presented

by a speaker. However, an AbbVie representative facilitated the workshop which was why there was a photograph of a representative speaking at the front of the meeting on 15 September 2017.

AbbVie stated that, in its view, there had been no breach of Clauses 15.2 and 15.9.

In conclusion, and for the reasons outlined above, AbbVie did not believe, based on the evidence provided, that there was a case to answer.

AbbVie specifically asked that the complainant was not provided with a copy of its response; the material was confidential by its nature.

In response to a request for further information, AbbVie stated that there was no additional information that it wished to submit in relation to the allegations, save for three points in response to the Authority's specific questions, namely:

- 1 AbbVie enclosed further email communications between the communications agency and the NHS trust. These emails were provided to AbbVie by the communications agency as the majority of them were not in AbbVie's possession given that AbbVie employees were not included in the recipients. Some of the emails were included with AbbVie's initial response.
- 2 AbbVie confirmed that the comments made on the poster at issue were made by an agency employee.
- 3 AbbVie confirmed that all 5 Embrace Stars posters were displayed at the Mini Embrace meeting in September 2017.

PANEL RULING

The Panel noted that Case AUTH/2997/12/17 and Case AUTH/3028/3/18 contained similar allegations with regard to a named AbbVie representative presenting clinical case studies which had not been certified at a meeting in September 2017. In Case AUTH/2997/12/17, the Panel ruled a breach of Clause 14.1 as a pathways document which consisted of three different scenarios (case studies) which were discussed in a session facilitated by a named AbbVie representative had not been certified, as acknowledged by AbbVie. The Panel noted that the complainant bore the burden of proof and considered that there was no evidence to show that in facilitating a discussion on the three scenarios within the pathways document, the representative in question, or the company, had failed to maintain high standards on this narrow point. No breach of Clause 15.2 was ruled. The Panel noted that it was **not necessarily unacceptable** under the Code for a representative to present case studies, as alleged, provided that the manner in which it was done complied with the Code.

Turning to the current case, Case AUTH/3028/3/18, the Panel noted the complainant's allegations regarding non-medical employees presenting uncertified case studies at regional Embrace meetings. The Panel noted that the complainant had

referred broadly to all regional Embrace meetings and had only subsequently referred to the meeting at issue in Case AUTH/2997/12/17 as an example of a relevant meeting when commenting on AbbVie's findings during his/her grievance proceedings. The Panel considered that the rulings in Case AUTH/2997/12/17 set out above were relevant. The Panel similarly ruled a breach of Clause 14.1 in the present case in relation to AbbVie's failure to certify the pathways document (case studies) and no breach of Clause 15.2 as the complainant in this case had not established that it was inappropriate for promotional staff to present case studies at promotional meetings as alleged. The Panel noted that as in the previous case, Case AUTH/2997/12/17, Clause 15.9 had been raised by the case preparation manager in this case. Clause 15.9 required that companies must prepare detailed briefing material that must not advocate, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code and is subject to the certification requirements of Clause 14. In Case AUTH/2997/12/17 the Panel did not consider that there was an allegation in this regard and therefore made no ruling in relation to this matter. The Panel noted the position was the same in this case and thus made no ruling with regard to Clause 15.9.

The Panel noted that a further allegation in this case, Case AUTH/3028/3/18, concerned AbbVie's involvement in the production of an Embrace Stars poster and its failure to accurately declare such involvement. The poster at issue included the statement 'This poster has been reviewed for compliance purposes by AbbVie with no influence on the content/opinions being presented'. The Panel noted that the entry pack for the submission of the posters stated that the programme was organised and funded by AbbVie and would be certified as promotional material given that the posters were intended for display at a series of promotional educational meetings. It also stated that AbbVie would have ownership of the posters created and would use the material promotionally subject to approval for the wider sharing of best practice in the field of RSV prevention. The entry pack stated that AbbVie would provide support in developing posters through its communications agency. In the Panel's view, AbbVie's role went beyond reviewing for compliance purposes as stated on the poster. The role of its communications agency, whilst made clear to the participants at the outset and not necessarily unacceptable, went beyond matters of compliance and as shown by the track change comments on the completed template, at the very least influenced the content of the poster. In addition, the Panel noted that the initial completed template submitted for the poster in question stated within the methodology section 'working in conjunction with [named AbbVie representative] a simple spreadsheet was formulated to identify babies all year round ...'. In the Panel's view, this supported the complainant's assertion and it appeared that the named AbbVie representative was involved in the project that was the subject of the poster. The Panel was concerned to note that the reference to the representative's involvement did not appear on the published poster. The Panel noted that whilst AbbVie's involvement might have been clear to those submitting posters, the Panel

did not consider that the declaration 'This poster has been reviewed for compliance purposes by AbbVie with no influence on the content/opinions being presented' accurately reflected AbbVie's involvement to readers of the poster. In addition, the Panel considered that the prominence of the health professional authors' names and pictures of the hospital compounded the misleading impression given by the declaration and a breach of Clause 9.10 was ruled.

The Panel noted its comments above in relation to the failure of AbbVie to accurately reflect its involvement in the production of the poster. High standards had not been maintained and a breach of Clause 9.1 was ruled.

The Panel had some concerns about email communications between AbbVie staff, between AbbVie staff and its communications agency and between the communications agency and the nurses said to be the authors of the poster, as well as concerns regarding AbbVie employees' involvement with regards to the Embrace Stars poster at issue. The Panel noted that the Code did not preclude the involvement of representatives in the creation of promotional material; companies should exercise caution in this regard and such material had to comply with all of the requirements of the Code including certification. The Panel noted its ruling above in relation to Clause 9.10 including its concerns about the role of the AbbVie representative. However, based on the narrow allegation, the Panel did not consider that the complainant had provided evidence to show that, on the balance of probabilities, the representative's role, and/or influence, was such that it could be stated that the representative had created the poster or that it was created at the express request of his/her manager and that the representative had not applied high standards in this regard. Based on the narrow allegation, the Panel ruled no breach of Clause 15.2.

The Panel noted its comments and rulings above and did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was as a sign of particular censure and reserved for such use. No breach of Clause 2 was ruled. This ruling was appealed by the complainant.

APPEAL BY THE COMPLAINANT

The complainant appealed the Panel's rulings of no breach of Clause 15.2 in relation to the poster and Clause 2 in relation to the poster and the case studies.

The complainant was extremely disappointed by AbbVie's response to the complaint and even more shocked that it would use the opportunity to make a personal attack on his/her motives for the initial complaint. The complainant alleged that AbbVie had in place a written protocol for whistleblowing, however, it was prone to ignore these and be extremely bullish and intimidating towards any staff member who dared to raise issues. The complainant alleged that this was highlighted extremely clearly by its 'vehement' denial of any wrong doing, intentional or otherwise.

The complainant alleged that as AbbVie had considered that it was necessary to provide some 'background' information as to why he/she would even dare to approach the PMCPA with any alleged breach of Code he/she also took the opportunity to provide some 'background' information. The complainant alleged that his/her submission was even more relevant in the demonstration of AbbVie's disregard of rules and regulations. In addition to his/her complaint, the complainant also made an independent complaint to the Information Commissioners (ICO), following AbbVie's failure to acknowledge a serious breach of data protection. In the interest of transparency the complainant provided his/her response from the ICO in entirety. Details of the ICO findings were provided. AbbVie was, however, still denying that there was any wrongdoing.

The complainant understood that the burden of proof regarding an alleged breach of Code was on the complainant and that it was the responsibility of the complainant to provide evidence to support allegations made. With this in mind and following AbbVie's submission that strongly refuted that the Embrace Stars Poster was in fact written by the complainant and not the nurses in question, the complainant had contacted the customer in question to obtain written confirmation that this was in fact the case and therefore prove without any doubt that his/her allegation had always been true. The complainant alleged that he/she had always stated that he/she had written the poster and he/she had invited the nurses; the alleged authors, to confirm his/her version of events. AbbVie never took that opportunity and the complainant alleged that this was due to the fact that it already knew the truth, but it suited AbbVie to deny it.

The complainant provided an email from one of the nurses that was listed as an author of the Embrace Poster. The complainant alleged this was written confirmation that he/she, acting as an AbbVie representative, had been the author of the poster, despite the disclaimer that was printed on the bottom of the said poster.

The email included confirmation that the poster presentation regarding the success of the RSV clinics was contributed to by two nurses with the complainant and then was produced by the complainant.

The complainant alleged that he/she was baffled that AbbVie was able to find emails from June 2017 as when he/she was making his/her initial complaint, he/she had submitted a subject access request (SAR) and AbbVie confirmed in writing, that no emails were kept on its systems for longer than 30 days and were therefore unable to provide him/her with anything outside of that timeframe. Clearly those emails predated 30 days. Furthermore, by AbbVie's own admission the 'author' did not respond directly to the communications agency contact. The poster was therefore produced off his/her verbal confirmation alone. Surely for something as important as a final sense check of a poster that was to be showcased it would have been vital to get written confirmation from the author? The fact of the

matter was the complainant's manager knew exactly who wrote the poster and he/she suggested the edits the complainant should make, which the Panel had commented on. It was sheer nonsense for AbbVie to claim that these comments were directed at the nurses. If this had been the case the comments would have been sent directly to the nurses from the agency just copying the complainant in, as the representative. The reality was that the nurses never saw the suggested track changes or input into those changes.

The complainant hoped that he/she had provided enough information to show the appalling way in which AbbVie had tried to deflect from the truth. Not only had AbbVie blatantly lied but due to its digging in of heels and not being 'brave and courageous', which was one of their own core values, it had left the complainant with no alternative other than to contact one of its customers to provide the evidence of the truth.

The complainant noted that despite previously remaining anonymous to AbbVie, the complainant alleged that it had gone out of its way to indicate it knew who made the complaint and therefore saw no reason to continue to hide his/her identity. The complainant alleged that all he/she had ever hoped for was that AbbVie would accept that it acted incorrectly and to be able to prevent such a situation arising for other staff members in the future. As AbbVie had acted in such an arrogant manner and was insistent that it was completely innocent the complainant felt he/she had little alternative.

RESPONSE FROM ABBVIE

AbbVie strongly refuted the unfounded allegation made by the complainant in his/her Appeal that it had acted in a 'bullish and intimidating' manner towards whistle blowers. As previously explained, AbbVie had a well-established whistleblowing process in place, including an independent ethics and compliance helpline and a strong track record of dealing with such issues and with the PMCPA. Rather than taking advantage of AbbVie's whistleblowing processes during the summer of 2017, when the events that were the subject of the complaint took place, the complainant did not raise his/her alleged concerns until December 2017 in the context of a separate grievance process relating to various employment matters.

AbbVie submitted that it had previously expressed concerns as to the intentions behind this complaint. The concern about this complaint (and the two complaints that AbbVie believed to be related) were genuine, and it was not, as the complainant suggested, using the complaint as an 'opportunity to make a personal attack'. While AbbVie did not want to repeat these points at length, the appeal only added to AbbVie's view that the complainant was abusing the PMCPA complaints process as a forum to air his/her personal grievances and cause disruption to AbbVie's business.

AbbVie noted that the PMCPA Guidance on Appeal Procedures stated that 'An appeal must be accompanied by detailed reasons as to why the

ruling was not accepted (7.3) and which clauses are appealed'. Far from providing detailed reasons why the ruling was not accepted, a large portion of the appeal related to a wholly separate complaint made to the Information Commissioner's Office (ICO). This was irrelevant to the appeal.

AbbVie submitted that the parts of the appeal that did relate to the complaint were in part made up of subjective and unspecified criticisms of AbbVie's conduct in responding to the complaint and were difficult to address. In fact, there did not appear to be a valid appeal point, the complainant simply did not agree with the Panel's decision. The purported reasons had no bearing on whether AbbVie breached Clauses 2 or 15.2.

AbbVie submitted that with respect to the Panel's rulings of no breach of Clause 15.2, the appeal only referred to Clause 2. AbbVie was unclear how this element of the appeal could proceed without detailed reasons.

AbbVie submitted that the appeal made only one substantive point that was not already addressed in its response to the complaint the inclusion of an email that attempted to substantiate the complainant's claim that he/she was the author of the 'Embrace Star poster'. As set out below, AbbVie did not consider that this email provided any substantiation of the claim, but in any event, it was inappropriate for the complainant to attempt to adduce new evidence at this stage of the process. The Guidance on Appeal Procedures stated that 'It should be borne in mind that it must have been possible to substantiate a claim etc. on the day it was made'. The complainant was unable to substantiate his/her claim that he/she was the author of the poster at the time he/she made the original complaint, and it should be dismissed as it was in the Panel's original ruling.

AbbVie submitted that it continued to acknowledge the importance of the complaints and appeals procedure and understood that the Panel must take each complaint seriously, it was difficult to see, in light of the points above, how the complainant's appeal could succeed. It was disappointing that AbbVie would have to spend further time and resources preparing for the appeal hearing.

The ICO Complaint

AbbVie submitted that as noted above, the majority of the appeal related to a separate complaint the complainant made to the ICO. Since this ICO complaint had no bearing on the PMCPA complaint, AbbVie did not wish to respond to this part of the appeal in detail.

AbbVie submitted that the complainant had also mischaracterised its response to his/her subject access request. The ICO concluded that AbbVie had complied with its obligations in this regard. The complainant stated that he/she 'was completely baffled that AbbVie was able to find emails to provide to the PMCPA from June last year'. The complainant's first SAR was limited in time from 26 July 2016 to 19 December 2017. Emails from June

2017 were provided in response so AbbVie did not understand this comment. In response to the first SAR, all data relating to records of employees who had left AbbVie was permanently deleted. AbbVie was able to provide emails to the PMCPA following the review of documents still in AbbVie's possession which included documents retrieved during the grievance process and collected in response to the first SAR which had been kept on file.

The complainant's alleged authorship of the Embrace Stars Poster

AbbVie noted that the Panel's ruling stated that 'based on the narrow allegation, the Panel did not consider that the complainant had provided evidence to show that, on the balance of probabilities, the representative's role, and/or influence, was such that it could be stated that the representative had created a poster or that it was created at the express request of his/her manager and that the representative had not applied high standards in this regard'. AbbVie submitted that in order to address this, the complainant had provided the text of an email from one of the nurses behind the Embrace Stars poster. Without prejudice to the point made above that the complainant should not be permitted to adduce new supporting evidence at this stage, this email did not prove that the complainant was the author of the poster. First, AbbVie noted that the complainant had not attached the entirety of the email chain but had instead copied and pasted the nurse's response.

AbbVie submitted that it was essential for fairness and transparency that the complainant provided a full unredacted copy of the email chain and any other reports of interactions. This was particularly important when operating under a self-regulatory framework. It was also a well-established principle that investigations required 'full and frank disclosure of the facts at the outset' (Case AUTH/2435/8/11). If there was confidentiality issues with this approach, then a full unredacted copy should be made available at least to the Appeal Board and, if necessary to an AbbVie representative who could sign a confidentiality undertaking if necessary. It went without saying that if the complainant had included his/her initial question, it might have provided some further clarity as to the meaning of the nurse's response.

AbbVie submitted that the response stated that two nurses contributed to the poster, along with the complainant. This was entirely consistent with the description of events in AbbVie's response to the complainant in which it concluded that from its review of the available information, and discussion it had had in the timeframe allowed by the PMCPA, the complainant might have been helping the nurses to prepare their application form, modifying it and 'hand holding' them through the process'. The email also stated that the complainant then 'produced' the poster. It was not clear what exactly was meant by 'produced', although the use of the word 'then' in this sentence (ie the 'production' took place after the contributions from the nurses and the complainant) suggests it was more likely to be referring to AbbVie's (and the communications agency's) role in converting the initial application

into the final poster (including adding graphics and making formatting changes, as well as editing the text). Again, this would be completely consistent with AbbVie's description of events in its response to the complaint.

AbbVie submitted that the complainant also cited the fact that AbbVie had not received written confirmation from the NHS trust that the edits of the poster were acceptable, but instead relied on verbal confirmation given to the complainant, as evidence that he/she was the true author of the poster. AbbVie's communication agency attempted to obtain written confirmation that the trust was happy with the poster on 31 July 2017 and again on 1 August 2017.

AbbVie submitted that however, when the trust did not respond, the complainant was asked to contact the trust to obtain its confirmation. AbbVie had no reason not to believe that the verbal confirmation passed on by the complainant was accurate, and if the complainant was suggesting that he/she deceived AbbVie, this was more the fault of the complainant than of AbbVie.

AbbVie submitted that finally, the complainant suggested that the fact that an AbbVie employee had sent comments to him/her rather than directly to the nurses suggested that he/she was the true author. In fact, this simply reflected standard lines of communication at AbbVie. The complainant was the one in direct contact with the nurses who were his/her customers.

FINAL COMMENTS FROM THE COMPLAINANT

There were a number of confidentiality issues which were resolved and relevant information was provided to the complainant.

The complainant noted that whilst he/she had previously had sight of some of the material, there were a number of emails/documents he/she had never seen. (This material fell within the timeframes of his/her SAR, but were previously not disclosed).

The complainant stated that having reviewed the document bundle it had become clear why AbbVie would not want him/her to have sight of the information as it presented clear evidence to substantiate his/her allegation. The complainant alleged that he/she had referred to those supporting documents throughout his/her response. The complainant had no other additional comments to make on the information supplied.

Firstly, the complainant addressed AbbVie's allegation that he/she was using this process to air any outstanding grievances, and stated that he/she was not, as there were no outstanding grievances. The complainant stated that he/she had fully exhausted AbbVie's grievance procedure and raised genuine concerns to the PMPCA after giving AbbVie ample opportunity to investigate and self-report. AbbVie had failed to do both. This was backed up by the fact that the Panel had already found AbbVie in breach of some of the clauses alleged.

The complainant alleged that he/she raised genuine issues of what he/she considered were breaches of the Code. The complainant noted that he/she stated this as AbbVie had been found in breach by two independent organisations. To be absolutely clear the complainant had only ever raised this **ONE** complaint regarding AbbVie. Any other complaints, whether they be linked or associated the complainant had absolutely no knowledge of. However there seemed to be an emerging pattern if there were further complaints relating to AbbVie and case studies/work ethics. The reason the complainant had provided the PMPCA with the ICO information was in response to AbbVie providing 'background information' to the PMPCA which was not relevant to the case and was only used to try to discredit his/her allegations, however the ICO findings the complainant provided were absolutely necessary in providing an insight into how AbbVie operated under such circumstances. The very fact that during AbbVie's 'robust process' it did not find ANY causes for concern. However, two independent, impartial organisations (ICO and PMCPA) upheld breaches, investigated and found failings, were yet further evidence of AbbVie's inability to deal with whistleblowing in a fair and transparent manner.

Specific comments on each point:

The complainant noted that AbbVie had mentioned the SAR requests which again had no relevance to this case. The complainant's comment on this was that AbbVie had failed to respond to the first SAR adequately, it was incomplete and it was asked by the ICO to share more details with the complainant. The second SAR was also incomplete, AbbVie did however manage to find some additional material which should have been shared in the first SAR. AbbVie had proven to be a non-complaint organisation which had a disregard for procedures and personal data protection, the complainant concluded on this point by noting that AbbVie was in fact found in breach of the first principle relating to the data protection act by the ICO.

The complainant noted that AbbVie had stated that he/she had not raised the issue until late 2017, when the events took place over the summer. The complainant gave details and stated that the grievance was raised at the first opportunity. The complainant was shocked AbbVie would be inclined to bring this up as it could be easily proved to be true. The complainant stated that he/she was more than happy for the PMCPA to ask AbbVie for he/her period of sick leave. In addition, the complainant had spoken with AbbVie's office of ethics and compliance in the early part of December, when he/she raised his/her concerns.

The complainant noted that AbbVie had stated that he/her appeal was subjective claiming it was motivated because he/she did not agree with the PMPCA response. Again, this was an example of AbbVie clearly not understanding the procedural importance of a process. A complainant had every right in appealing a process. It seemed that AbbVie was in fact not accepting his/her right to appeal.

The complainant noted that AbbVie was unhappy about his/her response. The complainant did not think his/her response could be any more detailed or fair. This case was based on the 'balance of probabilities' and not on the premise of 'beyond reasonable doubt'.

The complainant noted that AbbVie clearly did not want the evidence of the nurse who 'wrote' the poster to be admissible in the appeal. The complainant alleged that the nurses' evidence was absolutely essential and pertinent to the case. The complainant had been initially very reluctant to directly involve the nurses, as he/she did not want to put them into a difficult situation. However, following the initial PMPCA ruling, where it appeared that the complainant did not provide enough substantiating evidence to prove a breach of Clause 15.2 and subsequently a breach of Clause 2 the complainant felt he/she had absolutely no alternative other than to contact the nurses who then in turn confirmed his/her version of events.

The complainant categorically confirmed that the email provided by the nurses was the thread in its entirety, there was no other email exchange. The complainant stated that he/she could resubmit the initial evidence if AbbVie submitted that he/she had just 'Copied and pasted' the email. The complainant alleged that he/she had had a discussion with the nurses over the phone and asked them to confirm what actually happened via email in order for him/her to use it as evidence. The complainant noted that he/she had previously asked AbbVie to confirm this with the nurses which they clearly had not done.

The complainant alleged that the play on the word of 'then', which AbbVie was suggesting, was an inappropriate attempt to distort the truth. If AbbVie wanted to continue with the ambiguity of words then it should invite the nurse to the hearing to hear his/her truth. The complainant guaranteed it would be aligned to his/her submission.

Also critically, the complainant alleged that AbbVie claimed the agency attempted to make contact with the nurses to provide final approval and sign off. In none of the documentation AbbVie provided was it apparent that this occurred. AbbVie claimed that it asked him/her to contact the nurses verbally to obtain sign off. This did not occur. Quite frankly if the agency could not gain the necessary compliance sign off and paper trail then the poster should never have been produced and displayed. The complainant noted that assuming this was the case as no paper trail existed from the nurses giving permission or claiming the poster as their work or publication. AbbVie claimed to be very good at compliance and had a large team dedicated to it, so the complainant queried why this had slipped through the net. To be clear it was never the complainant's role to ensure poster compliance that was the role of the agency and other AbbVie internal departments.

The complainant alleged that AbbVie's submission that an AbbVie employee's (comments were sent to him/her rather than the nurses as it was 'standard procedure' was nonsense. The Abbvie employee had

met with many customers and would approach any national customer if he/she felt the need.

The complainant alleged that the email exchange from his/her manager to him/her in 2017, where his/her manager was clearly directing him/her was clear evidence they had discussed the preparation of the poster submission, despite AbbVie claiming the manager had no knowledge or input. Certain content was highlighted by the complainant.

Furthermore, the complainant drew attention to an email exchange between the nurse and the agency highlighting particular sections and asking why would the nurse who had written that specific poster be making such comments to the agency about clear factual inaccuracies to his/her service provision if he/she had written the poster? The complainant referred to email exchanges from one of the nurses and the communications agency and between an AbbVie employee and the complainant as yet more evidence of the fact that AbbVie produced the poster.

The complainant alleged that the reasons why the initial submitted work 'does not seem to align to the results described' was because the complainant was not a health professional, and this formed many subsequent verbal discussions with his/her manager. The complainant alleged that he/she had also discussed the stress that this caused him/her with immediate members of his/her team and, and HR were documented during AbbVie's internal investigations, but were not present in any evidence AbbVie had supplied in relation to the case.

In summary, the evidence that AbbVie provided, could not be seen to substantiate AbbVie's view that it was only 'Handholding' in the production of the poster. On the contrary, the evidence which was included in its own previously redacted evidence plus the evidence of the nurse, proved a clear breach of Clause 15.2 and Clause 2.

The complainant took the opportunity to thank the PMCPA for hearing the appeal and for its transparency in providing all the necessary information for him/her to make an informed decision about his/her appeal as it was clear AbbVie did not want to share information for him/her to appeal, and the question the complainant would ask was why?

The complainant noted that AbbVie's own core values included Integrity, transparency and honesty, being brave and courageous.

The complaint submitted that throughout this process he/she had behaved professionally and felt strongly that AbbVie had tried to make very personal attacks in its responses, in order to discredit him/her.

APPEAL BOARD RULING

The Appeal Board noted that the complainant alleged that he/she had been instructed by his/her manager to create a poster on behalf of nurses at an NHS trust for them to approve as their own work. AbbVie referred to the company representative 'hand holding' the nurses through the process.

The Appeal Board noted the difference of opinion in this case. Both parties acknowledged that there was some involvement by the complainant, the question to be considered by the Appeal Board was the extent of that involvement.

The Appeal Board noted from the AbbVie representative at the appeal (another person was, at the last minute, unable to attend due to major travel difficulties) that the company had not contacted the nurses regarding this complaint. The company had also not provided any testimony from the complainant's manager, colleagues or its HR department concerning the creation of the poster. The Appeal Board did not accept AbbVie's submission that it had carried out a thorough investigation into this complaint as its representative at the appeal was unable to answer certain questions which in the Appeal Board's view should have been covered by the investigation.

The Appeal Board noted that the Embrace Stars 2017 entry pack attached to an email of 26 May 2017 from the complainant to his/her manager could have been completed by a nurse/nurses. The Appeal Board considered that the inclusion of the patient testimonials and feedback in the completed entry pack implied the involvement of health professionals. Although the content of this submission appeared to have been completely re-written in the final poster with the patient testimonials removed, the themes were similar.

The Appeal Board noted that the emails sent in July/August 2017 to the nurses by AbbVie's agency that had worked to create the poster requested that the nurses look at the attached draft poster and confirm if they were happy. The emails also asked the nurses to supply photographs of themselves to include in the poster. The nurses' replies included that he/she was leaving his/her current post and away for the presentation date so was not sure it was meant for him/her and that he/she had looked at the poster and did not have fortnightly clinics. The Appeal Board did not consider that such responses would be expected from authors of a poster. In that regard the Appeal Board noted that the final poster did not include pictures of either of the nurses listed as authors nor did the company receive their written approval. The Appeal Board noted its comments above with regard to the nurse/nurses implied involvement in completion of the entry pack which was submitted to AbbVie and its agency to rework into a final poster which appeared to the Appeal Board to be based on the original completed submission.

The Appeal Board noted that an email dated 26 July provided by the complainant from one of the two nurses involved confirmed that the poster presentation regarding the success of the RSV clinics was contributed to by the nurses with the complainant myself and [named nurse] and then produced by the complainant'.

The Appeal Board considered that there was evidence to show that the complainant, the nurse(s) and AbbVie and its communications agency were involved with the production of the poster. In that

regard the Appeal Board noted the Panel's ruling of a breach of Clause 9.10 above in relation to AbbVie's declaration of its involvement in the production of the poster. The Appeal Board considered that on the information available it did not have sufficient evidence to show on the balance of probabilities that the complainant had created the poster *de novo* at the direction of his/her manager, as alleged. Consequently, on the narrow allegation, the Appeal Board considered that there was no evidence that the representative had not applied high standards in this regard. The Appeal Board upheld the Panel's ruling of no breach of Clause 15.2. The appeal on this point was unsuccessful.

The Appeal Board noted its comments and rulings above and those of the Panel and did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such use. The Appeal Board consequently upheld the Panel's ruling of no breach of Clause 2. The appeal on this point was unsuccessful.

Complaint received	9 March 2018
Case completed	17 October 2018

COMPLAINANT v GW PHARMACEUTICALS

Arrangements for a meeting, alleged promotion of Epidiolex and unapproved slides

A contactable complainant complained about the provision of inappropriate hospitality and the use of slides about cannabidiol (Epidiolex). Epidiolex was currently unlicensed, although an application for its marketing authorization had been submitted for its use as an adjunctive treatment for seizures associated with Lennox-Gastaut Syndrome and Dravet Syndrome.

The complainant stated that during a customer visit, an employee from a third party organisation engaged by GW Pharmaceuticals took a named health professional to lunch during which topics unrelated to epilepsy were discussed. The health professional did not treat epilepsy or paediatric epilepsy and was therefore according to the complainant not a relevant customer for GW Pharmaceuticals and lunch was provided despite there being no educational content to the meeting.

The complainant further stated that he/she was informed verbally by a doctor that he/she would complain to the PMCPA about the pre-licence promotion of a medicine in relation to a presentation to health professionals the complainant noted that a slide deck was approved by GW Pharmaceuticals but was subsequently amended before the meeting and as it had not been certified a breach was alleged. The complainant also stated that the presentation was solicited by the third party employee upon discussion with the meeting organisers. The complainant alleged that this type of proactive meeting would be considered to be 'promotional' before a market authorisation.

The detailed response from GW Pharmaceuticals is given below.

The Panel noted that the parties' accounts of the meeting differed.

The Panel noted GW Pharmaceuticals' submission that the named health professional was a relevant health professional in the field of epilepsy. The Panel further noted that an email from the third party employee to the health professional to arrange the meeting referred to the chance to catch up and understand his/her perspective on needs and treatments for hard to treat epilepsies and paediatric syndromes. In response, the health professional did not refer to the subject matter of the meeting but stated that it would be a pleasure to meet an old friend. According to GW Pharmaceuticals, matters discussed included the company's ethos in helping patients with complex epilepsies, discussion of a corporate brochure and his/her clinical interactions with paediatric neurologists and the burden of epilepsy in his/her patient population.

The Panel considered both the totality of the evidence in relation to the named health professional's professional interests and the subject matter of the meeting as described above and considered that he/she was a relevant health professional. The company had not failed to maintain high standards in this regard. No breach was ruled.

The complainant was concerned that hospitality had been provided without any educational content. The cost of the meal was £35.35 for three persons. The Panel noted the content of the meeting which lasted for approximately 1 hour according to GW Pharmaceuticals and 20-40 minutes according to the named health professional. The Panel noted that the complainant bore the burden of proof. Despite serious concerns about governance in relation to the meeting, based on the evidence and the very narrow allegation, the Panel did not consider that the complainant had established on the balance of probabilities that there had been no educational content and thus ruled no breaches of the Code including no breach of Clause 2.

The Panel noted that Case AUTH/3024/3/18 and the present case, Case AUTH/3029/4/18 contained similar allegations with regard to a presentation to a group of doctors at a hospital in February 2018 which the complainant alleged promoted a product prior to the grant of its marketing authorisation. The Panel considered that its rulings and comments in Case AUTH/3024/3/18 were relevant here. The Panel noted that there were some differences between Case AUTH/3024/3/18 and the present case.

In Case AUTH/3024/3/18 the Panel noted GW Pharmaceuticals' submission that the presentation was provided in response to an unsolicited verbal request from health professionals for a medical presentation on updated clinical data and properties of cannabidiol during a meeting in December 2017 between two employees working on behalf of GW Pharmaceuticals and two hospital doctors. The Panel noted that GW Pharmaceuticals provided some evidence in support of its position. The Panel queried whether it could be argued that an email to the hospital doctors was soliciting enquiries, however it did not appear that either doctor responded with any specific topics to be covered. The general points covered in the presentation provided by GW Pharmaceuticals appeared to be consistent with the points raised by the health professionals at the earlier meeting in December 2017. That the meeting in question (February 2018) resulted from an unsolicited request was also corroborated by further information provided.

In the previous case, Case AUTH/3024/3/18, the Panel noted the list of 12 attendees. From the evidence before the Panel it appeared that in requesting the meeting the two health professionals, rather than GW Pharmaceuticals, had taken the decision that the content was appropriate for the small specialized departmental group.

Based on the particular facts of Case AUTH/3029/4/18 and on the evidence before it, the Panel considered that, on balance, GW Pharmaceuticals could take the benefit of the exemption of the definition of promotion in relation to unsolicited requests and the presentation did not promote Epidiolex prior to the grant of its licence. The Panel ruled no breaches of the Code including Clause 2.

The Panel noted that a further allegation in the present case, Case AUTH/3029/4/18, concerned the slides being amended following approval by GW Pharmaceuticals, and that the amended version was not certified. The Panel noted GW Pharmaceuticals' submission that as the slides were non-promotional GW Pharmaceuticals did not consider that they required certification under the Code. The Panel noted its comments above with regard to GW Pharmaceuticals being able to take the benefit of the exemption from the definition of promotion in relation to unsolicited requests which did not require certification and the Panel therefore ruled no breaches of the Code including Clause 2.

A contactable complainant referred to an email from a third party which represented GW Pharmaceuticals. The complainant alleged that the email concerned the provision of inappropriate hospitality and the use of slides about cannabidiol (Epidiolex). Epidiolex was currently unlicensed, although an application for its marketing authorization had been submitted for its use as an adjunctive treatment for seizures associated with Lennox-Gastaut Syndrome and Dravet Syndrome.

COMPLAINT

The complainant stated that during a customer visit with a named health professional an employee from a third party engaged by GW Pharmaceuticals, asked the health professional if he/she would like to have lunch at a local café. During the lunch, attended by the complainant, the health professional discussed topics unrelated to epilepsy and stated that he/she did not treat epilepsy or paediatric epilepsy. The complainant maintained that the health professional was not a relevant customer for GW Pharmaceuticals and there was no educational content to the meeting. The employee paid for the lunch even though there was no educational content. The complainant alleged a breach of Clause 22.1.

The complainant further stated that he/she was informed verbally by a doctor that he/she would complain to the PMCPA about the pre-licence promotion of a medicine in relation to a presentation to health professionals at a hospital in February 2018. The complainant noted that a slide deck was approved by GW Pharmaceuticals but was subsequently amended before the meeting. The

complainant also stated that the presentation was solicited by the employee upon his/her discussion with the meeting organisers. The complainant alleged that this type of proactive meeting would be considered promotional, before the grant of a market authorisation in breach of Clause 3.1.

Additionally, as the slides were amended they had not been certified and so the complainant also alleged a breach of Clause 14.1.

When writing to GW Pharmaceuticals, the Authority asked it to consider the requirements of Clauses 15.2, 15.9, 9.1 and 2 in addition to Clause 22.1 as cited by the complainant with regards to the meeting and Clauses 3.1, 9.1, 14.1, 15.2 and 15.9 with regard to the slides used at the meeting in February 2018.

RESPONSE

GW Pharmaceuticals understood that to the extent that the meeting in February 2018 was said to be pre-licence promotion of a medicine, that it would be treated as falling under Case AUTH/3024/3/18. GW Pharmaceuticals responded below to each of the remaining points raised by the PMCPA, however, it considered it important to raise certain matters at the outset.

GW Pharmaceuticals wished to make it clear that it took compliance extremely seriously and strove at all times to operate responsibly, ethically and professionally. The company expected and took steps to ensure that all of its employees, and those acting on its behalf, always adhered to the same high standards of ethical conduct imposed by applicable regulatory regimes, including the Code, in line with best practice expected of a responsible corporate undertaking. On being advised of the complaint, GW Pharmaceuticals and its third party immediately launched in-depth investigations. GW Pharmaceuticals appreciated that it could be difficult to investigate and respond to this type of anonymous complaint, but after careful investigation it was comfortable that the complaint had no basis.

As part of its investigations GW Pharmaceuticals had obtained statements including from the employee of the third party and the named health professional.

GW Pharmaceuticals submitted that the third party employee in particular had provided a rigorous and detailed account of what happened at both meetings, backed by robust supporting materials, including a number of records of interactions with health professionals at, and before, the meetings and presentation. Together, these statements and the accounts, and the supporting materials provided with them, provided a clear, comprehensive and credible account of both events and their background.

GW Pharmaceuticals stated that it had taken particular care to re-assess in the context of the complaint, all relevant material, procedures, processes and instructions which might pertain to the alleged events, including anything which might have given rise to a representative inappropriately providing hospitality, soliciting, inappropriate amendment of materials, making promotional

statements or presenting promotional material in error. The company had reviewed in the context of the complaint the briefing and training materials. It had also considered the statements and their supporting documents. Further, GW Pharmaceuticals had reviewed the slides which were presented in February, including photographic evidence of the same, along with the detailed account including those provided in response to AUTH/3024/3/18.

The December 2017 lunchtime meeting at a café local to the hospital was attended by three people including the complainant. Full details of the meeting were provided in statements and supporting materials.

In summary, the third party employee knew the health professional as a relevant health professional in the field of epilepsy due to professional interactions while with another company active in the epilepsy field and considered it appropriate to re-introduce himself/herself in his/her new role. The support for this reasoning was provided.

The third party employee emailed the health professional to arrange to catch up and understand his/her perspective on needs and treatment for hard to treat epilepsies and paediatric syndromes. They went to lunch at a nearby café recommended by the health professional. As evidenced by respective accounts, the discussion was largely scientific and about the treatment of patients with complex epilepsies. They also discussed GW Pharmaceuticals and the third party employee responded to unsolicited questions from the health professional on cannabidiol. The interaction was fully documented including in summary reports. The cost of the lunch equated to a spend of roughly £11.80 on the health professional attendee. The meeting lasted around one hour. This summary of events was fully supported by the health professional's account.

GW Pharmaceuticals stated that in response to an unsolicited request and invitation by health professionals, various employees attended the hospital in February 2018 to exchange scientific and medical information about GW Pharmaceuticals' research interests and the development of cannabidiol. There was no formal agenda but the intention of what would be addressed at the meeting was set out in emails between the third party employee and health professionals at the hospital and contemporaneous notes. The purpose was to present tailored and appropriate data on cannabidiol in response to an unsolicited request. There was no promotional intent. A full list of attendees was provided.

GW Pharmaceuticals noted that the PMCPA had requested a copy of the approved slide deck and of the slide deck amended and used at the meeting. This request raised several issues that needed to be addressed upfront:

(i) **Approval of the slide deck:** as the slides were non-promotional GW Pharmaceuticals did not consider that they required certification under the Code. The supplementary information to Clause 14.3 required that 'other material ... which

is not promotional *per se*, such as corporate advertising ... should be examined to ensure that it does not contravene the Code or the relevant statutory requirements'. The employee of the third party who was highly experienced arranged the content of the presentation, and along with another experienced and previous Code signatory who examined the slides. Neither considered, then or now, that there had been any breach of the Code.

- (ii) **The slide deck that was used:** The employee of the third party provided a copy of the slide deck that he/she believed was presented, based on his/her recollection of the slides that he/she reviewed before the presentation, and took a contemporaneous photograph of one of the slides during the presentation which was consistent with these slides. Finally, although there was some confusion in the complainant's accounts, these were the slides which the complainant most recently and after some consideration, provided as the slides which were presented.
- (iii) **The slide deck:** GW Pharmaceuticals stated that the complainant presented the slides, not the third party employee as shown in a contemporaneous photograph of the presentation. The slides which the complainant provided had his/her name and title on them; they were presented using his/her laptop. The complainant also confirmed that he/she presented the slides and that he/she, or at least he/she in collaboration with the third party employee, added his/her name and title (see below).
- (iv) **Amendment of the slide deck by the third party employee:** Although this person amended the slide deck, and ultimately examined and approved it, these amendments were made jointly with the complainant, taking into account any concerns he/she had with the material on the morning of the meeting eg removing a data set with which the complainant was uncomfortable. Although the complainant's accounts were confused, the complainant confirmed that he/she amended the slides, in particular he/she added his/her name and title. These amendments were consistent with the slides which the complainant ultimately provided.

GW Pharmaceuticals stated that it was satisfied that all the circumstances of the meeting in December 2017 were entirely appropriate: the reason for and purpose of the meeting was to discuss with a relevant health professional the scientific and technical information about the treatment of complex epilepsies, the health professional was entirely appropriate and relevant to this aim, there was a short meeting conducive to this aim and, given the time of day, it was appropriate to go to a nearby café for lunch especially in light of the busy schedule and their valuable time. The content of the discussion was appropriate and the hospitality was secondary to the scientific content of the meeting and limited to subsistence only. This account was backed by the account of the health professional.

GW Pharmaceuticals stated that it was also satisfied that the presentation on 7 February 2018 was not

promotional in form or content. The employee of the third party did not solicit the meeting. His/her account was backed by: (i) contemporaneous records of his/her communications with health professionals with whom he/she interacted with as a result of unsolicited requests at another meeting and at the presentation at the meeting in question; (ii) his/her contemporaneous photograph of the February 2018 meeting which showed presentation slides; (iii) the slides themselves; and (iv) briefing materials upon which he/she was well-trained. The various statements etc provided corroborated the accounts. GW Pharmaceuticals considered that the amendments made to the slide deck, including in collaboration with the complainant, and the slides which were presented, were appropriate and did not breach the Code.

GW Pharmaceuticals stated that, in its view, the employee of the third party was highly experienced, had previously been a Code signatory and was fully aware of the Code and his/her responsibilities under it.

Having thoroughly investigated the complaint as set out above, GW Pharmaceuticals considered that the complainant's allegations were unfounded; it denied any wrongdoing or impropriety on the part of the company or its representatives. There were also many factual issues and inconsistencies in the complaint which led GW Pharmaceuticals to suspect that the complaint was unfounded and/or fabricated. GW Pharmaceuticals made a very detailed submission including about the complainant including his/her credibility and what the company considered to be his/her role in relation to the subject matter of the complaint.

Alleged promotion via solicitation

As to solicitation of the meeting in February 2018 which might constitute promotion GW Pharmaceuticals noted that the health professionals requested, unprompted, a 'medical presentation' on the updated clinical data and properties of cannabidiol. This was what was provided at the presentation. The request was corroborated by the email chain between the employee of the third party and the requesting health professionals which stated: 'Thanks for your request to present an update on cannabidiol data and progress'. There was clearly no solicitation.

The basis and nature of the presentation was clear from the above mentioned email chain and the disclaimer on slide 2 which stated 'This slide deck is being presented following an unsolicited request from a healthcare professional' 'particularly interested to hear more about study results, safety information, side effects, efficacy and also to get an update on recent trial data, when market approval might be expected and whether prescriptions on a named patient basis might be a possibility.

In relation to the materials which were presented, there was only a slide deck. Great care was taken to ensure that the presentation was balanced, noting trial design and balancing any efficacy data with

safety data including laboratory findings, common adverse events and serious treatment emergent adverse events. The information presented was balanced, fair, objective and unambiguous, and was as stated, based on an up-to-date evaluation of the evidence available'. The slides comprised scientific and medical information, genuine non-promotional information about GW Pharmaceuticals and its research interests and disease awareness information. One of the health professionals at the hospital agreed and stated that 'the presentation and meeting were of a scientific nature as new scientific data was shared to which he/she had not seen before.

Following the presentation, there followed from the health professionals a series of specific and unsolicited queries concerning the data and properties of cannabidiol. Again, GW Pharmaceuticals was satisfied from this material and accounts of attendees that the discussion/Q&A was non-promotional and there was no element of solicitation.

GW Pharmaceuticals stated that it was satisfied that the presentation and any interactions around it, were part of an appropriate response to an unsolicited request aimed to legitimately exchange medical and scientific information, and not promotional.

Implied allegation by a doctor of promotion

Although GW Pharmaceuticals noted that the allegation about the content of the slide decks would be separately addressed, the complainant stated that a doctor informed him verbally that he/she would complain about the promotion of a medicine before it had a marketing authorization. It was not clear when this interaction took place and very sparse information was provided to assist the investigation, but the complainant stated that this interaction was in reference to the presentation in February. GW Pharmaceuticals did not consider that this was credible.

GW Pharmaceuticals was comfortable from accounts of attendees and its review of supporting material, that it was simply implausible that anyone who had attended the presentation, even if only part of it, could have misunderstood, or worse been misled, as to the licensing status of cannabidiol.

On slide 2 there was a large and prominent disclaimer which stated 'Cannabidiol is an investigational product and is not FDA or EMA approved, for any indication'. In GW Pharmaceuticals' view, the licensing status could not be more clear. GW Pharmaceuticals understood that the complainant spent quite some time bringing this message to the attention of attendees. Even if the concerned doctor had missed slide 2, the following wording was prominently displayed in clear and large font on 21 out of 33 presentation slides: 'Cannabidiol is an investigational product and is not licensed in the EU'. This warning was featured throughout the slides including on the first and concluding ('Thanks') slides. The photograph taken of the presentation contemporaneously showed that

the wording was prominent and legible even at a distance. Anyone who attended the presentation at least had the opportunity to see this warning.

Further, GW Pharmaceuticals stated that it had no reason to believe, on the basis of the GW/third party representatives' professional background, experience and training, that they would have orally provided incorrect information on the licensing status or introduced uncertainty. Indeed to do so would have been problematic given the clarity of the wording on the slides; it would have required significant departure and contradiction which would have prompted queries from the attendees, especially as at least two of the health professionals had been expressly informed of the licensing status and availability in the previous meeting and again by email. One of the health professionals was apparently in no doubt before and at the presentation that the product was unapproved.

GW Pharmaceuticals rejected any allegation or implication that misleading information as to the status and availability of cannabidiol, or any promotional content, was presented at the meeting on 7 February 2018 which could have caused any attendee to state that they would complain to the PMCPA. GW Pharmaceuticals considered that the interaction was entirely fabricated.

Representatives' high standards and training

GW Pharmaceuticals stated that it was satisfied that it and the third party had discharged their duties to provide appropriate and comprehensive briefing and training to enable its representatives to meet high standards of ethical conduct in compliance with the Code. This also applied to the complainant. However, neither GW Pharmaceuticals nor the third party could, no matter how robust their systems and training, control and prevent individuals from making spurious allegations.

Standard of proof

GW Pharmaceuticals considered that the complaint was unmerited and implausible, if not fraudulent, and that it should be dismissed. However, the company appreciated that the apparent anonymity of the complainant and paucity of evidence in support of what was, in effect, one person's word, presented the Panel with particular difficulties in adjudicating this matter. In that regard, GW Pharmaceuticals noted the appropriate standard when adjudicating complaints involving conflicting claims, namely the 'balance of probabilities'.

GW Pharmaceuticals further noted that the burden of proof in the civil litigation context provided 'the standard to be attained in most cases is that the court must be satisfied "on a balance of probabilities" that what the client had alleged was correct'. In *Miller v Minister of Pensions* [1947] 2 All E.R. 372, QBD, Denning J. explained this as follows:

'If the evidence is such that the tribunal can say "We think it more probable than not," the burden is discharged, but if the probabilities are equal, it is not... In essence, in order to satisfy the judge that one party's version of the events is the version to be accepted, the judge has to be convinced that this version is more likely than not to be true—that the balance of evidence is tilted in the client's favour. If this were to be expressed in simple mathematical terms, at least a 51 per cent probability in favour of the client must be demonstrated, as suggested by Lord Simon in *Davies v Taylor* [1974] A.C. 207, HL (at p.219). If, on the other hand, the client's version is just as probable as the opponent's version, the client has failed to discharge the burden of proof.'

GW Pharmaceuticals noted that the Appeal Board considered the burden of proof in Case AUTH/2572/1/13 where it stated that where 'it is not always clear how/whether the material supported the complainant's allegation ... the Appeal Board [has] to decide how much weight to attach to this evidence'. In that case, the Appeal Board had before it emails and excerpts from published papers which it ruled were insufficient evidence and did not provide a 'fair and balanced reflection of the evidence available at the time'. The Appeal Board also made it clear that where the complainant failed to marshal sufficient evidence to discharge the burden of proof, there should not be a ruling of a breach.

In Case AUTH/2824/2/16 the Panel considered whether there was sufficient evidence to substantiate the allegation that company representatives went to a named location contrary to the terms of a verbal undertaking. The Panel found there was no evidence to substantiate the allegations and therefore no breaches were ruled. The essence of that case demonstrated the difficulty of substantiating an event where there was competing anecdotal or hearsay evidence. Allegations should be substantiated. Such allegations were not substantiated in that case nor were they, in GW Pharmaceuticals' view, substantiated in this case.

That reflected a general and widely-acknowledged strand in the law of evidence that 'the weight of evidence depends on the rules of common sense' (*R. v Madhub Chunder* (1874) 21 W.R Cr. 13 at 19 (Ind) per Birch J). GW Pharmaceuticals referred, in that regard, to the summary provided in its response to Case AUTH/3014/1/18 on the appropriate standard when adjudicating complaints involving conflicting claims, ie the 'balance of probabilities'.

Considering the points raised above and applicable case law, GW Pharmaceuticals considered that its version of events was clearly more probable than that put forward by the complainant. GW Pharmaceuticals had provided substantial evidence and careful assessment of the materials at issue and relevant events. Conversely, the complainant's allegations and account of events were simply not plausible. The complainant had provided no credible evidence to discharge the burden of proof on the balance of probabilities assessment. Indeed, as set out above, slides provided by the complainant

should be viewed, at best with caution, if not as being fraudulent. Therefore this 'evidence', rather than supporting the complainant's allegations, undermined his/her credibility.

GW Pharmaceuticals concluded that it was impossible on a common sense view to find against GW Pharmaceuticals on the basis of the simple, brief and false allegations put forward by the complainant, given its flaws and the weight of contradictory evidence and material submitted by the company.

GW Pharmaceuticals denied any breach of the Code.

FURTHER INFORMATION FROM GW PHARMACEUTICALS

GW Pharmaceuticals stated that on being advised of Cases AUTH/3014/1/18, AUTH/3024/3/18 and AUTH/3029/4/18, it and its third party immediately investigated the respective circumstances and merits of each complaint. Both GW Pharmaceuticals and the third party companies had serious misgivings about the legitimacy of the complaints, as well as concerns over the inaccuracies and inconsistencies in the complainants' accounts. Further details were supplied.

PANEL RULING

The Panel noted that the parties' accounts differed. The Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was often impossible in such circumstances to determine precisely what had happened. The introduction to the Constitution and Procedure stated that a complainant had the burden of proving their complaint on the balance of probabilities.

The response from GW Pharmaceuticals implied that it was aware of the complainant's identity. The Panel noted that it did not know the identity of the complainant who was nonetheless contactable.

The Panel noted that it was an established principle under the Code that companies were responsible for the acts/omissions of third parties acting on their behalf.

The Panel noted that Epidiolex was unlicensed, an application for a marketing authorisation was submitted on 29 December 2017 for its use as an adjunctive treatment for seizures associated with Lennox-Gastaut Syndrome and Dravet Syndrome.

The Panel noted the complainant's concern that the meeting between himself/herself the employee from the third party organisation and the health professional at a café was in breach of the Code because the health professional was not a relevant customer as he/she did not treat epilepsy or paediatric epilepsy and he/she was provided with hospitality despite the meeting having no educational content.

The Panel noted GW Pharmaceuticals' submission that the health professional was a relevant health professional in the field of epilepsy. The Panel

further noted that an email from the third party employee to arrange the meeting stated that he/she would welcome the chance to catch up with the health professional and understand his/her perspective on needs and treatments for hard to treat epilepsies and paediatric syndromes. In response he/she did not refer to the subject matter of the meeting but stated that it would be a pleasure to meet an old friend. According to a statement, matters discussed included the company's ethos in helping patients with complex epilepsies, discussion of a corporate brochure, discussion of his/her clinical interactions with paediatric neurologists and the burden of epilepsy in his/her patient population. The statement noted that unsolicited questions about cannabidiol were answered. This was supported, in part, by a report written shortly after the meeting in question which noted discussion about the narrow nature of the licence. The Panel queried whether such discussions were truly unsolicited whilst noting that this aspect was not the subject of the complaint.

The Panel noted GW Pharmaceuticals' assertion, that the individual was a relevant health professional and referred to his/her website biography and signature on an epilepsy consensus statement. The Panel also noted that a transcript of a telephone conversation with the health professional, signed by him, stated that the submission that he/she did not treat epilepsy patients was incorrect. Whilst he/she did not treat epilepsy patients under the age of 17 and was not an expert in Dravet Syndrome, many patients survived into adulthood and thus he/she had an interest in and connection to paediatric epilepsy.

The Panel considered both the totality of the evidence in relation to the health professional's professional interests and the subject matter of the meeting as described above and considered that he/she was a relevant health professional. The company had not failed to maintain high standards in this regard. No breach of Clause 9.1 was ruled.

The Panel was very concerned to note that the meeting, at the health professional's request, was held at a local café. The Panel noted the public nature of the venue, the impression given, the lack of a formal agenda and the matters discussed as outlined above and queried whether such a venue was appropriate. The Panel noted however that there was no allegation about these matters including the venue, the complainant was concerned that hospitality had been provided without any educational content. The Panel noted the cost of the meal was £35.35 for three persons. The Panel noted the content of the meeting as described above. The meeting lasted for approximately 1 hour according to the employee of the third party and 20-40 minutes according to the health professional. The Panel noted that the complainant bore the burden of proof. Despite its serious concerns about governance in relation to the meeting as set out above, based on the evidence and the very narrow allegation the Panel did not consider that the complainant had established on the balance of probabilities that there had been no educational content and thus ruled no breach of Clause 22.1. The Panel subsequently ruled no breach of Clauses 15.2, 9.1 and 2.

The Panel noted that the case preparation manager had raised Clause 15.9, which related to briefing material, as potentially being relevant. The Panel did not consider that there was an allegation in this regard and made no ruling.

The Panel noted that Case AUTH/3024/3/18 and the present case, Case AUTH/3029/4/18 contained similar allegations with regard to a presentation to a group of doctors at a hospital in February 2017 which the complainant alleged promoted a product prior to the grant of its marketing authorisation. The Panel considered that its rulings and comments in Case AUTH/3024/3/18 were relevant here. The Panel noted that there were some differences between Case AUTH/3024/3/18 and the present case. In Case AUTH/3024/3/18 the complainant provided photographs, some cropped, of 9 presentation slides. In the present case the complainant provided a printout of 33 slides which were similar to those provided by GW Pharmaceuticals save that they did not include the disclaimer 'Cannabidiol is an investigational product and is not licensed in the EU' at the top of 21 of the 32 slides. According to GW Pharmaceuticals, it appeared that the slides provided by the complainant to the PMCPA had been modified after the meeting at issue.

In the previous case, Case AUTH/3024/3/18, the Panel noted that GW Pharmaceuticals had asserted that the meeting in question in February 2018 was the legitimate exchange of medical and scientific information in response to an unsolicited enquiry about the development of cannabidiol. The Panel noted that Clause 3.1 prohibited the promotion of a medicine prior to the grant of its marketing authorization, its supplementary information stated that the legitimate exchange of medical and scientific information during the development of a medicine was not prohibited provided that this did not constitute promotion which was prohibited by Clause 3 or any other Clause. The Panel queried whether a product subject to Phase III trials and for which a licence had been applied for in the US and Europe would be considered an investigational molecule or otherwise in development. The Panel noted that the GW Pharmaceuticals' version of the slides presented included the proposed indications, usage and dosage. In the Panel's view and given the content of the presentations provided by each party, health professionals were likely to view Epidiolex as a pre-licence product. The Panel considered that its view was supported by the list of questions asked by those present which included questions about cost, shelf life, storage and others relevant to the product's use. There did not, on the information before the Panel, appear to be an exchange of medical and scientific information about the development of the product. In the Panel's view the presentation could not take the benefit of the supplementary information to Clause 3.1.

In the previous case, Case AUTH/3024/3/18, the Panel noted that GW Pharmaceuticals had also asserted that the presentation was provided in response to an unsolicited enquiry. The Panel noted that Clause 1.2 provided an exemption to the definition of promotion stating that replies made in response to individual enquiries from members of the health

professions or other relevant decision makers or in response to specific communications from them whether of enquiry or comment, were excluded from the definition of promotion, but only if they related solely to the subject matter of the letter or enquiry, were accurate and did not mislead and were not promotional in nature. The Panel noted that the exemption only applied to unsolicited enquiries, an enquiry made without any prompting from the company. If an enquirer subsequently requests further information this could be provided and would be exempt from the Code provided the additional information met the requirements of this exemption. The Panel noted that when relying on this limited exemption in relation to a meeting about an unlicensed product documentation was very important.

In Case AUTH/3024/3/18 the Panel noted GW Pharmaceuticals' submission that the presentation was provided in response to an unsolicited verbal request from health professionals for a medical presentation on updated clinical data and properties of cannabidiol during a meeting with two named doctors from the hospital. The Panel noted that GW Pharmaceuticals provided some evidence in support of its position. The third party employees statement and notes of the meeting indicated that the health professionals had requested that GW Pharmaceuticals present at the departmental multi-disciplinary meeting on cannabidiol and clinical data. A follow up email dated to the two doctors referred to their request to present an update on cannabidiol data and progress at the weekly department meeting and asked for specific questions around cannabidiol to ensure that the company presented the most pertinent information. The Panel queried whether it could be argued that this email was soliciting enquiries, however it did not appear that either doctor responded with any specific topics to be covered. The general points covered in the presentation provided by GW Pharmaceuticals appeared to be consistent with the points raised by the health professionals at the earlier meeting. That the meeting in February resulted from an unsolicited request was also corroborated by various signed documents including one of the health professionals who stated that he/she and a colleague had asked GW Pharmaceuticals to arrange the presentation. Whilst he/she did not remember whether or not the presentation included any disclaimers that the product was not yet licensed, that would not be something he/she would have paid special attention to as he/she was already aware that it was not. The health professional was particularly interested to hear more about study results, safety information, side effects, efficacy and also to get an update on recent trial data, when market approval might be expected and whether prescriptions on a named patient basis might be a possibility.

In Case AUTH/3024/3/18 the Panel noted the list of 12 attendees. From the evidence before the Panel it appeared that in requesting the meeting the two health professionals, rather than GW Pharmaceuticals, had taken the decision that the content was appropriate for the small specialized departmental group.

Whilst the Panel in Case AUTH/3024/3/18 had some concerns about the meeting including the lack of an agenda, it noted that based on the company's account there was no evidence that the meeting went beyond the original information requested by the two health professionals. The Panel noted that the complainant bore the burden of proof and had not established that the meeting was promotional and not in response to an unsolicited request. On the evidence before it, the Panel considered that, on balance, GW Pharmaceuticals could take the benefit of the exemption of the definition of promotion at Clause 1.2 in relation to unsolicited requests and therefore did not consider on the particular facts of this case, that the meeting promoted Epidiolex prior to the grant of its license as alleged. The Panel therefore ruled no breach of Clause 3.1 and subsequently no breach of Clauses 15.2, 9.1 and 2.

Turning to the present case, Case AUTH/3029/4/18, the Panel noted the complainant's allegations and considered that the comments and rulings set out above in Case AUTH/3024/3/18 were relevant.

Based on the particular facts of this case and on the evidence before it, the Panel considered that, on balance, GW Pharmaceuticals could take the benefit of the exemption of the definition of promotion at Clause 1.2 in relation to unsolicited requests and the presentation did not promote Epidiolex prior to the grant of its licence. The Panel ruled no breach of Clauses 3.1, 15.2, 9.1 and 2.

The Panel noted that as in Case AUTH/3024/3/18, Clause 15.9 had been raised by the case preparation

manager. Clause 15.9 required that companies must prepare detailed briefing material that must not advocate, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code. In Case AUTH/3024/3/18 the Panel did not consider that there was an allegation in this regard and therefore made no ruling in relation to this matter. The Panel noted the position was the same in this case, Case AUTH/3029/4/18, and thus made no ruling with regard to Clause 15.9.

The Panel noted that a further allegation in the present case, Case AUTH/3029/4/18, concerned the slides being amended by the employee of the third party agency following approval by GW Pharmaceuticals, and that the amended version was not certified. The Panel noted GW Pharmaceuticals' submission that as the slides were non-promotional GW Pharmaceuticals did not consider that they required certification under the Code. The Panel noted its comments above with regard to GW Pharmaceuticals being able to take the benefit of the exemption from the definition of promotion at Clause 1.2 in relation to unsolicited requests which did not require certification and the Panel therefore ruled no breach of Clause 14.1. The Panel subsequently ruled no breach of Clauses 15.2, 9.1 and 2.

Complaint received **5 April 2018**

Case completed **21 December 2018**

HEALTH PROFESSIONAL v ASTRAZENECA

Patient engagement webpages

An anonymous complaint was received about a page on AstraZeneca UK's Medicines website. Within the diabetes section there was a 'Fixing Dad' video which was about an ordinary family's battle with type 2 diabetes. The introductory text stated 'To support you and your patients, AstraZeneca has partnered with Fixing Dad to delve deeper in to patient engagement through four new documentaries designed specifically for you as HCPs [healthcare professionals]' and gave the viewer the option to arrange a meeting with an AstraZeneca representative. The meeting request form stated 'The meeting that you are requesting is an educational meeting, which will also include a promotional element containing information on AstraZeneca's diabetes prescription medicines'.

The complainant alleged that the webpage was promotional given the viewer's ability to contact a representative but he/she noted, however, that there was no prescribing information provided for the products that would be promoted. The video stated that the content was funded by AstraZeneca although it was not clear who had editorial control.

AstraZeneca submitted that the AstraZeneca UK Medicines website was solely for health professionals in the UK and included both promotional and non-promotional information and resources regarding the company's core areas of interest including diabetes. Prior to entering the website, visitors were required to confirm that they were a UK health professional. Any UK resident that did not provide confirmation of this was redirected to the corporate website.

The detailed response from AstraZeneca is given below.

The Panel noted that the Code required prescribing information to be provided in a clear, legible manner in all promotional material. In audio-visual material such as films, DVDs etc and in interactive data systems, the prescribing information might be provided either by way of a document made available to everyone to whom the material was shown/sent or by inclusion on the audio-visual recording or in the interactive data system itself.

In the Panel's view, noting the broad definition of promotion in the Code, the section of the AstraZeneca Medicines website at issue, directed solely towards health professionals, was promotional. The Panel noted AstraZeneca's submission that neither the Fixing Dad video nor the webpage were promotional as they did not refer directly or indirectly to the treatment of type 2 diabetes with an AstraZeneca medicine. The Panel noted that the homepage of the AstraZeneca Medicines website listed AstraZeneca

medicines for cardiovascular, diabetes, oncology and respiratory with a link to their respective prescribing information. There were two ways of accessing the Fixing Dad webpage. Firstly, by selecting the diabetes tab on the homepage from which a drop-down menu listed diabetes, the company's diabetes products and Fixing Dad. Alternatively, if the viewer selected diabetes from the aforementioned drop-down list, a Medicines tab opened which listed the company's diabetes products in promotional logo format with their indications and a link to the prescribing information. Adjacent to the aforementioned Medicines tab, the tabs Resources and Fixing Dad appeared, clicking on the latter took the reader to the relevant webpage. In addition the Panel noted that it appeared from the relevant briefing document that representatives introduced Fixing Dad at the end of a promotional call and sent consenting health professionals an email which directed them to the Fixing Dad page on the AstraZeneca Medicines website to view the trailer and book a meeting. Customer Service Associates could show the trailer from the website and introduce the Fixing Dad films in the context of patient engagement. Job bag information indicated that the page was also to be shown at conferences.

In the Panel's view, the fact that the Fixing Dad page gave readers the option to request a meeting with a representative, which the company stated would include a promotional element containing information on AstraZeneca's diabetes prescription medicines, did not automatically mean that the particular webpage was promotional as implied by the complainant. The Panel noted that the trailer did not refer to specific medicines. The Panel, however, considered that the content of the webpage, its context and how it could be accessed were relevant when deciding whether the trailer was promotional. The Panel noted that a health professional might access the webpage from the AstraZeneca Medicines website as described above, or via a link in an email used by the field force to introduce the Fixing Dad/AstraZeneca Partnership. The Panel noted its comments above and considered that the context in which the Fixing Dad page appeared was promotional. It was an integral part of a promotional site. The requirement to include prescribing information was not met and breaches of the Code were ruled.

The Panel noted that the supplementary information to the Code, stated, *inter alia*, that the declaration of sponsorship must be sufficiently prominent to ensure that readers of sponsored material were aware of it at the outset. The wording of the declaration must be unambiguous so that readers would immediately understand the extent of the company's involvement and influence over the material.

The Panel noted AstraZeneca's submission that the following message was displayed for the first 16 seconds of the 3 minute trailer:

'Fixing Dad and AstraZeneca are now working in collaboration to bring you four new documentaries throughout 2018, exploring patient engagement from both the [health professional's] and patients' perspective.'

AstraZeneca have funded this project.'

The Panel noted that above this it was stated 'In 2016, the original Fixing Dad documentary explored an ordinary family's battle with type 2 diabetes and how a patient can become engaged with their disease'.

The Panel noted the complaint concerned the trailer alone. The trailer which concluded with a display of the AstraZeneca and Fixing Dad logos, was commissioned by AstraZeneca using the format and content previously independently developed by Fixing Dad for its documentary.

In the Panel's view it was clear from the trailer that AstraZeneca had commissioned the trailer and going forward it would be funding a project in which it collaborated with Fixing Dad to create further documentaries. The Panel ruled no breach in relation to the declaration displayed on the trailer; in its view the role of the company was sufficiently clear.

An anonymous complainant who described him/herself as a 'concerned UK health professional' complained about a page on AstraZeneca UK Limited's AstraZeneca Medicines website. Within the diabetes section there was a 'Fixing Dad' video which was about an ordinary family's battle with type 2 diabetes. The introductory text stated 'To support you and your patients, AstraZeneca has partnered with Fixing Dad to delve deeper in to patient engagement through four new documentaries designed specifically for you as HCPs [healthcare professionals]' and gave the viewer the option to arrange a meeting with an AstraZeneca representative. The meeting request form stated 'The meeting that you are requesting is an educational meeting, which will also include a promotional element containing information on AstraZeneca's diabetes prescription medicines'.

COMPLAINT

The complainant alleged that the material which he/she described as a diabetic service was promotional given the viewer's ability at the end to contact a representative. The complainant noted, however, that there was no prescribing information provided for the products that would be promoted. The video stated that the content was funded by AstraZeneca although it was not clear who had editorial control.

When writing to AstraZeneca, the Authority asked it to consider the requirements of Clauses 4.1, 4.5 and 9.10.

RESPONSE

AstraZeneca explained that the video and webpage were part of a larger audio-visual and face-to-face project that it had undertaken in partnership with Fixing Dad Ltd to help health professionals engage their type 2 diabetes patients. The difficulties encountered by the founders of Fixing Dad in engaging their father in his diagnosis were the core motivations that led to their original Fixing Dad documentary which aired in 2016. AstraZeneca also recognised poor patient engagement as a key challenge to the successful management of type 2 diabetes. Through its engagement with Fixing Dad, AstraZeneca hoped to support optimal patient care and fulfil its responsibilities in an area of healthcare in which it had a significant scientific interest. This project and the supporting materials were non-promotional; they contained information about human health and diseases with no direct or indirect reference to specific medicines.

AstraZeneca submitted that neither the video nor the webpage were promotional; they contained no direct or indirect reference to the treatment of type 2 diabetes with an AstraZeneca medicine. They were certified as non-promotional, educational material and, in line with the Code, did not require the incorporation of prescribing information or the other obligatory information laid out in Clause 4.

AstraZeneca noted the complainant's submission that the webpage was promotional because it enabled the viewer to arrange a promotional meeting. In AstraZeneca's view, a communication to arrange a promotional meeting where the communication itself was free from product information, promotional claims and branding, did not promote the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicine.

AstraZeneca recognised and strongly supported the inclusion of prescribing information on promotional material where it served to ensure the proper administration of medicines but it rejected the complainant's alleged breaches of Clauses 4.1 and 4.5 as neither in keeping with the letter nor the spirit of the Code.

AstraZeneca noted that the beginning of the video displayed the message:

'Fixing Dad and AstraZeneca are now working in collaboration to bring you four new documentaries throughout 2018, exploring patient engagement from both the [health professional's] and patients' perspective.'

AstraZeneca have funded this project.'

This statement was displayed for the first 16 seconds of the 3 minute trailer. The trailer, which concluded with a display of the AstraZeneca and Fixing Dad logos, was commissioned by AstraZeneca using the format and content previously independently developed by Fixing Dad for its BBC documentary. The contractual agreement supporting this

collaboration allowed AstraZeneca to comment on and, if necessary, reject work produced by Fixing Dad. The video was hosted on AstraZeneca's own webpage, and not as discussed in the supplementary information to Clause 9.10, circulated by an otherwise wholly independent party. AstraZeneca considered the statement above fulfilled the requirements of Clause 9.10 and genuinely reflected a collaborative project which it had funded. The company denied a breach of Clause 9.10.

In response to a request for further information AstraZeneca submitted that the AstraZeneca Medicines website was an online resource for health professionals. It provided promotional and non-promotional information including:

- Prescribing information for AstraZeneca medicines
- Clinical trial information for some of AstraZeneca medicines
- Promotional information on AstraZeneca medicines
- Support resources for health professionals for their own education and for their use with and patients prescribed AstraZeneca medicines.

AstraZeneca provided details of the certification of the AstraZeneca UK Medicines website. The company explained that the website pages were approved separately and added to a core shell. The document providing job bag information relating to the specific Fixing Dad webpage was highlighted.

AstraZeneca submitted that AstraZeneca Medicines was AstraZeneca UK's health professional's website and was solely for doctors, nurses and pharmacists in the UK. It included both promotional and non-promotional information and resources regarding the company's core areas of interest - cardiovascular, diabetes, oncology, and respiratory medicine - and some relevant information about its supply chain. The metadata for the AstraZeneca website shell visible on search engine results page was:

'FOR HEALTHCARE PROFESSIONALS ONLY –
The AstraZeneca medicines portal provides
information on AstraZeneca products'

Before entering the website, visitors were required to confirm that they were a UK health professional and it was explained that the website contained both promotional and non-promotional content. UK residents that did not provide confirmation of this were redirected to the corporate website at www.astrazeneca.co.uk.

AstraZeneca provided the site map of AstraZeneca Medicines and explained that the video could only be accessed via the Fixing Dad page and was not available via any other method.

AstraZeneca gave details as to how to access the Fixing Dad webpage. Firstly, by selecting the diabetes tab on the homepage from which a drop down menu listed diabetes, the company's diabetes products and Fixing Dad. Alternatively, if the viewer selected diabetes from the aforementioned drop down list, a Medicines tab opened which listed

the company's diabetes products in promotional logo format with their indications and a link to the prescribing information. Adjacent to the aforementioned Medicines tab, the tabs Resources and Fixing Dad appeared, clicking on the latter took the reader to the relevant webpage. The Fixing Dad video was embedded into the Fixing Dad page and could not be viewed in isolation.

AstraZeneca noted that on the Fixing Dad website page it was stated 'Alongside this, we will create some resources to help support you during your conversations with patients. They will be released throughout 2018 to further explore the impact of patient engagement to both HCPs and patients'. AstraZeneca submitted that, to date, the only resource available to health professionals, via AstraZeneca personnel, was the first documentary (ref GB-10790 DOP March 2018). This was for use with health professionals only and in its current form and must not be used with patients or the public. As detailed in the Works Agreement, 'each film will be accompanied by a short video intended for HCPs to share with their patients in the order of 2 minutes duration'. This material was currently being created and in early stages of development. These videos would provide a resource for the health professional to use with patients to support their management, ownership and engagement with their type 2 diabetes.

PANEL RULING

The Panel noted that Clause 4.1 required prescribing information to be provided in a clear, legible manner in all promotional material. Clause 4.5 stated that in the case of audio-visual material such as films, DVDs and suchlike and in the case of interactive data systems, the prescribing information might be provided either by way of a document which was made available to all persons to whom the material was shown or sent or by inclusion on the audio-visual recording or in the interactive data system itself.

In the Panel's view, noting the broad definition of promotion at Clause 1.2, the section of AstraZeneca Medicines website at issue, which was directed solely towards health professionals, was promotional. The Panel noted AstraZeneca's submission that neither the Fixing Dad video nor the webpage were promotional as they contained no direct or indirect reference to the treatment of type 2 diabetes with an AstraZeneca medicine. The Panel noted that the homepage of the AstraZeneca Medicines website listed AstraZeneca medicines for cardiovascular, diabetes (Bydureon, Forxiga, Onglyza and QTERN), oncology and respiratory with a link to their respective prescribing information. There were two ways of accessing the 'Fixing Dad' webpage. Firstly, by selecting the diabetes tab at the top of the homepage from which a drop down menu listed diabetes, the company's diabetes products, Forxiga (dapagliflozin), Onglyza (saxagliptin) and QTERN (saxagliptin and dapagliflozin) and Fixing Dad. Alternatively, if the viewer selected Diabetes from the aforementioned drop down menu, a Medicines tab appeared open which listed the diabetes products referred to above in promotional logo format, and their indications with a link to the

relevant prescribing information. Adjacent to the aforementioned Medicines tab, the tabs Resources and Fixing Dad appeared, clicking on the latter took the reader to the relevant webpage. In addition the Panel noted that it appeared from the briefing document for guidance on the AstraZeneca and Fixing Dad partnership, and the use of associated assets, that representatives were introducing Fixing Dad at the end of a promotional call and sending consenting health professionals an email which directed them to the Fixing Dad page on the AstraZeneca Medicines website to view the trailer and book a meeting. Customer Service Associates could show the trailer from the website and introduce the Fixing Dad films in the context of patient engagement. Job bag information indicated that the page was also to be shown at conferences.

In the Panel's view, the fact that the Fixing Dad page gave readers the option to request a meeting with an AstraZeneca representative, which the company stated would include a promotional element containing information on AstraZeneca's diabetes prescription medicines, did not automatically mean that the particular webpage was promotional as implied by the complainant. The Panel noted that the trailer did not refer to specific medicines. The Panel, however, considered that the content of the webpage, its context and how it could be accessed were relevant when deciding whether the trailer was promotional. The Panel noted that a health professional might access the webpage as described above, or via a link in an email used by the field force to introduce the Fixing Dad/AstraZeneca Partnership. The Panel noted its comments above and considered that the context in which the Fixing Dad page appeared was promotional. It was an integral part of a promotional site. The requirement to include prescribing information was not met and breaches of Clauses 4.1 and 4.5 were ruled.

The Panel noted that the supplementary information to Clause 9.10, Declaration and Sponsorship, stated, *inter alia*, that the declaration of sponsorship must

be sufficiently prominent to ensure that readers of sponsored material were aware of it at the outset. The wording of the declaration must be unambiguous so that readers would immediately understand the extent of the company's involvement and influence over the material.

The Panel noted AstraZeneca's submission that the following message was displayed for the first 16 seconds of the 3 minute trailer:

'Fixing Dad and AstraZeneca are now working in collaboration to bring you four new documentaries throughout 2018, exploring patient engagement from both the [health professional's] and patients' perspective.

AstraZeneca have funded this project.'

The Panel noted that above this was the statement 'In 2016, the original Fixing Dad documentary explored an ordinary family's battle with type 2 diabetes and how a patient can become engaged with their disease'.

The Panel noted the complaint concerned the trailer alone. The trailer which concluded with a display of the AstraZeneca and Fixing Dad logos, was commissioned by AstraZeneca using the format and content previously independently developed by Fixing Dad for its BBC documentary.

In the Panel's view it was clear from the trailer that AstraZeneca had commissioned the trailer and going forward it would fund a collaborative project with Fixing Dad to create further documentaries. The Panel ruled no breach of Clause 9.10 in relation to the declaration displayed on the trailer; in its view the role of the company was sufficiently clear.

Complaint received **25 April 2018**

Case completed **4 October 2018**

ANONYMOUS HEALTH PROFESSIONAL v BAYER

Promotion of Xarelto

An anonymous complainant who described him/herself as a 'concerned UK health professional' complained about an Xarelto (rivaroxaban) advertisement by Bayer. Xarelto was a novel oral anticoagulant (NOAC) licensed to prevent thrombotic events in differing groups of patients. The advertisement at issue was headed 'Xarelto Protects Your High-Risk NVAF [non-valvular atrial fibrillation] Patients with Confidence'; the second of three bullet points below read 'In your patients with renal impairment'.

The complainant submitted that renally impaired patients were difficult to treat and in that regard, the Xarelto summary of product characteristics (SPC) stated:

'Limited clinical data for patients with severe renal impairment (creatinine clearance 15-29 ml/min) indicate that rivaroxaban plasma concentrations are significantly increased. Therefore, Xarelto is to be used with caution in these patients. Use is not recommended in patients with creatinine clearance <15 ml/min.'

In the complainant's view there was a big difference between using something with confidence and there being limited data and using it with caution or its use not being recommended. The complainant accepted that although this was technically within the licence, patients could still be put at risk.

The detailed response from Bayer is given below.

The Panel noted that the Xarelto SPC stated that limited data for patients with severe renal impairment indicated that rivaroxaban plasma concentration levels were significantly increased and so because of the possible increased risk of bleeding, Xarelto was to be used with caution in these patients. Use was not recommended in those with creatinine clearance CrCl of <15ml/min. In patients with moderate (CrCl 30-49ml/min) or severe (CrCl 15-29ml/min) renal impairment a reduced dose of Xarelto was recommended in patients with non-valvular atrial fibrillation.

The Panel queried Bayer's submission that 'renal impairment' was used in good faith to account for the majority of such patients who presented to a treating physician ie those with mild-to-moderate renal impairment and that a further detailed explanation about the severity of renal impairment and Xarelto dosing was addressed in the explanatory footnote. The Panel noted its comments above with regard to the reduced dose required in patients with moderate renal impairment and that rivaroxaban plasma levels might increase in these patients which could potentially lead to an

increased bleeding risk. The Panel did not consider that the statement 'A single consideration for dose reduction (moderate and severe renal impairment, CrCl 15-49mL/min. CrCl 15-29mL/min: to be used with caution)' which appeared in very small font above the prescribing information as a footnote to the third bullet point 'With the simplest dosing algorithm of any NOAC' negated the otherwise misleading impression of the claim at issue in relation to renal impairment.

The Panel disagreed with Bayer's submission that the complainant's concerns were unfounded because 'confidence' in the claim 'Xarelto Protects Your High-Risk NVAF Patients with Confidence' referred to efficacy in preventing stroke, which was the possible consequence of NVAF. The Panel did not consider that this was clear, the indication was not stated in the body of the advertisement.

In the Panel's view the claim 'In your patients with renal impairment' was ambiguous as acknowledged by Bayer; the unqualified claim, read in conjunction with the prominent headline 'Xarelto Protects your High-Risk NVAF Patients with Confidence', implied that Xarelto could be used with confidence in all NVAF patients with renal impairment which was not so. The Panel considered that the misleading implication was compounded by the claim 'Tested in more high-risk patients than any other NOAC and prescribed to over 33 million patients across 7 indications'. The Panel considered that the claim was misleading and was not capable of substantiation and breaches of the Code were ruled. In the Panel's view Bayer had failed to maintain high standards and a breach of the Code was ruled.

The Panel considered that the claim at issue could potentially put the safety of NVAF patients with severe renal impairment (CrCl 15-29ml/min) and those with CrCl <15ml/min at risk and thus brought discredit upon and reduced confidence in the pharmaceutical industry, a breach of Clause 2 of the Code was ruled.

An anonymous complainant who described him/herself as a 'concerned UK health professional', complained about a Xarelto (rivaroxaban) advertisement (ref UKXAR01180037d) placed by Bayer Plc in Pulse, April 2018. Xarelto was a novel, oral anticoagulant (NOAC) licensed to prevent thrombotic events in a number of different patient groups. The advertisement at issue had the headline 'Xarelto Protects Your High-Risk NVAF [non-valvular atrial fibrillation] Patients with Confidence'; the second of three bullet points below read 'In your patients with renal impairment'.

COMPLAINT

The complainant noted the bullet point 'In your patients with renal impairment' and submitted that such patients were difficult to treat and in that regard, he/she noted that the Xarelto summary of product characteristics (SPC) stated:

'Limited clinical data for patients with severe renal impairment (creatinine clearance 15-29 ml/min) indicate that rivaroxaban plasma concentrations are significantly increased. Therefore, Xarelto is to be used with caution in these patients. Use is not recommended in patients with creatinine clearance <15 ml/min.'

The complainant stated that in his/her view there was a great difference between using something with confidence and there being limited data and use with caution/use was not recommended. The complainant accepted that this was technically within the licence but he/she still considered that it could put patients at risk.

When writing to Bayer the Authority asked it to consider the requirements of Clauses 2, 7.2, 7.4, 7.9 and 9.1 of the Code.

RESPONSE

Bayer noted that the complainant was concerned about the claim 'Xarelto Protects Your High-Risk NVAF Patients with Confidence [...] in your patients with renal impairment'. Specifically, the complainant's concern appeared to be about the interpretation of confidence in NVAF patients with severe renal impairment (creatinine clearance (CrCl) ≤29ml/min).

Within the context of NVAF, the licensed indication for Xarelto was:

'Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack.'

And with regard to renally impaired patients, the SPC stated:

'Limited clinical data for patients with severe renal impairment (creatinine clearance 15 - 29 ml/min) indicate that rivaroxaban plasma concentrations are significantly increased. Therefore, Xarelto is to be used with caution in these patients. Use is not recommended in patients with creatinine clearance < 15 ml/min (see sections 4.4 and 5.2).

In patients with moderate (creatinine clearance 30 - 49 ml/min) or severe (creatinine clearance 15 - 29 ml/min) renal impairment the following dosage recommendations apply:

- for the prevention of stroke and systemic embolism in patients with non-valvular atrial

fibrillation, the recommended dose is 15 mg once daily (see section 5.2).'

Therefore, patients with mild renal impairment were treated at the normal dose of 20mg, patients with moderate renal impairment (CrCl 30-49ml/min) at the reduced dose of 15mg, and patients with severe renal failure (CrCl 15-29ml/min) might be treated with caution at the reduced dose of 15mg. Use was not recommended in patients with a CrCl <15ml/min. Bayer noted that the majority of patients with renal impairment had mild-to-moderate impairment (CrCl >30ml/min).

Bayer acknowledged the complainant's concerns in that renally impaired NVAF patients could be difficult to treat which was why that important patient cohort was included in the pivotal Phase III study for Xarelto, as well as being in focus in the advertisement.

Bayer submitted, however, that the complainant's concerns were unfounded, as the 'confidence' referred to efficacy in preventing stroke, which was the possible consequence of NVAF in the claim 'Xarelto Protects Your High-Risk NVAF Patients with Confidence'. Additionally, the advertisement contained the following explanatory statement 'A single consideration for dose reduction (moderate and severe renal impairment, CrCl 15-49ml/min. CrCl 15-29ml/min: to be used with caution).'

Consequently, Bayer did not agree that the advertisement placed patients at risk. Bayer submitted that the mention of renal impairment was highly relevant to efficacy claims in high-risk NVAF because:

- the prevalence of both atrial fibrillation (AF) and renal impairment increased with age
- both conditions shared major risk factors, common comorbidities and polypharmacy
- irrespective of geographic location, observational studies revealed that older patients with AF and those with renal dysfunction were undertreated with anticoagulants (Fox *et al* 2011)
- both AF and renal impairment independently increased the risk of stroke and systemic thromboembolism (Olesen *et al* 2012, Fox *et al*)
- AF was known to increase the risk of stroke by a factor of approximately five
- renal impairment had also been shown to increase the risk of stroke or systemic embolism cumulatively in patients with AF (Olesen *et al*)
- In a registry of 132,372 patients with AF, non-end-stage chronic kidney disease increased the risk of stroke or systemic thromboembolism compared with no renal disease (hazard ratio, 1.49; 95% confidence interval [CI], 1.38 to 1.59; p<0.001) as did those requiring renal-replacement therapy (hazard ratio, 1.83; 95% CI, 1.57 to 2.14; p<0.001) (Olesen *et al*).

Bayer stated that the efficacy for Xarelto in patients with NVAF and renal impairment was substantiated by the following:

- in ROCKET AF (the pivotal Phase III study for Xarelto in NVAF), patients with mild renal

impairment (CrCl 50-80ml/min), and moderate renal impairment (CrCl 30-49ml/min) were included per protocol (Fox *et al*). Out of all the Phase III NOAC studies, ROCKET AF had the greatest proportion of high risk patients both in terms of stroke risk and bleeding risk

- patients with moderate renal impairment comprised 20.7% of the ROCKET AF study population (n=2950) (Fox *et al*). These patients with moderate renal impairment were administered a reduced dose of rivaroxaban (15mg once a day). ROCKET AF was the only Phase III NOAC study to have prospectively tested a specific renal dose
- 26.3% of the final analysis population in ROCKET AF had worsening renal function (WRF), defined as a decrease of >20% in CrCl from the screening CrCl measurement at any time during the study period. A number of these patients would have progressed to severe renal impairment during the course of the study. WRF patients who were randomized to receive rivaroxaban had a reduction in stroke or systemic embolism compared with those who took warfarin (1.54 vs 3.25 events per 100 patient-years) that was not seen in patients with stable renal function who were randomized to receive rivaroxaban (p=0.050). There was no difference in major or non-major clinically relevant bleeding among WRF patients randomized to warfarin vs rivaroxaban. (Fordyce *et al* 2016)
- The efficacy and safety (bleeding) results from ROCKET AF subjects with mild-to-moderate renal insufficiency behaved homogeneously with the study population overall. Specifically, the reduced dose of rivaroxaban preserved the treatment effect of warfarin without increasing bleeding and with fewer fatal bleeds than warfarin (Fox *et al*).

Consequently, Xarelto was licensed for use in patients with mild, moderate and severe (CrCl>15ml/min) renal impairment, as well as in those with normal renal function. 'Confidence' in the advertisement pertained not only to the quality and quantity of data in high risk patients, but to the consistent safety and efficacy profile seen in these patients, including those with mild- to-moderate renal impairment, treated with rivaroxaban in the ROCKET AF study.

As with many disease areas or organ dysfunctions, renal impairment existed on a spectrum of severity and pathology, from the mildest, through to moderate then severe, or more granularly classified as Stage 1-5 renal impairment. It was generally well understood by clinicians that disease or pathophysiological processes such as renal impairment, were a spectrum, and that 'renal impairment' did not describe, on an individual patient basis, the full clinical spectrum of the condition to which they referred, and that there was more clinical granularity beyond this. 'Renal impairment' was used in good faith in the advertisement to account for the majority of such patients who presented to a treating physician ie those with mild-to-moderate renal impairment. Further detailed explanation about the severity of renal impairment and Xarelto dosing was addressed

in the explanatory statement. In addition, other than the inclusion of the prescribing information, the main body of the advertisement contained no information about the posology or method of administration on which to make a prescribing decision. Bayer thus did not agree with the complainant's assertion that the advertisement could put patients at risk.

Bayer denied breaches of Clauses 2, 9.1, 7.4 and 7.9.

Bayer acknowledged, however, after careful consideration of the complaint, that there was the possibility for ambiguity in the claim in question. The wording of the advertisement could be further optimised and clarified in future, through the addition of a specific description of the classification of renally impaired patients included within the efficacy claim. Bayer thus accepted a breach of Clause 7.2. The advertisement, and all materials with related claims, had been withdrawn. Bayer submitted that it had amended relevant materials for future advertising.

PANEL RULING

The Panel noted that the advertisement in question had the headline 'Xarelto Protects Your High-Risk NVAF Patients with Confidence' followed by three bullet points: 'With a well-established efficacy and safety profile; In your patients with renal impairment' and 'With the simplest dosing algorithm of any NOAC'. Below these bullet points it stated 'Tested in more high-risk patients than any other NOAC and prescribed to over 33 million patients, across 7 indications'.

The Panel noted that Section 4.2 of the Xarelto 20mg SPC Special populations, Renal Impairment, stated that limited data for patients with severe renal impairment indicated that rivaroxaban plasma concentration levels were significantly increased. Therefore, Xarelto was to be used with caution in these patients. Use was not recommended in patients with CrCl in <15ml/min. In patients with moderate (CrCl 30-49ml/min) or severe (CrCl 15-29ml/min) renal impairment the reduced dose of 15mg once daily was recommended for the prevention of stroke and systemic embolism in patients with NVAF.

The Panel noted that Section 4.4 of the Xarelto 20mg SPC stated that in patients with severe renal impairment (CrCl <30ml/min) rivaroxaban plasma levels might be significantly increased (1.6 fold on average) which might lead to an increased bleeding risk. Xarelto was to be used with caution in patients with creatinine clearance 15-29ml/min. Use was not recommended in patients with CrCl <15ml/min.

Section 5.2 stated that there was an increase in rivaroxaban exposure correlated to decrease in renal function, as assessed via creatinine clearance measurements. In individuals with mild (CrCl 50-80ml/min), moderate (CrCl 30-49ml/min) and severe (CrCl 15-29ml/min) renal impairment, rivaroxaban plasma concentrations (AUC) were increased 1.4, 1.5 and 1.6 fold respectively. Corresponding increases in pharmacodynamic effects were more pronounced.

In individuals with mild, moderate and severe renal impairment the overall inhibition of factor Xa activity was increased by a factor of 1.5, 1.9 and 2.0 respectively as compared to healthy volunteers; prolongation of PT was similarly increased by a factor of 1.3, 2.2 and 2.4 respectively. There were no data in patients with CrCl <15ml/min.

The Panel queried Bayer's submission that 'renal impairment' was used in good faith in the advertisement to account for the majority of such patients who presented to a treating physician ie those with mild-to-moderate renal impairment and that a further detailed explanation about the severity of renal impairment and Xarelto dosing was addressed in the explanatory footnote. The Panel noted its comments above with regard to the reduced dose required in patients with moderate renal impairment and that rivaroxaban plasma levels might increase (1.5 fold on average) in these patients which could potentially lead to an increased bleeding risk. The Panel did not consider that the statement 'A single consideration for dose reduction (moderate and severe renal impairment, CrCl 15-49ml/min. CrCl 15-29mL/min: to be used with caution)' which appeared in very small font above the prescribing information as a footnote to the bullet point 'With the simplest dosing algorithm of any NOAC' negated the otherwise misleading impression of the claim at issue in relation to renal impairment.

The Panel disagreed with Bayer's submission that the complainant's concerns were unfounded, as 'confidence' in the claim 'Xarelto Protects Your High-Risk NVAF Patients with Confidence' referred to efficacy in preventing stroke, which was the possible consequence of NVAF. The Panel did not consider that this was clear, the indication was not stated in the body of the advertisement.

In the Panel's view the claim 'In your patients with renal impairment' was ambiguous as acknowledged by Bayer and as a standalone claim it did not make grammatical sense. In the Panel's view the unqualified claim would be read in conjunction with the prominent headline claim 'Xarelto Protects your High-Risk NVAF Patients with Confidence' and implied that Xarelto could be used with confidence in all NVAF patients with renal impairment which was not so. The Panel considered that the misleading

implication was compounded by the claim 'Tested in more high-risk patients than any other NOAC and prescribed to over 33 million patients across 7 indications'.

The Panel considered that the claim was misleading and was not capable of substantiation and a breach of Clauses 7.2 and 7.4 were ruled.

The Panel noted that Clause 7.9 was raised by the case preparation manager. Clause 7.9 stated that information and claims about adverse reactions must reflect available evidence or be capable of substantiation by clinical experience and it must not be stated that a product has no adverse reactions, toxic hazards or risks of addiction or dependency. The word 'safe' must not be used without qualification. The Panel did not consider that there was an allegation in this regard and therefore made no ruling.

The Panel noted its comments and rulings above and considered that Bayer had failed to maintain high standards and a breach of Clause 9.1 was ruled. The Panel noted Bayer's submission that the wording of the advertisement could be further optimised and clarified in future, through the addition of a specific description of the classification of renally impaired patients included within the efficacy claim. The advertisement, and all materials with related claims, had been withdrawn. Nonetheless, the Panel noted that examples of activities that were likely to be in breach of Clause 2 included prejudicing patient safety. The Panel noted the relevant sections of the SPC referred to above and the correlation between decrease in renal function and increase in rivaroxaban exposure, which might lead to an increased bleeding risk in some NVAF patients with renal impairment. The Panel considered that the claim at issue could potentially put the safety of NVAF patients with severe renal impairment (creatinine clearance 15-29ml/min) and those with CrCl <15ml/min at risk and thus brought discredit upon and reduced confidence in the pharmaceutical industry and a breach of Clause 2 was ruled.

Complaint received **26 April 2018**

Case completed **8 October 2018**

HEALTH PROFESSIONAL v NOVARTIS

Conduct of an employee on LinkedIn

An anonymous contactable complainant who described themselves as a concerned UK health professional complained about a named Novartis employee using LinkedIn to promote medicines. The medicines at issue were Entresto (sacubitril/valsartan) used in adults with chronic heart failure, and Cosentyx (secukinumab) used in adults with moderate to severe plaque psoriasis.

The complainant noted that he/she had received information on LinkedIn that had been shared ('liked' posts) and considered it inappropriate for company employees to use LinkedIn to promote information, including studies, about their companies' products. It was promotion to non-prescribers and the complainant doubted that the materials shared had undergone appropriate internal review. The material at issue included: an article which discussed the prescribing behaviour of cardiologists and how to price new medicines in relation to the Entresto launch; Vivinda TV which appeared to be a resource solely intended for health professionals but was being advertised to the public; and advertising of a Novartis press release regarding Phase III data for Cosentyx.

The detailed response from Novartis is given below.

The Panel noted that the complaint concerned LinkedIn activity on an employee's personal LinkedIn account. In the Panel's view, it was of course not unacceptable for company employees to use personal LinkedIn accounts and the Code would not automatically apply to all activity on a personal account; if activity was found to be within the scope of the Code, the company would be held responsible.

The Panel noted that material could be disseminated or highlighted by an individual on LinkedIn in a number of ways including posting, sharing, commenting or liking. The algorithms applied by LinkedIn were relevant including whether an individual could opt out of material being disseminated by such algorithms. In the Panel's view, activity conducted on social media that could potentially alert one's connections to the activity might be considered proactive dissemination of material. In addition an individual's activity and associated content might appear in the individual's list of activities on his/her LinkedIn profile page which was visible to his/her connections; an individual's profile page was also potentially visible to others outside his/her network depending on the individual's security settings.

The Panel noted that the complaint concerned three specific activities:

- 1 Sharing an article on the prescribing behaviour of cardiologists and how to price new medicines in relation to the Entresto launch

The Panel noted Novartis' submission that the hyperlink provided by the complainant had been proactively shared by the named employee with his/her connections on the LinkedIn platform.

The Panel noted that the original article appeared to have been authored and posted by a journalist at LinkedIn as part of a weekly 'Premium report' which highlighted healthcare news. The original post contained a video and written report of an interview with a named Novartis senior leader. The Panel noted Novartis' submission that the content of the article was focussed on the business approach to a product launch and lessons learnt from the launch of Entresto. The Panel noted that Entresto was mentioned several times, predominantly in relation to the US health environment, its sales and cost-effectiveness data. The Panel disagreed with Novartis' submission that the article did not position Entresto positively. The article referred to the Institute for Clinical and Economic Review categorising Entresto as cost-effective and the American College of Cardiology and the American Heart Association issuing guidelines which referred to Entresto as the standard of care for certain heart-failure patients, a decision, that the article stated, was often seen as a gold standard in pharmaceutical commercialisation. In the Panel's view, an employee of Novartis proactively sharing the article with his/her connections on LinkedIn was considered to be promotion of Entresto, a prescription only medicine, and the 'share' and its associated content should have been certified. A breach was ruled.

The Panel considered that on the balance of probabilities not all the employee's connections would have been health professionals and therefore sharing of the article with his/her network constituted promotion of a prescription only medicine to the public and a breach was ruled. Furthermore, and on balance, the Panel considered that the positive statements in the article could on the balance of probabilities have encouraged members of the public to ask their health professional to prescribe Entresto and therefore a breach was ruled.

- 2 Advertising VivindaTV, a resource intended for health professionals, to the general public

The Panel noted that the hyperlink provided by the complainant led to a Novartis post on LinkedIn that referred to the latest research in dermatology and referred to Vivinda TV and sessions from a dermatology congress. Readers were invited to

register. The linked registration page clearly stated that to create an account the individual had to declare that he/she was a health professional and their country of practice. The Panel noted that neither the original post nor the linked registration page directly or indirectly referred to specific medicines. The Panel noted Novartis' submission that it appeared the employee in question had 'liked' not 'shared' this Novartis post. Regardless of whether it was liked or shared, the Panel considered that neither the post nor the linked registration page contained any product related information. The viewer would have to register as a health professional to see further material. The Panel therefore did not consider that the employee's endorsement constituted promotion of a prescription only medicine to the public; no information about medicines was supplied to the public and no breaches were ruled accordingly.

The Panel noted that the complainant alleged that materials shared had not undergone internal review. The complainant referred to 'shared (liked posts)' and thus the Panel considered that the allegation covered both 'shared' and 'liked' posts. The Panel noted its comments above that the original post and the linked registration page made no direct or indirect reference to a specific medicine and therefore was not considered as promotional material that required certification. Nor did the Panel consider that it was non-promotional material which required certification. No breaches of the Code were ruled.

3 Advertising a Novartis press release about Cosentyx Phase 3 data

The Panel noted that the third hyperlink provided by the complainant led to a Novartis post announcing data in psoriasis at a 2018 dermatology annual meeting. The post itself did not contain any reference to a product but according to Novartis the 'find out more' link led to a press release about Cosentyx data from the congress. The complainant referred to a press release and Phase III data for Cosentyx. The Panel noted that Novartis had not provided a copy of the press release. The company submitted that the press release was initiated by the Swiss based headquarters and had not been examined by the UK company.

The Panel noted Novartis' submission that the post was 'liked' by the named employee and not 'shared'. The Panel noted its comments above about the number of ways an individual could endorse a post which included 'liking'. The Panel noted Novartis' submission that following receipt of the complaint it had identified information about how activity on LinkedIn was visible to one's connections on their feed. Although it appeared that Novartis had known that a 'share' would alert an individual's connections to the activity, it had not realised that a 'like' could also alert one's connections. Novartis submitted that LinkedIn appeared to have an algorithm which decided which 'likes' it would alert one's connections to. The Panel was surprised that this issue had not come to light previously. It was not inconceivable that similar issues might have occurred previously wherein a 'liked' post

had been disseminated to a Novartis employee's connection(s). The Panel understood that if an individual 'liked' a post it increased the likelihood that the post would appear in his/her connections' LinkedIn feeds, appearing as '[name] likes this'. In the Panel's view, companies should remain vigilant and needed to ensure that they took reasonable steps to highlight the potential compliance issues that might arise from 'liking' certain posts if such posts could thereby potentially be pushed to their connections' feed.

The Panel noted Novartis' explanation that the nature of such an algorithm meant that an individual could not anticipate the outcome of 'liking' a post therefore Novartis did not accept that 'liking' a LinkedIn post was proactively disseminating information in the same way that 'sharing' a post was. Novartis acknowledged that if the named employee had 'shared' the post it might constitute promotion to the public.

The Panel noted that whilst the complainant had provided a copy of the original Novartis post, beneath which was a list of likes, he/she referred to 'receiving information' on LinkedIn. The Panel therefore considered that on the balance of probabilities the employees 'like' had been disseminated by the algorithm to his/her contacts and further considered that such dissemination was the subject of complaint.

In the Panel's view that an algorithm had disseminated an individual's 'like' did not absolve Novartis from responsibility. The Panel considered that the proactive dissemination of a press release about a prescription only medicine to those who were not health professionals or other relevant decision makers promoted that medicine to the public and might encourage such recipients to ask their doctor to prescribe it. Breaches were ruled. The Panel considered that the 'like' of the post and its associated content would constitute promotional material and would require certification under the Code. A breach was ruled.

The Panel was mindful of the complex issues that had to be addressed by companies when advising staff about personal social media use. The increasing use of social media, both in personal and business capacity presented challenges. In addition, many social media platforms used algorithms and had settings which individuals and companies might not be fully aware of.

The Panel was aware that the types of activity performed by the named employee on LinkedIn was not uncommon across the industry. In the Panel's view, employees might feel inclined to endorse articles related to their senior colleagues on LinkedIn or their company's corporate social media posts and depending on the content such activity might or might not fall within the scope of the Code, therefore companies needed to issue specific and unambiguous guidance on personal use of social media. This was particularly important if UK employees were likely to follow the social media accounts of overseas affiliates which might have codes, laws and regulations that differed to the

UK. In the Panel's view it was very important that companies regularly reviewed such guidance.

In the Panel's view, the global social media guidance issued by Novartis to its employees prior to the complaint and dated 2016 was open to interpretation. The Panel was concerned that at the time of the LinkedIn activity in question there was no UK local guidance. The Panel noted that after Novartis was notified of this complaint a UK wide communication was sent. The Panel was concerned about the absence of UK specific guidance at the relevant time. The Panel noted its comments and rulings of breaches of the Code as set out above. Overall, the Panel considered that high standards had not been maintained and ruled accordingly. On balance the Panel did not consider that the circumstances warranted a breach of Clause 2.

An anonymous contactable complainant who described themselves as a concerned UK health professional complained about a Novartis employee using LinkedIn to promote medicines. The medicines at issue were Entresto (sacubitril/valsartan) used in adults with chronic heart failure, and Cosentyx (secukinumab) used in adults with moderate to severe plaque psoriasis.

COMPLAINT

The complainant noted that he/she had received information on LinkedIn that had been shared ('liked' posts) by a named Novartis employee. The complainant did not consider that it was appropriate for company employees to use LinkedIn to promote information including studies about their companies' own products. The complainant stated that it was promotion to non-prescribers. The complainant doubted that the materials shared had undergone appropriate internal review. The material at issue included: an article which discussed the prescribing behaviour of cardiologists and how to price new medicines in relation to the Entresto launch; Vivinda TV which appeared to be a resource solely intended for health professionals but was being advertised to the public; and advertising of a Novartis press release regarding Phase III data for Cosentyx.

When writing to Novartis, the Authority asked it to consider the requirements of Clauses 2, 9.1, 14.1, 14.3, 26.1 and 26.2 of the Code.

RESPONSE

Novartis submitted that social media platforms were an important channel of communication, through which the industry could and should engage society in high level topics about science and build the reputation of the industry as an essential component of health care. The company recognised that social media played an increasingly important role in the professional and personal lives of its employees. However, the company took its responsibilities under the Code very seriously and, as such, appreciated this and other opportunities to understand the perspectives of others, to re-examine how it conducted its business, and to continually learn and adapt how it might appropriately manage the use of these rapidly evolving platforms and technologies.

Novartis stated that it was very concerned to receive the complaint. Novartis stated that it was clear that whilst company employees had the right to use personal accounts on social media platforms to communicate their own views and perspectives, the Code might, in some circumstances, apply to such posts and that the company might therefore be held responsible for them; each case would need to be decided by a consideration of all of the circumstances. That said, in such a complex and nuanced regulatory environment, where the effect of self-regulation was decided on a case-by-case basis after the fact, it might be difficult for employees to decide how to approach their personal social media activity. This potential difficulty was even more evident in fora such as LinkedIn which was a business and employment network associated with an employee's professional interests.

Novartis understood the complainant was concerned that information had potentially been shared with him/her by a named Novartis employee through the employee having 'liked' some LinkedIn posts. Novartis noted that the complainant was concerned about the use of LinkedIn to '... promote information ...' and that he/she was concerned that this had included studies about Novartis products. Novartis also noted that the complainant was concerned that this might constitute '... promotion to non-prescribers ...' and was doubtful whether the shared materials had been appropriately reviewed internally.

These concerns were referenced specifically to three discrete LinkedIn activities by the employee.

Novartis fully understood that proactive sharing of detailed information about a company medicine by a company employee would likely constitute promotion, regardless of whether the channel of communication was digital, paper or verbal. Novartis also recognized that in determining whether the activities cited by the complainant in this case were appropriately conducted or not, all of the circumstances should be taken into account, as summarized in both the PMCPA's 'Guidance About Digital Communication' and in Case AUTH/2988/10/17.

Novartis noted that this consideration should include the nature of the material disseminated, the audience in receipt of the material, any product references, the company's role in creating the material posted and whether the posting was directed, encouraged or otherwise acquiesced by the company. Novartis also believed it important in this case to understand the degree to which information was proactively disseminated as opposed to it being available to view. Specifically, the differences between the LinkedIn activities of 'post', 'share' (or 're-post') and 'like' were relevant considerations.

Hyperlink 1

Novartis noted that the complainant provided a hyperlink and stated that it discussed the prescribing behaviour of cardiologists and how to price new medicines in relation to the Entresto launch. The hyperlink led to a 'share' by the named employee. Novartis submitted that a share effectively meant

an individual had proactively shared content from a third party with his/her 'connections' on the LinkedIn platform and was shown as a 'share' in the individual's list of activity provided on his/her LinkedIn profile page. The employee had not commented on the share and he/she was not the original 'poster' of the initial content. Novartis noted that the hyperlink provided by the complainant no longer linked to the 'share' in contention and the 'share' was no longer visible on the list of activity on the named employee's profile page. This was because Novartis considered it important that the employee remove the post until this case had been ruled upon.

Novartis stated that the original article was a business news article from a series entitled 'LinkedIn Premium Report, Healthcare' which was generated and posted by LinkedIn. The introduction to the article stated that the Premium Report series '... highlight industry trends, job moves and healthcare openings ...' making it clear that the material was focussed on the conduct of business and employment within healthcare.

The material appeared to be based upon an interview with a named senior leader at Novartis conducted by a LinkedIn journalist. The post consisted of a short video clip and a written report, which were broadly similar in context and content. The original content was provided.

Novartis submitted that the content of the written article was centred on questions from the LinkedIn journalist as to why Entresto did not meet the expectations of finance analysts. In the opening paragraph the journalist provided the following opinion:

'It's never made much sense to me why Novartis's Entresto, a fairly priced heart-failure drug that was the first new medicine in its category in more than a decade, largely failed to excite cardiologists' and goes on to describe how the medicine '... underperformed in its first two years on the market.'

The named Novartis senior leader explained that it was a struggle to get use in the system, despite having data that led to inclusion in guidelines and which demonstrated the level of cost-effectiveness of the product. He/she described two issues (pricing and the need to enable changes in behaviour when clinicians were provided with a new treatment option) that prevented the expected uptake.

Novartis submitted that the article focussed on understanding the business approaches to pharmaceutical product launches and the business lessons Novartis had learned from a recent launch. Although the further discussion referred to Entresto and its clinical and cost-effectiveness data, the content did not position Entresto positively, did not focus on detailed descriptions of Entresto use or clinical data and did not include promotional claims. Novartis thus did not consider that the article encouraged the administration, consumption, prescription, purchase, recommendation, sale, supply or use of Entresto. In that regard, Novartis did not believe that the proactive sharing of this

content by the Novartis employee constituted promotion as defined in Clause 1, or advertising to the public as defined in Clause 26.1 (nor did it meet the definition of an advertisement as provided in Section 3.3 of the MHRA 'Blue Guide'). Novartis also considered that, as such, it did not need certification as required by Clause 14.1.

As the information provided was business focussed, rather than being about the medicines *per se* and there was no detailed discussion about how diseases were managed or how treatments were clinically used, Novartis believed that the information provided did not fall into any of the three categories of 'information to the public' described in the supplementary information to Clause 26.2 (proactive information about a medicine, reference information or reactive information), or that it constituted 'educational material for the public or patients ... relating to diseases or medicines ...' as covered by Clause 14.3 of the Code. As such, Novartis did not believe that the employee's re-post of this material constituted a breach of Clause 26.2 or that there was any requirement to examine the 'share', as would otherwise be required by the supplementary information to Clause 14.3.

Hyperlink 2

The second hyperlink provided by the complainant led to a Novartis post on LinkedIn which advertised the availability of educational content on dermatology, intended for health professionals, which was accessed via a Novartis proprietary platform called VivindaTV. The VivindaTV platform was used to enable registered health professionals to 'attend' scientific congresses and/or access their content remotely. A screenshot of the content accessed at the address cited by the complainant was provided.

Novartis could find no evidence that this content was proactively 'shared' by the employee (the employee was not named on the post as accessed via the link provided by the complainant and this LinkedIn activity did not appear as a 'share' on the list of activity which was provided on the employee's profile page). Novartis submitted that the post was 'liked' by the named employee. When it was accessed, 122 'likes' of this post could be seen. The list of those who 'liked' the post could be accessed, only if the viewer clicked in the vicinity of the word 'likes'. When Novartis accessed this the named Novartis employee was towards the end (details provided) of the list of 122 who had 'liked' it. Novartis submitted that, in practical terms, this required scrolling through and scanning many names before seeing the name of the employee. Only his/her name was given. A viewer would need to click on the name to see any detail about that individual and, importantly, to be able to see if they were an employee of a company.

With regard to the link to VivindaTV itself, Novartis stated that if a viewer followed the advertised link marked as 'Register Now', he/she would not see any educational content on dermatology. Instead, he/she would land on a page which required him/her to create an account. On clicking 'create an account'

the viewer was taken to a registration page and had to provide details including name, contact details, country and healthcare speciality. He/she must then confirm that he/she was a health professional in that country in order to complete registration.

Regardless of whether this post had been 'liked' or 'shared' by the Novartis employee, Novartis noted that neither the content of the original post nor the pages it linked to, contained any information about medicines, disease or healthcare and as such the pages were not subject to the Code. Furthermore, Novartis submitted that good practice had been demonstrated in that a viewer must register to gain access to any such content and to register, the viewer must actively confirm that he/she was a health professional.

Hyperlink 3

Novartis stated that the third hyperlink provided by the complainant led to a Novartis initiated news article announcing data in psoriasis at the 2018 American Academy of Dermatology Annual Meeting in San Diego. The news post itself did not contain any actual data or refer to a product, but if the 'find out more' link was followed, the viewer was taken to a press release about Cosentyx which gave details about Cosentyx data at the congress. The press release was initiated by the Swiss based headquarters of Novartis, in Basel, on 16 February 2018; as it was not released in the UK and not intended for a solely UK audience, Novartis submitted that the press release had not been examined by the UK company.

Novartis could find no evidence that the article was 'shared' by the named employee (the employee was not named on the post as accessed via the link provided by the complainant and this LinkedIn activity did not appear as a 'share' on the list of activity which was provided on the employee's profile page). Novartis submitted that this post was 'liked' by the named employee, and when this was accessed, there were 440 'likes' of this post. As above, the list of those who 'liked' the post could be accessed; the name of the employee referred to by the complainant appeared well down the list of names (details provided). Novartis noted that the screenshot provided showed 439 likes, not 440. When this was accessed for the investigation, there were 440 likes. However, the screenshot taken at the time of Novartis' investigation did not save properly and would not open, so a second screenshot was made at a later date in order to provide an attachment for this response.

Novartis could find no evidence that the post which referred to psoriasis data release was proactively shared by the employee. It did not appear as a 'share' on the list of activity on his/her profile page and the hyperlink provided by the complainant did not show a 'share' (in contrast to the LinkedIn premium article, which was clearly shared by the employee and shown as such in the hyperlink provided by the complainant and the list of activity on the employee's profile page).

Novartis noted that the complainant clearly stated that the material was 'shared' with him/her by it being 'liked' by the Novartis employee, but Novartis was not able to explain how the complainant had had this 'shared' with him/her, given the absence of this as a 'share' on the list of activity on the employee's profile page and the absence of the employee's name or recognition of him/her sharing the material at the hyperlink provided by the complainant.

During the course of this investigation, Novartis had identified some information which might help the company and the Panel to understand how the complainant had seen content that a contact had 'liked' even if it had not been proactively shared. On the LinkedIn help pages, there was some advice provided to members as to how the visibility and impact of social activity was managed on an individual's 'feed' (the 'feed' being the content that was presented to an individual when they accessed LinkedIn). This help page stated that an individual's LinkedIn feed contained information from his/her network, his/her own likes, shares, posts etc and, importantly, '... other information that we believe you may be interested in'. The help page explained that 'LinkedIn's systems track and analyze social actions such as writing a post or article, liking content, or commenting on another members posts or articles' and that 'This data is used by our algorithms to provide content relevant to you in your LinkedIn feed'.

Novartis stated that it did not have access to LinkedIn proprietary algorithms and it found it hard to understand how an industry could regulate for what appeared to be an Artificial Intelligence approach by LinkedIn in managing the content which was seen by another individual. The very nature of such an algorithm meant that the various potential outcomes of the algorithm could not be anticipated by an individual employee of a company when 'liking' a third-party post. Whilst this was important in terms of the industry learning about how to use LinkedIn and similar platforms appropriately, the fact remained that Novartis could find no evidence that this post was proactively disseminated by its employee.

Novartis recognized the principle that, had the press release about Cosentyx data been proactively disseminated by the employee on his/her personal LinkedIn account, this might constitute promotion to the public for which the company might be responsible. However, as stated above, Novartis considered that the employee's 'like' was not proactive dissemination and, as such, did not constitute promotion to the public. Novartis did not believe that the employee's 'like' of this content was in breach of Clause 26.1 and as it would not require certification or examination it denied breaches of Clauses 14.1 or 14.3.

Instructions to Novartis staff about the use of social media

Novartis submitted that its employees were all given clear instruction on the business and personal use of social media. The UK employee handbook,

given to all Novartis staff when their contracts were issued, contained some of the major policies about employee relations and professional practices. The global social media guidance for both business and personal use was explicitly referred to in the main text of the document and required employees to read the full guidance provided as an appendix within the document. Novartis noted that an employee's contract required them to read and accept the content of the employee handbook when he/she signed. The guidance within the employee handbook was taken from two global guidance documents. Novartis confirmed that the named employee had completed training on these documents.

Summary and additional information

Novartis noted that it was clear from an interview with the named employee that he/she fully understood the global guidance that had been provided and the application of the Code to social media activity. He/she was clear that his/her intent was never to promote, and that he/she believed that the LinkedIn premium article was an interesting business article rather than information about a medicine or disease, and therefore could compliantly share this article. He/she was unsure about sharing the VivindaTV advertisement and so decided to 'like' it rather than 'share' it, in the belief that a 'like' would not proactively disseminate the content. He/she realized that sharing the news article about product data release would constitute promotion, and so deliberately did not 'share' that, but clicked 'like' instead, again in the belief that a 'like' would not proactively disseminate the information.

On receipt of the complaint, Novartis considered it important to remind employees of their responsibilities about the use of personal social media channels; it was important to do this before the ruling in this case as this was such an important area to manage appropriately. Action taken had included a UK company-wide communication from a Novartis UK senior leader, to reinforce the guidelines and remind employees that information about a medicine should not be shared by employees on any social media platform.

In the spirit of learning from all dialogue and complaints within the self-regulatory system, Novartis convened a cross-functional team with representation from communications, compliance, medical, legal and pharmacovigilance to look at its existing guidelines and training and to consider any lessons that could be learned from this complaint. The work of this team would be further informed by the ruling in this case.

Novartis did not consider that it had failed to maintain high standards or had brought the industry into disrepute given the evidence above about the three cited pieces of LinkedIn activity in contention, the intent and conduct of the employee in his/her approach to social media and the company's approach to use this case to both learn from, and adapt to, this rapidly changing technology. The company denied a breach of Clauses 9.1 and 2.

PANEL RULING

The Panel noted the broad definition of promotion as stated in Clause 1.2; it encompassed any activity undertaken by a pharmaceutical company or with its authority which promoted the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicines.

The Panel noted that the complaint concerned LinkedIn activity on an employee's personal LinkedIn account. The Panel noted that LinkedIn was different to some other social media platforms in that it was a business and employment-orientated network and was primarily, although not exclusively, associated with an individual's professional heritage and current employment and interests. In the pharmaceutical industry, the Panel noted that an individual's network might, albeit not exclusively, be directly or indirectly associated with the healthcare industry. In the Panel's view, it was of course not unacceptable for company employees to use personal LinkedIn accounts and the Code would not automatically apply to all activity on a personal account; whether the Code applied would be determined on a case-by-case basis taking into account all the circumstances including: the content, any direct or indirect reference to a product, how the information was disseminated on LinkedIn, the company's role in relation to the availability of the content and whether such activity was instructed or encouraged by the company. If activity was found to be within the scope of the Code, the company would be held responsible.

The Panel noted that material could be disseminated or highlighted by an individual on LinkedIn in a number of ways, by posting, sharing, commenting or liking. The algorithms applied by LinkedIn were relevant including whether an individual could opt out of material being disseminated by such algorithms. In the Panel's view, activity conducted on social media that could potentially alert one's connections to the activity might be considered proactive dissemination of material. In addition an individual's activity and associated content might appear in the individual's list of activities on his/her LinkedIn profile page which was visible to his/her connections; an individual's profile page was also potentially visible to others outside his/her network depending on the individual's security settings.

The Panel noted that the complaint appeared to be limited to matters that had been shared or liked.

The Panel noted that Clause 26.1 prohibited the promotion of prescription only medicines to the public. Clause 26.2 stated that information about prescription only medicines which was made available either directly or indirectly to the public must be factual, presented in a balanced way, must not raise unfounded hopes of successful treatment and must not encourage members of the public to ask their health professional to prescribe a specific prescription only medicine.

The Panel noted that the complaint concerned three specific activities of a named Novartis employee on LinkedIn which were considered as follows.

1 Sharing an article discussing the prescribing behaviour of cardiologists and how to price new medicines in relation to the Entresto launch

The Panel noted Novartis' submission that the hyperlink provided by the complainant had been proactively shared by the named employee with his/her connections on the LinkedIn platform. The Panel further noted Novartis' submission that the employee did not post the original article on LinkedIn and had not commented on it.

The Panel noted that the original article appeared to have been authored and posted by a journalist at LinkedIn as part of a weekly 'Premium report' which highlighted healthcare news. The original post contained a video and written report of an interview with a named Novartis senior leader. The Panel noted Novartis' submission that the content of the article was focussed on the business approach to a product launch and lessons learnt from the launch of Entresto. The Panel noted that Entresto was mentioned several times, predominantly in relation to the US health environment, its sales and cost-effectiveness data. The Panel disagreed with Novartis' submission that the article did not position Entresto positively. The article referred to the Institute for Clinical and Economic Review categorising Entresto as cost-effective and the American College of Cardiology and the American Heart Association issuing guidelines which referred to Entresto as the standard of care for certain heart-failure patients, a decision, that the article stated, was often looked at as a gold standard in pharmaceutical commercialisation. In the Panel's view, an employee of Novartis proactively sharing the article with his/her connections on LinkedIn was considered to be promotion of Entresto, a prescription only medicine, and the 'share' and its associated content should have been certified as required by Clause 14.1. A breach was ruled.

The Panel did not know how many connections the named employee had on LinkedIn and if they were all health professionals; the company made no submission in that regard. However, as it was a personal LinkedIn account, the Panel considered that on the balance of probabilities not all the employee's connections would have been health professionals and therefore sharing of the article with his/her network constituted promotion of a prescription only medicine to the public and a breach of Clause 26.1 was ruled. Furthermore, and on balance, the Panel considered that the positive statements in the article could on the balance of probabilities have encouraged members of the public to ask their health professional to prescribe Entresto and therefore a breach of Clause 26.2 was ruled.

2 Advertising VivindaTV, a resource intended for health professionals, to the general public

The Panel noted that the hyperlink provided by the complainant led to a Novartis post on LinkedIn that referred to the latest research in dermatology

and referred to VivindaTV and sessions from a dermatology congress. Readers were invited to register. The linked registration page clearly stated that to create an account the individual had to declare that he/she was a health professional and their country of practice. The Panel noted that neither the original post nor the linked registration page directly or indirectly referred to specific medicines. The Panel noted Novartis' submission that it appeared the employee in question had 'liked' not 'shared' this Novartis post. Regardless of whether it was liked or shared, the Panel considered that neither the post nor the linked registration page contained any product related information. The viewer would have to register as a health professional to see further material. The Panel therefore did not consider that the employee's endorsement of the original Novartis post by liking it constituted promotion of a prescription only medicine to the public, nor was it contrary to the requirements of Clause 26.2 as no information about prescription only medicines was provided to the public in the original post or linked registration page. The Panel ruled no breach of Clauses 26.1 and 26.2 accordingly.

The Panel noted that the complainant alleged that materials shared had not undergone internal review. The complainant referred to 'shared (liked posts)' and thus the Panel considered that the allegation covered both 'shared' and 'liked' postings. The Panel noted its comments above that the original post and the linked registration page made no direct or indirect reference to a specific medicine and therefore was not considered as promotional material that required certification and ruled no breach of Clause 14.1 accordingly. Nor did the Panel consider that it was non-promotional material covered by Clause 14.3; no breach of that Clause was ruled accordingly.

3 Advertising a Novartis press release about Cosentyx Phase 3 data

The Panel noted that the third hyperlink provided by the complainant led to a Novartis posting announcing data in psoriasis at a 2018 dermatology annual meeting. The post itself did not contain any reference to a product but according to Novartis the 'find out more' link led to a press release about Cosentyx data from the congress. The complainant referred to a press release and Phase III data for Cosentyx. The Panel noted that Novartis had not provided a copy of the press release. The Panel further noted Novartis' submission that the press release was initiated by the Swiss based headquarters and had not been examined by the UK company.

The Panel noted Novartis' submission that the post was 'liked' by the named employee and not 'shared'. The Panel noted its general comments above about the dissemination of material on LinkedIn and that an individual could endorse a post on LinkedIn in a number of ways including 'sharing', 'liking' or 'commenting'. The Panel noted Novartis' submission that following receipt of the complaint it had identified information about how activity on LinkedIn

was visible to one's connections (their network) on their feed. Although it appeared that Novartis had known that a 'share' would alert an individual's connections to the activity, it had not realised that a 'like' could also alert one's connections. Novartis submitted that LinkedIn appeared to have an algorithm which decided which 'likes' it would alert one's connections to. The Panel was surprised that this issue had not come to light previously. It was not inconceivable that similar issues might have occurred previously wherein a 'liked' post had been disseminated to a Novartis employee's connection(s). The Panel understood that if an individual 'liked' a post it increased the likelihood that the post would appear in his/her connections' LinkedIn feeds, appearing as '[name] likes this'. In the Panel's view, companies should remain vigilant and needed to ensure that they took reasonable steps to highlight the potential compliance issues that might arise from 'liking' certain posts if such posts could thereby potentially be pushed to their connections' feed. The Panel noted Novartis' explanation that the nature of such an algorithm meant that an individual could not anticipate the outcome of 'liking' a post and therefore Novartis did not accept that 'liking' a LinkedIn post was proactively disseminating information in the same way that 'sharing' a post was. Novartis acknowledged that if the named employee had 'shared' this post it might constitute promotion to the public.

The Panel noted that whilst the complainant had provided a copy of the original Novartis post, beneath which was a list of likes, he/she referred to 'receiving information' on LinkedIn. The Panel therefore considered that on the balance of probabilities the employee's 'like' had been disseminated by the algorithm to his/her contacts and further considered that such dissemination was the subject of complaint.

In the Panel's view that an algorithm had disseminated an individual's 'like' did not absolve Novartis from responsibility. The Panel considered that the proactive dissemination of a press release about a prescription only medicine to those who were not health professionals or other relevant decision makers promoted that medicine to the public and might encourage such recipients to ask their doctor to prescribe it. Breaches of Clauses 26.1 and 26.2 were ruled.

The Panel considered that the 'like' of the post and its associated content would constitute promotional material and would require certification under the Code. A breach of Clause 14.1 was ruled.

The Panel was mindful of the complex issues that had to be addressed by companies when advising staff about personal social media use. The increasing use of social media, both in the personal and business capacity, presented challenges. In addition, many social media platforms used algorithms and

had settings which individuals and companies might not be fully aware of. In Case AUTH/2851/6/16, which related to a posting on LinkedIn, the Panel considered that the fact that it had occurred as a result of an algorithm did not absolve the company from responsibility.

The Panel was aware that the types of activity performed by the named employee on LinkedIn was not uncommon across the industry. In the Panel's view, employees might feel inclined to endorse articles related to their senior colleagues on LinkedIn or their company's corporate social media posts and depending on the content such activity might or might not fall within the scope of the Code; therefore, companies needed to issue specific and unambiguous guidance on personal use of social media. This was particularly important if UK employees were likely to follow the social media accounts of overseas affiliates which might have Codes, laws and regulations that differed to the UK. In the Panel's view it was important that companies regularly reviewed such guidance.

In the Panel's view, the global social media guidance issued by Novartis to its employees prior to the complaint and dated 2016 was open to interpretation; it stated:

'In general you can share public Novartis posts. But be aware that any comments you add to a Novartis post may create a risk of violation of rules regarding the promotion of our products or our company. You must also understand and follow any divisional or local guidance that may limit your ability to share such posts'.

The Panel was concerned that at the time of the LinkedIn activity in question there was no UK local guidance. The Panel noted that after Novartis was notified of the present complaint a UK company wide communication was sent by a UK senior leader which stated:

'Please do not post, re-post or share content that makes any reference to a specific medicine, including Novartis products. This includes product-specific information emanating from Novartis corporate social media feeds.'

The Panel was concerned about the absence of UK specific guidance at the relevant time. The Panel noted its comments and rulings of breaches of the Code as set out above. Overall, the Panel considered that high standards had not been maintained and ruled a breach of Clause 9.1. On balance the Panel did not consider that the circumstances warranted a breach of Clause 2 and ruled accordingly.

Complaint received	25 April 2018
Case completed	5 December 2018

BIAL PHARMA v PROFILE PHARMA

Promotion of Xadago

Bial Pharma UK complained about material distributed from a promotional exhibition stand by Profile Pharma to support its promotion of Xadago (safinamide). Xadago was indicated as add-on therapy for adults with idiopathic Parkinson's disease. Bial marketed Ongentys (opicapone) which was indicated as adjunctive therapy in patients with Parkinson's disease.

The materials at issue were two study summaries: 'Opicapone as adjunct to levodopa therapy in patients with Parkinson's Disease and motor fluctuations' which detailed Lees *et al* (2017) (BIPARK II); and 'Assessment of safety and efficacy of safinamide as a levodopa adjunct in patients with Parkinson's Disease and motor fluctuations: A randomised clinical trial' which detailed Schapira *et al* (2016) (SETTLE).

Bial stated that Ongentys and Xadago were indicated in similar patient populations but they had different mechanisms of action. Bial submitted that for Profile Pharma to selectively produce a standalone clinical trial summary of its competitor's product to use alongside summaries of clinical trials of its own product, and to distribute these as promotional materials, encouraged an indirect comparison of the two products where there were no direct comparative clinical studies.

Bial alleged that the summaries available on the exhibition stand did not provide a balanced summary of all of the available evidence and the selection of the summaries and the selective way they were written, was intended to indirectly favour Xadago over Ongentys.

The detailed response from Profile is given below.

The clinical trial summaries had been produced using PICO (population, intervention, comparator and outcome) methodology. The Panel noted the briefing document to support the use of the summaries stated that they were to be used by key account managers proactively with all relevant health professionals to support the formulary and market access of Xadago. The briefing stated that as there were no head-to-head trials, the summaries were a key tool to differentiate Xadago from other adjunct therapies.

It was clear to the Panel that the summaries would inevitably lead to comparisons of the products. This was not necessarily unacceptable, it was a question of whether the content of each summary was fair, whether health professionals were provided with an overview of all the data and if not, what was the basis of selection and was such selection fair.

The materials were used to promote Xadago. The document which detailed the Xadago study included prescribing information. It appeared from Profile's submission that a number of criteria were used when selecting the studies to be summarised, ie was the medicine one of the most relevant? was it a pivotal study? and was there data in order to present the summary using a PICO format? Profile stated that the PICO methodology would highlight differences in studies. Health professionals would use data from a number of sources in making decisions. In the Panel's view it was disingenuous to claim that material produced using similar methodology would not encourage health professionals to make comparisons. Profile's approach facilitated indirect comparisons.

The Panel noted Profile's submission that it had produced a summary on study 016 and if there were none available on the stand it might have been because it had run out. Profile submitted that it always sent equal quantities of the summaries. It appeared that Bial did not accept Profile's submission in this regard. The Panel noted that the PICO summaries briefing document listed study 016. The Panel considered all the circumstances and ruled that there was no breach of the Code in relation to the summary of study 016.

It was not clear to the Panel why one of the key papers referenced in the Xadago EPAR, study 018, had not been summarised because it failed to meet its primary endpoint. In the Panel's view this was an important study and the failure to reach its primary end point would be of interest. Profile stated that the two year study was of interest to health professionals as no other medicine in this therapy area had long-term data. The Panel further queried Profile's submission that the limitations of the methodology and hierarchical statistics were not easy to explain in the PICO format so it was not used as it would be misleading. It was not entirely clear to the Panel why study 018 could not be presented in this format or in an alternative format if necessary.

Overall the Panel did not consider that use of the material to make indirect comparisons was misleading as alleged. That the studies were separate and there was no direct comparison would be apparent from the use of individual documents. The Panel ruled no breach of the Code. However, the Panel was concerned that taking all the factors into account the absence of a summary for a pivotal study on Profile's product which did not meet its primary endpoint meant that the basis of selection was unfair and did not reflect all the evidence. A breach of the Code was ruled. This meant the indirect comparison was misleading and the Panel ruled a breach of the Code.

Bial Pharma UK Limited complained about material produced by Profile Pharma Ltd to support its promotion of Xadago (safinamide). Xadago was indicated as add-on therapy for adults with idiopathic Parkinson's disease. Bial marketed Ongentys (opicapone) which was indicated as adjunctive therapy in patients with Parkinson's disease.

The materials at issue were two study summaries: 'Opicapone as adjunct to levodopa therapy in patients with Parkinson's Disease and motor fluctuations' (ref UK_XAD_187) which detailed Lees *et al* (2017) (BIPARK II) and 'Assessment of safety and efficacy of safinamide as a levodopa adjunct in patients with Parkinson's Disease and motor fluctuations: A randomised clinical trial' which detailed Schapira *et al* (2016) (SETTLE). The study summaries were distributed from Profile's stand at a promotional meeting.

COMPLAINT

Bial stated that although Ongentys and Xadago had different mechanisms of action, they were indicated in similar patient populations. The company submitted that for a pharmaceutical company to selectively produce a standalone clinical trial summary of its competitor's product, with the intention that the summary be used alongside summaries of clinical trials of its own product, and distribute these as promotional materials, could only have one purpose ie to encourage and/or facilitate health professionals and other decision makers to indirectly compare the two products.

Bial stated that the summaries available on the Profile stand were a selection of the pivotal studies of Ongentys and Xadago and as such did not provide a balanced summary of all of the available evidence. The selection of the summaries and the selective way they were written, was intended to favour Xadago over Ongentys in indirect comparisons.

Indirect comparisons

Bial stated that it was concerned that, in the absence of comparative studies, Profile had produced promotional materials in the form of individual clinical study summaries; these were distributed via the salesforce with the intention that it would directly or indirectly encourage health professionals and other decision makers to indirectly compare the efficacy and safety of Xadago and other competing products. In Bial's view, the only reason that a salesforce would be supplied with summaries of clinical trials of competitor products, as promotional items, would be to encourage or facilitate indirect comparisons between products.

Bial stated that its concerns about indirect comparisons fell into two areas:

1 The encouragement by Profile's salesforce (or otherwise) of indirect comparisons, by health professionals and other decision makers, between products where there were no direct comparative clinical studies. Bial noted that breaches of the Code had previously been ruled in relation to the use of indirect comparisons. In this instance:

- a) Profile's view was that because the clinical study summaries used a recognised methodology, they could be distributed as standalone promotional items. In Bial's view, and in consideration of previous PMCPA cases, it was not acceptable for a company to encourage indirect comparisons between two competitive products. Bial alleged a breach of Clause 7.
- b) During an inter-company meeting Profile stated that the materials were intended to be used to facilitate indirect comparisons by health professionals and other decision makers. Furthermore, in response to a request for clarification by Bial during the meeting, this statement was reiterated by Profile. Profile subsequently denied the statement had been made and as a result the minutes of the meeting had not been agreed. Based on Profile's statement on indirect comparisons made at the meeting, though subsequently retracted, Bial remained of the view that the study summaries were provided to the salesforce as promotional items simply for the purpose of encouraging indirect comparisons, in breach of the Code.
- c) Profile had not otherwise explained why the study summaries were used as promotional items.

2 The study summaries and their availability at promotional and other meetings was selective, such that the data provided to health professionals to make indirect comparisons did not reflect all the available evidence, and the selection and the presentation of data appeared, by design, to favour Xadago.

- a) At the promotional meeting at which the materials in question were obtained, there was no summary available from the Profile stand of the second pivotal study of Xadago in the licensed indication (Study 016). The size of the mean estimate of the improvement in the primary variable in this study was approximately 50% of the mean estimate of Schapira *et al*. Once again this appeared to be selective, failed to take account of all of the relevant clinical data of Xadago and was part of a deliberate strategy to bias any indirect comparison by health professionals of Xadago and Ongentys in favour of Xadago.
- b) Although during inter-company dialogue, Profile indicated that an additional study summary (Study 016) had been produced, this was not available at the meeting in question. If this item was available, not making it available on the meetings stand could also be considered selective, as the summarised data would reflect Xadago in a less favourable light. As Bial had not seen this item, it relied on Profile's statement that the item was available.
- c) As the study summaries were distributed as separate items, rather than bound together, selectivity in distribution was almost inevitable and had been shown to be established as practice by Profile as evidenced by the summaries available at the promotional

meeting at which these materials were obtained.

Bial stated that its fundamental concern was that the use of the materials would encourage health professionals and other decision makers to make indirect comparisons. The original selection of certain clinical studies, in this summarised form, without taking into account all of the available published data, was a concern. Profile's intention with these materials, and the indication that clear briefing materials were not initially considered, was a concern. Further, Bial's suggestion that all published and available clinical studies were provided in one bound document, to prevent any selective use in a promotional context by the salesforce, had been rejected by Profile, compounding Bial's concern that the study summaries were, by design, to be used selectively.

Bial alleged that this approach was in breach of Clause 7, particularly Clause 7.2 but equally a breach of Clause 7.3 could be argued.

RESPONSE

Profile explained that it produced a series of purely factual summaries of the key papers for the most used or newest medicines for Parkinson's patients in need of adjunct therapy to levodopa. It had not made any claims beyond presenting results. It had presented the results of the same endpoints where available and made clear where they were not published in the paper. The endpoints presented were those the European Medicines Agency (EMA) required for registration studies in Parkinson's disease. This was done in conjunction with experts in the therapy area to advise on the most relevant medicines and the pivotal studies for each. The studies were summarised using a PICO (population, intervention, comparator and outcome) methodology. The National Institute for Health and Care Excellence (NICE) guideline manual had endorsed this methodology which would highlight differences in studies. Profile did not make any comparisons nor direct its salesforce to make them. Profile provided the summaries as individual items and could not be responsible for how a decision maker used a purely factual summary of a clinical paper or even a full clinical paper. Profile's aim was to summarise the data as fairly and accurately as possible.

Profile noted Bial's accusation that Profile's intention of the materials was for its salesforce to make indirect comparisons with health professionals, yet no evidence of this was offered. Further, this point could be applied to a lot of promotional materials. Profile stated that its intention was to aid decision making through producing factual summaries with an established methodology, not to encourage indirect comparisons. Of course, health professionals made indirect comparisons daily when making prescribing decisions and so, if Bial's logic was accepted, all promotional material could be used to make indirect comparisons.

Profile categorically refuted Bial's version of what was said at the meeting and provided its version of

the meeting minutes. Profile noted that Bial wrote up the minutes and that Profile corrected them in track change. Bial refused to accept the changes, even to remove its post meeting suppositions and factual errors. Profile stated that Bial rejected all of Profile's changes and made no attempt to reach an agreement.

Profile stated that without accepting that it intended indirect comparison to be made it would address how the materials might be in breach of the Code. Bial had not stated where in the Code indirect comparisons were not allowed. Profile accepted there were many limitations with an indirect comparison but Clause 7.3 did not prohibit them *per se* and therefore Bial's statement that by having an indirect comparison without further clarification Profile did not accept as being in breach.

Profile noted that Bial offered no evidence that Profile salesforce encouraged indirect comparisons. Bial did not cite particular PMCPA cases to substantiate that all indirect comparisons were in breach. The rulings in Case AUTH/2199/1/09 and Case AUTH/2778/8/15 related to indirect comparison where studies had different endpoints. This did not necessarily mean all indirect comparisons would be in breach of the Code. There were very few instances where head-to-head studies were available for all comparisons. In Cases AUTH/2440/10/11 and AUTH/2441/10/11 the Panel ruled that head-to-head studies were not needed to substantiate a claim for 'class-comparable efficacy'. The Panel considered 'comparable' meant that the two products were worthy of comparison or able to be compared. The Panel did not consider that comparability implied equivalence. This would indicate that in some circumstances comparisons without head-to-head studies ie an indirect comparison might be acceptable.

Profile noted that Bial alleged that the summaries only had one purpose ie to encourage indirect comparisons, without offering any evidence of this or considering that most promotional materials had many purposes.

Listing the requirements of Clause 7.3, Profile stated that an indirect comparison would not be in breach of the Code if, in effect, it met those requirements:

Profile reiterated that it did not make an indirect comparison but if the materials were to be used by a health professional or other decision maker for this purpose then none of the listed requirements of Clause 7.3 would have been breached.

Profile categorically refuted Bial's version of what was said during an inter-company meeting and noted that, in addition to the incorrect comment about indirect comparisons, there were many other errors in the minutes. Profile never stated that the intention was for indirect comparisons to be made. Profile submitted that it stated during the meeting that the PICO methodology was an accepted method for the basis of indirect comparisons as used by Cochrane, NICE and other decision makers precisely because it highlighted the differences in studies. This was totally misconstrued by Bial. The intention was to

summarise the key studies to facilitate decision making. The salesforce was not directed to make indirect comparisons and Profile only stated that it could not be responsible for health professionals making indirect comparisons as they must do this continually to make appropriate prescribing decisions, as there were rarely head-to-head studies to help them. Throughout the subsequent inter-company dialogue Bial refused to acknowledge that and continued to incorrectly state that Profile had stated the materials were intended to make indirect comparisons. The Code allowed comparisons as long as they complied with Clause 7.3 and Profile did not accept that it had breached Clause 7.3.

Profile considered that each summary was a balanced presentation of the key data in each paper. Only results were presented and no inferences or claims about the data were made. The choice of papers was such as to present a pivotal study or studies for each medicine. Profile stated that it ensured both its pivotal studies were summarised and that its choice of studies for other medicines represented the data for those medicines. Profile noted that Bial did not state how the data was not balanced or how the summaries and how they were written favoured Xadago. The Code did not prohibit the use of competitor data in promotion.

Profile noted that Bial refused to believe that Profile had summarised both of its pivotal studies namely study 016 and SETTLE. Bial did not find the summary for Study 016 so accused Profile of not having one and therefore 'cherry picking' its data. Bial would not accept Profile's explanation that if there were none on the stand maybe it was because it had run out as it was more popular. Profile stated that it always sent equal quantities of the summaries. As the meeting in question had not been identified, Profile could not confirm the exact quantities of the summaries provided. Profile provided copies of all of the summaries in the series.

Profile stated that it explained to Bial in the inter-company meeting, that rather than cherry picking data it had actually not summarised a key paper that was referenced in Xadago's European Public Assessment Report (EPAR) and summary of product characteristics (SPC), Study 018, as it failed to meet its primary endpoint. This was the results of a 2-year study, and as such was of interest to health professionals as no other medicine in this therapy area had long-term data. The limitations of the methodology and hierarchical statistics were not easy to explain in the PICO format so Profile did not present the data in that format because it considered that it would be misleading. A copy of the paper was provided. Bial then incorrectly stated that Profile was using data from a study in an unlicensed indication (Motion study in early Parkinson's disease), which apart from forming part of the reference safety information, Profile never used. Bial also incorrectly referred to its own pivotal phase III trial as a phase IV open label study.

Profile refuted that the summaries were written in a way that was selective, it had only summarised the papers for each medicine, provided the results for the same endpoints where possible and where the

endpoints were different, made sure this was clear. There had been no cherry picking.

As for the summaries not presenting all the available evidence, Profile submitted that it was not feasible to produce summaries of all papers in this this area, nor would that be useful to prescribers and decision makers. The company took expert advice that the data presented was representative and not misleading. Profile did not set out to favour Xadago. The data was factual, if there were differences that were more favourable to one medicine over another then so be it. It was up to prescribers or decision makers to draw their own conclusions. Profile had not drawn any conclusions on any of the studies.

Profile noted Bial's request that the summaries be bound together but did not understand how this would remove the accusation of an indirect comparison. Conversely, Profile considered that binding them together made indirect comparisons more likely which was why it did not agree to it. Bial offered no evidence that the materials were used selectively to support its inflammatory comment 'established as practice'. Profile noted that, in the course of inter-company dialogue, it offered to brief the salesforce to make sure all summaries were available on promotional stands and to tell health professionals and decision makers of all the paper summaries available so they could choose which they wanted.

In conclusion Profile refuted any breach of Clause 7.2 or 7.3. Bial had not been clear in how Profile might have done that and what aspects of the materials breached each clause. Profile did not consider that all indirect comparisons would be in breach of the Code but accepted they had many limitations. For that very reason, Profile produced individual summaries of key papers for prescribers and decision makers in order to avoid bias. This was done to help those in the NHS as many formulary committees used the PICO methodology when reviewing papers.

PANEL RULING

The Panel noted the briefing document to support the use of the PICO key study leaflets stated that they were to be used by key account managers proactively with all relevant health professionals to support the formulary and market access of Xadago within the UK. The briefing stated that as there were no head-to-head trials, the PICO leaflets were a key tool to differentiate Xadago from other adjunct therapies. It further stated that the PICOs looked at each trial and compared using the following criteria: population, intervention comparison and outcome.

It was clear to the Panel that the summaries would inevitably lead to comparisons of the products. This was not necessarily unacceptable it was a question of whether the content of each summary was fair, whether health professionals were provided with an overview of all the data and if not, what was the basis of selection and was such selection fair.

The materials were used to promote Xadago. The document which detailed the Xadago study included prescribing information. It appeared from Profile's

submission that a number of criteria were used when selecting the studies to be summarised, firstly was the medicine one of the most relevant, secondly was the study a pivotal study and thirdly was there data in order to present the summary using a PICO format. Profile stated that the PICO methodology would highlight differences in studies. Health professionals would use data from a number of sources in making decisions. In the Panel's view it was disingenuous to claim that material produced using similar methodology would not encourage health professionals to make comparisons. Profile's approach facilitated indirect comparisons.

The Panel noted Profile's submission that it had produced a summary on study 016 and if there were none available on the stand it might have been because it had run out. Profile submitted that it always sent equal quantities of the summaries. It appeared that Bial did not accept Profile's submission in this regard. The Panel noted that the PICO summaries briefing document listed study 016. The Panel considered all the circumstances and ruled that there was no breach of Clause 7.2 and 7.3 in relation to the summary of study 016.

It was not clear to the Panel why one of the key papers referenced in the Xadago EPAR, study 018, had not been summarised because it failed to meet its primary endpoint. In the Panel's view this was an important study and the failure to reach its primary end point would be of interest. Profile

stated that the two year study was of interest to health professionals as no other medicine in this therapy area had long-term data. The Panel further queried Profile's submission that the limitations of the methodology and hierarchical statistics were not easy to explain in the PICO format so it was not used as it would be misleading. The Panel noted that using the PICO format the data would be set out as population, intervention, comparator and outcome. It was not entirely clear to the Panel why study 018 could not be presented in this format or in an alternative format if necessary.

Overall the Panel did not consider that use of the material to make indirect comparisons was misleading as alleged. That the studies were separate and there was no direct comparison would be apparent from the use of individual documents. The Panel ruled no breach of Clauses 7.2 and 7.3. However, the Panel was concerned that taking all the factors into account the absence of a summary for a pivotal study on Profile's product which did not meet its primary endpoint meant that the basis of selection was unfair and did not reflect all the evidence. A breach of Clause 7.2 was ruled. This meant the indirect comparison was misleading and the Panel also ruled a breach of Clause 7.3.

Complaint received	7 June 2018
Case completed	10 October 2018

ANONYMOUS, NON-CONTACTABLE HEALTH PROFESSIONAL v ABBVIE

Promotion of Synagis

An anonymous, non-contactable complainant complained about a meeting held by AbbVie in May 2018. The day-long meeting was a BPD (bronchopulmonary dysplasia) Masterclass which, *inter alia*, discussed the use of Synagis (palivizumab) marketed by AbbVie. Synagis was indicated for the prevention of serious lower respiratory tract disease requiring hospitalization caused by respiratory syncytial virus (RSV) in children at high risk of RSV disease.

The complainant had decided to go after careful consideration of the detailed agenda sent to him/her by the AbbVie representative. The complainant stated that one of the sessions, however, was cut considerably short and the named representative used the time to forcefully interrogate the audience about their prescribing habits and their views on immunising infants outside of both the Joint Committee on Vaccination and Immunisation (JCVI) guidance and the product licence, namely twins. The complainant stated that the representative's conduct made him/herself and other members of the audience feel uncomfortable and had left him/her feeling that this was completely inappropriate and questioning the intent of the meeting. It was inappropriate for a representative to initiate group discussions about the off-licence prescribing habits of clinicians and he/she left the meeting perplexed about the possibility of any hidden agenda.

The detailed response from Abbvie is given below.

The Panel noted AbbVie's submission that there was some correlation between the events described in the complaint and what occurred at the meeting. AbbVie suspected that the presentation in question was 'The Real Impact of RSV – Think About What You Can't See', which addressed the factors that put children at risk of RSV, in particular BPD and prematurity, and included a discussion of the JCVI Guidelines.

The Panel noted that according to AbbVie the health professional completed the presentation in around 35 minutes, rather than the hour allocated; the presentation was not deliberately cut short by AbbVie. The remaining 25 minutes were questions from the audience, many of which related to AbbVie-specific information and were answered by the AbbVie representative. The Panel noted AbbVie's submission that its representative facilitated further discussion on topics related to the presentation including the use of Synagis in premature twins and multiples.

The Panel considered that according to the SPC each child that was part of a twin or other multiple birth might potentially meet the licensed criteria for Synagis. The Panel noted AbbVie's submission that that the preceding presentation listed multiple births as a risk factor for RSV and the discussion was limited to premature twins and using Synagis within the scope of its licence.

In the Panel view the complainant's allegation regarding out of license discussion 'namely twins' was not specific. The Panel considered that the complainant had not provided evidence to show that Synagis had been promoted outside of its licensed indication as alleged and thus no breach of the Code was ruled.

An anonymous, non-contactable complainant complained about a meeting held by AbbVie Ltd at a hotel in London in May 2018. The day-long meeting was a BPD (bronchopulmonary dysplasia) Masterclass which, *inter alia*, discussed the use of Synagis (palivizumab) marketed by AbbVie. Synagis was indicated for the prevention of serious lower respiratory tract disease requiring hospitalization caused by respiratory syncytial virus (RSV) in children at high risk of RSV disease. One group of children who would be indicated for Synagis treatment were those born at 35 weeks gestation or less and less than 6 months of age at the onset of the RSV season.

COMPLAINT

The complainant submitted that he/she had attended the meeting at issue, which had been organised by the local named AbbVie representative, to gain additional insight and knowledge on BPD. The complainant had decided to go after careful consideration of the detailed agenda sent to him/her by the representative. The complainant stated that one of the sessions, however, was cut considerably short and the named representative seized the opportunity to use the time to forcefully interrogate the audience about their prescribing habits and their views on immunising infants outside of both the Joint Committee on Vaccination and Immunisation (JCVI) guidance and the product licence, namely twins. The complainant stated that the representative's conduct made him/herself and other members of the audience feel uncomfortable and had left him/her feeling that this was completely inappropriate and questioning the intent of the meeting and whether he/she would consider any future meetings facilitated by AbbVie.

The complainant considered that it was inappropriate for a representative to initiate group discussions about the off-licence prescribing habits of clinicians and he/she left the meeting perplexed about the possibility of any hidden agenda.

When writing to AbbVie, the Authority asked it to consider the requirements of Clauses 3.1 and 3.2 of the Code.

RESPONSE

AbbVie submitted that the vague nature of the complaint gave it reason to believe that it was not genuine. The substance of the complaint was contained in a single sentence in which it was alleged that one of the meeting sessions was cut short and the AbbVie representative 'seized the opportunity to use the time to forcefully interrogate the audience regarding their prescribing habits and their views on immunising infants outside of both JCVI guidance and product licence namely twins'.

Other than the passing reference to twins, the complainant provided no details as to the alleged breach of the Code. If this were a genuine complaint, AbbVie would have expected the complainant to specify the practices allegedly discussed by the representative and how/why they fell outside of both JCVI guidance and product licence. Furthermore, the complainant waited for nearly two months after the meeting to submit the complaint. If the complainant was genuinely concerned about the meeting, AbbVie would have expected him/her to act more quickly.

AbbVie submitted that there was some correlation between the events described in the complaint and what occurred at the meeting. However, the lack of detail in the complaint, the delay in making it and the discrepancies between the events described in the complaint and reality suggested that the complainant was not present at the meeting.

AbbVie had discussed the matter with the representative in question and his/her line manager, who were the only AbbVie personnel at the meeting in question. AbbVie had also reviewed the related documents.

BPD Masterclass

AbbVie explained that Synagis was a monoclonal antibody which provided passive immunity to respiratory syncytial virus (RSV) in infants. The Synagis summary of product characteristics (SPC) listed three therapeutic indications for Synagis, covering three categories of children who were deemed to be at a high risk of contracting RSV:

- i) premature babies who were less than six months old at the onset of RSV season (October);
- ii) children who were less than two years old with bronchopulmonary dysplasia (BPD); and
- iii) children who were less than two years old with haemodynamically significant congenital heart disease (CHD).

The BPD Masterclass was a promotional meeting organised and funded by AbbVie. The purpose was to bring paediatric and neonatal communities together to share and discuss hot topics in the current management of BPD and ensure continued optimal patient care. As explained above, children with BPD were one of the three populations included in the licensed indications for Synagis.

The Masterclass consisted of a mixture of talks and panels/Q&A sessions on topics related to BPD, led by various expert health professionals engaged by AbbVie. The attendees were paediatric and neonatal nurses and consultants. The representative and line manager both confirmed that the meeting appeared to be well-received on the day. This was confirmed by the attendees' feedback scores. The attendees were asked to score each session between 1 and 5 for 'Quality of Content', 'Relevance to You', and 'Improvement of Knowledge', and virtually every session averaged at least 4 out of 5 in each category. No complaints or concerns were raised by any attendee on the day and nor were any concerns recorded in the feedback documents (copies provided).

The alleged comments made by the representative

Although the complainant did not state which session of the Masterclass had been cut short, AbbVie suspected that it was the one entitled 'The Real Impact of RSV – Think About What You Can't See'. The slides for this session were provided. The presentation addressed the factors that put children at risk of RSV, in particular BPD and prematurity, and included a discussion of the JCVI Guidelines and what categories of patients fell within their scope.

The health professional completed the presentation in around 35 minutes, rather than the hour allocated, however if the complainant was alleging that AbbVie deliberately cut the presentation short, this was not so. The remaining 25 minutes of the session were filled by questions from the audience. Many of the questions related to AbbVie-specific information (eg the pricing of Synagis) and were not able to be answered by the presenter. The AbbVie representative responded appropriately to these questions and facilitated further discussion within the group on topics related to the presentation. There was no evidence that the representative 'forcefully interrogated the audience' and this was disputed by AbbVie.

Among the topics raised for discussion by the representative was that of the use of Synagis in twins and multiples. It was made clear that this was for premature twins and multiples. As stated in the response to Case AUTH/2997/12/17, the Code did not prohibit the promotion of medicines within their marketing authorisation but that were not funded by NHS England (to which the JCVI Guidelines related).

Since premature twins or multiples could fall within the indications listed in the Synagis SPC, discussion of this topic initially raised by the representative did not inherently constitute a breach of Clauses 3.1 or 3.2 of the Code. The discussion was limited

to premature twins and to using Synagis within the scope of its licence. AbbVie noted that the preceding presentation listed multiple births as a risk factor for RSV and so it would therefore have been a reasonable topic for discussion in the context of the meeting.

AbbVie noted the complainant's comments that he/she and other members of the audience felt uncomfortable with the representative's conduct. However, as noted above, none of the attendees complained at the time and they appeared happy to discuss this topic. The feedback for this particular session was positive, as was the feedback for the other sessions.

Conclusion

For the reasons set out above, AbbVie seriously doubted whether the complaint was genuine. Furthermore, it was strongly of the view that the complainant had not and could not discharge the burden of proof due to the vague nature of the complaint. As such, the case should not proceed. Despite this primary position, AbbVie stated that it took its obligations to comply with the Code very seriously and had thus responded in detail as set out above.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. Like all complaints, anonymous complaints were judged on the evidence provided. The complainant bore the burden of proving his/her complaint on the balance of probabilities.

The Panel noted AbbVie's submission that there was some correlation between the events described in the complaint and what occurred at the meeting. Whilst the complainant had not identified the presentation AbbVie suspected that the presentation in question was 'The Real Impact of RSV – Think About What You Can't See', which addressed the factors that put children at risk of RSV, in particular BPD and prematurity, and included a discussion of the JCVI Guidelines and what categories of patients fell within their scope.

The Panel noted that according to AbbVie the health professional completed the presentation in around 35 minutes, rather than the hour allocated; the presentation was not deliberately cut short by AbbVie. The remaining 25 minutes of the session were filled by questions from the audience, many of which related to AbbVie-specific information and were therefore answered by the AbbVie

representative. The Panel noted AbbVie's submission that its representative facilitated further discussion within the group on topics related to the presentation including the use of Synagis in premature twins and multiples.

The Panel noted that the promotion of a medicine must be in accordance with the terms of its marketing authorization and must not be inconsistent with the particulars listed in its summary of product characteristics. The Panel noted that the Code did not state that a medicine must be promoted in a manner that was consistent with JCVI guidance as implied by the complainant. It did however, require that all information, claims and comparisons must be accurate and must not be misleading either directly or by implication, by distortion, exaggeration or undue emphasis.

The Panel noted that according to its SPC, Synagis was indicated for the prevention of serious lower respiratory tract disease requiring hospitalisation caused by RSV in children at high risk for RSV disease:

- children born at 35 weeks of gestation or less and less than 6 months of age at the onset of the RSV season
- children less than 2 years of age and requiring treatment for bronchopulmonary dysplasia within the last 6 months
- children less than 2 years of age and with haemodynamically significant congenital heart disease

The Panel considered that each child that was part of a twin or other multiple birth might potentially meet the licensed criteria for Synagis. The Panel noted AbbVie's submission that that the preceding presentation listed multiple births as a risk factor for RSV and the discussion was limited to premature twins and using Synagis within the scope of its licence.

The Panel noted the complainant's allegation that the discussion was both out of licence and outside of the JCVI guidance. The Panel noted its comments above in this regard. The complainant referred to twins but otherwise gave little detail about his/her concerns. The Panel considered that the complainant had not provided evidence to show that Synagis had been promoted outside of its licensed indication as alleged and thus no breach of Clauses 3.1 and 3.2 was ruled.

Complaint received	29 June 2018
Case completed	14 November 2018

COMPLAINANT v ALEXION

Promotional material posted on LinkedIn

A contactable complainant who described themselves as a concerned UK health professional complained about material received on his/her LinkedIn feed from Alexion Pharmaceuticals. The posted message informed readers that, *inter alia*, Alexion had submitted an EU application for approval of ALXN1210 as a treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH).

The complainant submitted that it seemed that the posting appeared in his/her feed since Alexion employees in the UK had liked it which then presented it to their connections which included a variety of people including many people in the UK who were not health professionals. The post detailed the company, the medicine and what it was used for.

The detailed response from Alexion is given below.

The Panel noted the complainant's allegation that the LinkedIn post, which led to a press release about Alexion and ALXN1210, appeared in his/her LinkedIn feed because Alexion UK employees had liked it which then presented it to their connections. The Panel noted that the complainant had not named or otherwise referred to a specific Alexion UK employee that was in his/her network on LinkedIn. The Panel further noted Alexion's submission that when it was advised of the complaint, the post had received over 300 'likes' on LinkedIn including a 'small handful' of likes from Alexion UK employees.

The Panel noted that material could be disseminated or highlighted by an individual on LinkedIn in a number of ways, including by posting, sharing, commenting or liking. The Panel understood that if an individual 'liked' a post it increased the likelihood that the post would appear in his/her connections LinkedIn feeds thereby disseminating the post. In the Panel's view, activity conducted on social media that could potentially alert one's connections to the activity might be considered proactive dissemination of material. In addition, an individual's activity and associated content might appear in the individual's list of activities on his/her LinkedIn profile page which was visible to his/her connections; an individual's profile page was also potentially visible to others outside his/her network depending on the security settings. The Panel considered it was likely that Alexion UK employees' connections would include UK members of the public and might include UK health professionals. The Panel noted that the LinkedIn post and associated press release was 'liked' by a number of Alexion UK employees. In the Panel's view the act of liking the material amounted to proactive dissemination of the material within the UK and brought it within the scope of the Code.

The Panel noted Alexion's submission that the post and press release in question were factual, non-promotional, corporate announcements relevant, in their entirety, to the investor community and that they originated from a LinkedIn account operated by Alexion Pharmaceuticals Inc. based in the US with no involvement of the UK affiliate. The Panel noted Alexion's submission that the post did not target UK users or directly mention the UK. The Panel noted, however, that in liking the post, Alexion UK employees had, on the balance of probabilities, proactively disseminated it within the UK to an audience far wider than the intended financial community.

The Panel noted that the LinkedIn posting informed readers that Alexion had submitted an application for approval of ALXN1210 as a treatment for patients with paroxysmal nocturnal haemoglobinuria (PNH) in the European Union (EU). The US filing and Japanese submission were also referred to. The linked press release provided more detail. It described the results of two large Phase 3 studies and included statements such as 'We are excited about this next important step towards our goal of establishing ALXN1210 as the new standard of care for patients with PNH...' and 'Building on 10 years of proven efficacy and safety with Soliris and 25 years of leadership in complement biology...'. Soliris (eculizumab) was an Alexion prescription only medicine, available in the UK, indicated in adults and children for the treatment of PNH. Soliris was described in the press release as 'a first-in-class complement inhibitor ...' and ALXN1210 was described as an 'innovative, long acting C5 inhibitor discovered and developed by Alexion ...'. The press release also stated that Alexion and Soliris had received some of the pharmaceutical industry's highest honours for medical innovation in complement inhibition.

The Panel noted its comments above and considered that on the balance of probabilities not all the Alexion UK employees' connections to whom the post might have been disseminated to by virtue of their 'like' would have been health professionals. Thus, in the Panel's view and on the balance of probabilities the LinkedIn post and associated press release had been disseminated to members of the public.

The Code prohibited the promotion of prescription only medicines to the public. The Panel noted that the product, ALXN1210, was not classified as a prescription only medicine when the LinkedIn post and associated press release at issue were liked by the UK employee and on this very narrow technical point the Panel ruled no breach of the Code.

However, the Panel considered that the Alexion UK employees' like of the LinkedIn post and associated press release regarding an unlicensed medicine and the potential subsequent dissemination to all of their connections meant that Alexion had failed to maintain high standards and a breach of the Code was ruled.

The Panel considered that the Code required companies that wished to rely on prior permission to be able to demonstrate that recipients had agreed to receive promotional material by such means. Nonetheless, the Panel noted that the complainant bore the burden of proof and considered that he/she had not provided evidence to show that there had been a breach of the Code in this regard and no breach was ruled.

The Panel noted Alexion's submission that the Alexion Global Social Media Policy stated, *inter alia*, that employees were permitted to 'like' Alexion's social media posts but might not provide further comment. The Panel noted that Alexion was, however, reviewing the social media policy to see whether changes were necessary for the UK and might guide UK employees not to 'like' certain posts on social media in future. The Panel was concerned that there appeared to be no UK specific guidance at the time of the complaint. The Panel considered that the lack of adequate UK specific social media guidance at the time of the complaint meant that Alexion had failed to maintain high standards and a breach of the Code was ruled.

The Panel did not consider that the circumstances warranted a breach of Clause 2 which was used as a sign of particular censure and was reserved for such circumstances. No breach of Clause 2 was ruled.

A contactable complainant who described themselves as a concerned UK health professional complained about material received on his/her LinkedIn feed from Alexion Pharmaceuticals. The posted message informed readers that, *inter alia*, Alexion had submitted an EU application for approval of ALXN1210 as a treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH).

COMPLAINT

The complainant noted that the LinkedIn posting linked through to a long press statement about Alexion and its new compound ALXN1210.

The complainant submitted that it seemed that the posting appeared in his/her feed since Alexion employees in the UK had liked it. This had, in turn, been presented to all of their links which included a variety of people.

The complainant imagined that there was a very small number of people that needed updates about a compound before it was approved, but this posting had gone well beyond that.

The complainant alleged that the link would include many people in the UK who were not health professionals. The post detailed the company, the medicine and what it was used for.

When writing to Alexion, the Authority asked it to consider the requirements of Clauses 2, 9.1, 9.9, 26.1 and 26.2 of the Code.

RESPONSE

Alexion stated that it had escalated the matter internally in the UK and in the US where its parent company (which issued the LinkedIn post in question) was based. Whilst the company was reviewing its position, subject to receiving further information, it had taken the immediate and precautionary measure of taking the post down from LinkedIn. The company was also reviewing its social media policy to consider whether any changes were needed to deal more specifically with such instances in the UK.

Alexion noted that the post and press release were international in nature, wholly attributable to the US-based parent company, Alexion Pharmaceuticals Inc., with no involvement of the UK affiliate, and did not target UK users, nor indeed directly mention the UK. Therefore, the company considered that the activity did not fall within the scope of the Code and asked for the complaint to be dismissed as such.

That said, Alexion responded to the complaint. In summary, Alexion submitted that it was clear that the post and press release in question were factual, non-promotional, corporate announcements relevant, in their entirety, to the investor community. Such communications were permitted under the Code. Moreover, given the highly specialised nature of Alexion's products, the company did not understand how the posts could, even inadvertently, have a promotional effect. As such, it did not see grounds to support the alleged breaches. Moreover, the company had developed a robust social media policy for its employees and considered that it had maintained high standards at all times.

Background and context

Alexion was a US-headquartered group that focused on the development and sales of products for orphan and ultra-orphan conditions such as paroxysmal nocturnal hemoglobinuria (PNH). Alexion Pharma UK Ltd (Alexion UK) was the group's UK affiliate. Alexion UK's promotional activities were limited to the very small number of specialist centres and clinicians that diagnosed and treated patients with rare diseases; it did not target GPs with any kind of promotional material, since they would not usually be in a position to prescribe Alexion products and/or be directly responsible for the diagnosis and treatment of very rare diseases. Alexion submitted that because of the specialist nature of its products, and their classification as prescription only, it did not promote its products on open social media platforms.

The post in question came from a LinkedIn account operated by Alexion Pharmaceuticals Inc. based in the US. This account exclusively contained general information relevant to investors, the financial community and others with an interest in Alexion

Pharmaceuticals Inc. It did not contain product promotional materials of any kind.

When Alexion was advised of the complaint, the post had received over 300 'likes' on LinkedIn largely from users who were not employees of, nor associated with, Alexion. Of those that were from Alexion, only a small handful were employees of Alexion UK; the rest were Alexion employees based outside the UK and would not be expected to have any professional dealings with UK-based clinicians and certainly not UK GPs. It was therefore not clear whether the complainant received the post in his/her feed as a result of following the Alexion LinkedIn account, being linked to a person not employed by Alexion who 'liked' the post, or being linked to an Alexion UK employee or ex-employee who 'liked' the post.

Jurisdiction and scope of Code

Alexion noted that Section 14 of the PMCPA Digital Guidelines effectively confirmed that UK companies should not be held responsible for information placed on the Internet outside the UK by a parent company unless: (i) such activities were on the instigation or authority of the UK company; and (ii) the information referred to the availability of a product in the UK.

According to the above test, the post and the press release would not be attributable to Alexion UK and would fall outside the scope of the Code because:

- The source of the post was Alexion Pharmaceuticals Inc., the US-based parent company. The LinkedIn account of Alexion Pharmaceuticals Inc. had a global audience, predominantly based in the US. Source of feed was 'news.alexion.com'. The press release was from Alexion Inc, to NASDAQ – a US-based stock exchange. The press release had US-based contact addresses. Publishing such content was clearly under the authority and at the instigation of Alexion Pharmaceuticals Inc. without involvement of the UK company.
- The LinkedIn post and press release were addressed to the global investor community and not specifically to UK users. Both the feed and the press release focused on US, EU and forthcoming Japanese regulatory filings, and the mention of the EU was simply part of that continuum.

Based on advice and information received about previous PMCPA cases, Alexion submitted that the LinkedIn post in question clearly fell outside the scope of the Code.

Non-promotional nature of post

As noted above, the post originated from a corporate LinkedIn account, containing general company and investor-relations news at an international level. Consistent with this, the post itself and the press release provided factual, non-promotional information about an important corporate update. The contents were, in their entirety, relevant to investors and the financial community.

Alexion noted that Alexion Pharmaceuticals Inc. was under obligation under various securities laws to bring such news to the attention of markets in full.

Alexion referred to the Supplementary Information to Clause 26.2 of the Code:

'Information made available in order to inform shareholders, the Stock Exchange and the like by way of ... announcements etc. may relate to both existing medicines and those not yet marketed. Such information must be factual and presented in a balanced way....'

The LinkedIn post clearly adhered to these requirements, as follows:

- The post accurately summarised and provided a link to a press release made to the NASDAQ. The nature and purpose of the communication, as a corporate announcement, would be abundantly clear to the average user. For example: the press release (i) mentioned NASDAQ ticker; (ii) and contained a 'Forward Looking Statements' disclaimer. Alexion did not understand how this could be interpreted as product-promotional material.
- No product claims were made. The press release only mentioned clinical trial results in the context of updating corporate news, as supporting the marketing authorization application.
- No product name was mentioned – ALXN1210 was not a brand name. The post did not stimulate patient or health professional interest in a specific product, as no product with that name existed. No marketed product would be available for a number of years, as the EU marketing authorisation application was very recent.
- The risk of the post being misconstrued as promotional, or inadvertently having a product promotional effect, was virtually zero. PNH was an ultra-rare condition and the handful of patients with the disease or few clinicians operating in that field were already likely to be aware of Alexion's products and pipeline. The post simply provided that information to the wider financial and investor community, which might not have such awareness, but in any event, would not be in a position to prescribe, recommend, use, request etc treatment with any Alexion product. While it remained unclear to Alexion how a GP would have received the post, its receipt could not possibly have a promotional effect since GPs would not be in a position to prescribe or recommend its products.
- Under general principles set out in the Code, companies might mention an indication in a non-promotional context so long as they did not also mention a product by name (analogy with 'Reply Paid Cards', per Supplementary Information to Clause 9.8 of the Code). A proportionate approach had been taken here, since it might be misleading to the market not to be clear about which indication and which development molecule was in question.

Complainant's receipt of content

It was unclear as to how the complainant received the post in his/her LinkedIn feed. There was a suggestion that this was because the post received a 'like' from an Alexion employee to whom Alexion assumed the complainant was connected through LinkedIn, however, the complaint did not elaborate. As a general observation, Alexion noted that LinkedIn users would have consented to receiving posts from their contacts, except where users had disabled such a setting, so the post could have been liked by anyone in the complainant's network. Nonetheless, Alexion maintained that the intention and content of the post was not promotional and so it denied a breach of Clause 9.9.

Social media activities of employees

Alexion understood that the PMCPA addressed the responsibility of a company with respect to the social media activities of its employees on a case-by-case basis. With respect to Clauses 2 and 9.1 of the Code, a key factor was whether companies had appropriate social media policies in place for their employees.

Alexion was aware of the sensitivities of the use of social media by its employees and took its responsibilities very seriously in this regard. For instance, the Alexion Global Social Media Policy required that employees:

- were 'expected to act responsibly and professionally, exercise good judgement ...' (Section A)
- were expected not to speak on the company's behalf on social media (Section C.III)
- were permitted to 'like' Alexion's social media posts but might not provide further comment (Section C.V.i)
- should have awareness of interactions with professional acquaintances over social media (Section C.V.ii).

Alexion considered that the company had strong policies in place to guide employees on the appropriate use of social media and had maintained high standards. Without understanding how the complainant received the LinkedIn post in question, it was difficult to comment further at this stage. However, Alexion was reviewing the social media policy to see whether changes were necessary for the UK. Alexion might, for example, guide UK employees not to 'like' certain posts on social media in future.

Conclusions

Subject to receiving further information, Alexion's interim conclusions were as follows:

- Alexion's position was that the post in question fell outside the scope of the Code as there was no relationship with the UK.
- Notwithstanding this, the materials were clearly corporate announcements relevant, in full, to the investment community. As such they were a form of general communication permitted under the Code and acknowledged to be non-promotional.

As such, it was Alexion's position that it had fully complied with the requirements of Clauses 9.9, 26.1 and 26.2.

- Alexion had maintained high standards by establishing a clear social media policy for employees, which discouraged any comment on materials posted. This ensured employees did not make promotional claims as a follow-up to non-promotional information. Alexion therefore believed that it had complied with the requirements of Clause 9.1.
- In light of the above, Alexion submitted that it had always complied with the requirements of Clause 2 in not bringing discredit upon, or reducing confidence in, the pharmaceutical industry.

Alexion had not been provided with any evidence to support the suggestion that the actions of a specific Alexion employee might have triggered the complaint. Even if the LinkedIn post appeared in the complainant's feed because it was liked by an Alexion employee, Alexion maintained that the post was not promotional. LinkedIn users who received items in their LinkedIn feed had consented to this by agreeing to the terms of use. Alexion did not have any control over the use of 'likes' by non-Alexion employees, and the social media actions of its own employees were managed by the Alexion social media policy. The liking of the post by any LinkedIn user (Alexion employee or not) did not make a non-promotional post become promotional.

Alexion had taken, and would take; the measures outlined above and might take further remedial actions following the PMCPA's investigation if required.

PANEL RULING

The Panel noted that Alexion referred to the complainant as a general practitioner (GP) in its response. The Panel noted that the company had been advised by the case preparation manager at the outset that the complainant was a GP. That was not so, the contactable complainant described themselves as a 'concerned HCP'. The Panel noted that the complaint concerned alleged promotion to the public rather than to health professionals and thus his/her professional status was not relevant to the subject matter of the complaint.

The Panel noted the complainant's allegation that the LinkedIn post, which led to a press release, appeared in his/her LinkedIn feed because Alexion UK employees had liked it which then presented it to their connections. The Panel noted that the complainant had not named or otherwise referred to a specific Alexion UK employee that was in his/her network on LinkedIn. The Panel further noted Alexion's submission that when it was advised of the complaint, the post had received over 300 'likes' on LinkedIn including a 'small handful' of likes from Alexion UK employees.

The Panel noted that material could be disseminated or highlighted by an individual on LinkedIn in a number of ways, including by posting, sharing, commenting or liking. The Panel understood that if an individual 'liked' a post it increased the

likelihood that the post would appear in his/her connections LinkedIn feeds thereby disseminating the material. In the Panel's view, activity conducted on social media that could potentially alert one's connections to the activity might be considered proactive dissemination of material. In addition, an individual's activity and associated content might appear in the individual's list of activities on his/her LinkedIn profile page which was visible to his/her connections; an individual's profile page was also potentially visible to others outside his/her network depending on the individual's security settings. The Panel considered it was likely that Alexion UK employees' connections would include UK members of the public and might include UK health professionals. The Panel noted that the LinkedIn post and associated press release was 'liked' by a number of Alexion UK employees. In the Panel's view the act of liking the material amounted to proactive dissemination of the material within the UK and brought it within the scope of the Code.

The Panel noted that LinkedIn was different to some other social media platforms in that it was a business and employment-orientated network and was primarily, although not exclusively, associated with an individual's professional heritage and current employment and interests. In the pharmaceutical industry, the Panel noted that an individual's network might, albeit not exclusively, be directly or indirectly associated with the healthcare industry. In the Panel's view, it was of course not unacceptable for company employees to use personal LinkedIn accounts and the Code would not automatically apply to all activity on a personal account; whether the Code applied would be determined on a case-by-case basis taking into account all the circumstances including: the content, any direct or indirect reference to a product, how the information was disseminated on LinkedIn, the company's role in relation to the availability of the content and whether such activity was directed or encouraged by the company. If activity was found to be within the scope of the Code, the company would be held responsible.

The Panel noted Alexion's submission that the post and press release in question were factual, non-promotional, corporate announcements relevant, in their entirety, to the investor community and that they originated from a LinkedIn account operated by Alexion Pharmaceuticals Inc. based in the US no involvement of the UK affiliate. The Panel noted Alexion's submission that the post did not target UK users or directly mention the UK. The Panel noted, however, that in liking the post, Alexion UK employees had, on the balance of probabilities, proactively disseminated it within the UK to an audience far wider than the intended financial community. In the Panel's view, the broad dissemination of the material beyond the financial community meant that such dissemination was beyond that referred to in the supplementary information to Clause 26.2 Financial Information which, *inter alia*, permitted financial information within the scope of the supplementary information to relate to both existing medicines and those not yet marketed.

The Panel noted that the LinkedIn posting informed readers that Alexion had submitted an application for approval of ALXN1210 as a treatment for patients with paroxysmal nocturnal haemoglobinuria (PNH) in the European Union (EU). The US filing and Japanese submission were also referred to. The linked press release provided more detail. It described the results of two large Phase 3 studies and included statements such as 'We are excited about this next important step towards our goal of establishing ALXN1210 as the new standard of care for patients with PNH...' and 'Building on 10 years of proven efficacy and safety with Soliris and 25 years of leadership in complement biology...'. Soliris (eculizumab) was an Alexion prescription only medicine, available in the UK, indicated in adults and children for the treatment of PNH. Soliris was described in the press release as 'a first-in-class complement inhibitor ...' and ALXN1210 was described as an 'innovative, long acting C5 inhibitor discovered and developed by Alexion ...'. The press release also stated that 'Alexion and Soliris have received some of the pharmaceutical industry's highest honours for medical innovation in complement inhibition.

The Panel noted that Clause 26.1 prohibited the promotion of prescription only medicines to the public. Clause 26.2 stated that information about prescription only medicines which was made available either directly or indirectly to the public must be factual, presented in a balanced way, must not raise unfounded hopes of successful treatment and must not encourage members of the public to ask their health professional to prescribe a specific prescription only medicine.

The Panel noted its comments above and considered that on the balance of probabilities not all the Alexion UK employees' connections to whom the post might have been disseminated to by virtue of their 'like' would have been health professionals. Thus, in the Panel's view and on the balance of probabilities the LinkedIn post and associated press release had been disseminated to members of the public.

The Panel noted that the product, ALXN1210, was not classified as a prescription only medicine when the LinkedIn post and associated press release at issue were liked by the UK employee. Clauses 26.1 and 26.2 only applied to prescription only medicines. On this very narrow technical point the Panel ruled no breach of Clauses 26.1 and 26.2 of the Code. However, the Panel considered that the Alexion UK employees' like of the LinkedIn post and associated press release regarding an unlicensed medicine and the potential subsequent dissemination to all of their connections meant that Alexion had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted that the press release also referred to Soliris, which was a prescription only medicine available in the UK. There was no allegation with regard to Soliris and, therefore, the Panel could make no ruling in this regard.

The Panel noted that Clause 9.9 stated that the telephone, text messages, email, telemessages,

facsimile, automated calling systems and other electronic data communications must not be used for promotional purposes, except with the prior permission of the recipient. The Panel noted Alexion's submission that LinkedIn users would have consented to receiving posts from their contacts, except where users had disabled such a setting. There was no evidence before the Panel detailing what information was provided to users when signing up to use LinkedIn and to existing users when new functionalities were introduced. It was thus unclear whether prior permission had been given to receive such posts. The Panel considered that Clause 9.9 required companies that wished to rely on prior permission to be able to demonstrate that recipients had agreed to receive promotional material by such means. Such consent should be explicit and the nature of the material to be sent electronically made clear. Clause 9.9 applied to all medicines within the scope of the Code. Nonetheless, the Panel noted that the complainant bore the burden of proof and considered that he/she had not provided evidence to show that there had been a breach of Clause 9.9 and no breach was ruled.

The Panel was mindful of the complex issues that had to be addressed by companies when advising staff about social media use. The increasing use of social media, both in the personal and business capacity, presented compliance challenges. In addition, many social media platforms used algorithms and had settings which individuals and companies might not be fully aware of. In the Panel's view, companies should remain vigilant and ensure that they took reasonable steps to highlight the potential compliance issues that might arise from interacting on social media including 'liking' certain posts on LinkedIn given such posts could thereby potentially be pushed to their connections' feeds. The Panel was aware that the types of activity performed by the Alexion UK employees on LinkedIn was not uncommon across the industry.

In the Panel's view, employees might feel inclined to endorse posts that were published by their company's corporate social media account or which related to their company and depending on the content such activity may or may not fall within the scope of the Code. Companies therefore needed to issue specific and unambiguous guidance on use of social media including relevant personal use. This was particularly important if UK employees were likely to follow the social media accounts of overseas affiliates which might have codes, laws and regulations that differed to the UK. It was therefore critical that companies provided clear and tailored guidance for its employees which was frequently reviewed. In the Panel's view it was important that companies regularly reviewed such guidance.

The Panel noted Alexion's submission that the Alexion Global Social Media Policy stated, *inter alia*, that employees were permitted to 'like' Alexion's social media posts but might not provide further comment. The Panel noted that Alexion was, however, reviewing the social media policy to see whether changes were necessary for the UK and might guide UK employees not to 'like' certain posts on social media in future. The Panel was concerned that there appeared to be no UK specific guidance at the time of the complaint. The Panel considered that the lack of adequate UK specific social media guidance at the time of the complaint meant that Alexion had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel did not consider that the circumstances warranted a breach of Clause 2 which was used as a sign of particular censure and was reserved for such circumstances. No breach of Clause 2 was ruled.

Complaint received

28 June 2018

Case completed

14 February 2019

ANONYMOUS, NON-CONTACTABLE v PHARMAMAR

Meeting in Madrid

An anonymous, non-contactable complainant who appeared to be an NHS employee complained about a meeting in Madrid organised by PharmaMar.

The complainant explained that he/she was invited by PharmaMar to attend the meeting and was told that new Yondelis (trabectedin) data would be presented. PharmaMar would be willing to pay for his/her flights and accommodation. The complainant stated that he/she attended a gala dinner at a named venue on Friday, 31 March 2017 along with other UK delegates and described the event as a 'social gathering'. The complainant attended the promotional meeting the following day where no new data on the company's product was presented and felt very much misled by PharmaMar's representative. The complainant stated that, along with other delegates, he/she was offered the opportunity to stay the Saturday night even though there was no meeting on Sunday, 2 April.

The detailed response from PharmaMar is given below.

The Panel noted that when a meeting was held outside the UK in a European country where the national association was a member of EFPIA the limits in the host country code would apply. The Panel noted that the cost of the meal including drinks and taxes was €59.95 per head which was marginally below the limit in the Spanish Code of €60.

The Panel considered that it was not necessarily unacceptable to offer subsistence to delegates who had arrived the day prior to the meeting – however, the arrangements had to comply with the Code. The Panel noted that the dinner invitation, provided by the complainant, referred to the dinner being held at the named venue in celebration of the second international sarcoma meeting. The Panel noted PharmaMar's submission that the meeting invitation for UK delegates contained no pictures or website address for the dinner venue, however, the meeting invitation implied that it was the venue for the entire meeting. The Panel noted that the dinner venue was selected because it could accommodate a large number of delegates. The Panel noted that the programme referred to the meeting occurring from 31 March - 1 April. However, there was no agenda, presentations nor educational content provided on 31 March and PharmaMar provided no justification as to why all delegates needed to be together for dinner. The Panel noted that delegates appeared to be seated by country on separate tables. The impression from the photographs was that the venue was lavish and deluxe. It was a 2 Michelin star restaurant*. The capacity of the dinner venue was not a justifiable reason for selecting it.

The Panel considered that it was important for a company to be mindful of the impression created by its activities. Taking all the circumstances into account the Panel did not consider that the hospitality on 31 March 2017 was secondary to the main purpose of the event ie subsistence only. The level was not appropriate and was out of proportion to the occasion. A breach was ruled. The Panel considered that high standards had not been maintained and a further breach was ruled.

The Panel noted that the invitation to delegates was made face-to-face, with the programme being used as an introduction to the event. The Panel had no knowledge of what representatives had told health professionals about the meeting during the face-to-face invitation. The programme listed 'STS update: Latest news' as an agenda item. The complainant alleged he/she was told that new data was going to be presented on PharmaMar's product and that this was not the case and in that regard he/she felt very much misled. The Panel considered that the complainant had not proved his/her complaint on the balance of probabilities and therefore ruled no breach.

The Panel noted that the meeting was scheduled to finish at 16:20 on Saturday, 1 April. The Panel noted PharmaMar's initial submission that there were five UK delegates for whom evening flights were not available from Madrid to their home locations on 1 April, and these delegates were offered an additional one-night stay. The Panel considered that, in such circumstances, it was not unreasonable for PharmaMar to offer an extra night's accommodation. The complainant had provided no evidence to support his/her allegation that the additional one night stay offered was inappropriate. The Panel ruled no breach on that particular point.

The Panel noted that the cost of the meal per head at the Friday night dinner venue was €59.95 (including taxes) and therefore just below the Spanish Code limit of €60. The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2, which was a sign of particular censure and was reserved for such use, and therefore no breach was ruled.

* Following the completion of the case, PharmaMar advised the Authority that although a 2 Michelin star restaurant was one of the facilities available at the venue, PharmaMar had not used the restaurant. Rather it had rented a room at the venue and used the venue's catering rather than that of the 2 Michelin star restaurant.

An anonymous, non-contactable complainant who appeared to be an NHS employee complained about a meeting in Madrid organised by PharmaMar. The

complainant stated that he/she had recently seen Case AUTH/2979/9/17 on the PMCPA website which concerned Yondelis (trabectedin). Yondelis was used in adults with advanced soft tissue sarcoma.

COMPLAINT

The complainant explained that he/she was invited to attend a meeting in Madrid organised by PharmaMar and was told that new data would be presented on its product. PharmaMar would be willing to pay for his/her flights and accommodation. The complainant stated that he/she attended a gala dinner at a named venue on 31 March 2017 along with other UK delegates and described the event as a 'social gathering'. Photographs were provided. The complainant attended the promotional meeting on 1 April 2017 where no new data on the company's product was presented and felt very much misled by PharmaMar's representative. The complainant stated that, along with other delegates, he/she was offered the opportunity to stay the Saturday night even though there was no meeting on Sunday, 2 April.

The complainant wished to remain anonymous as he/she had not declared the trip to his/her NHS employers.

When writing to PharmaMar, the Authority asked it to consider the requirements of Clauses 22.1, 9.1 and 2 of the Code.

RESPONSE

PharmaMar submitted that PharmaMar Ltd was ceasing the promotional activities of Yondelis. It was closing its UK operation from 31 July 2018. PharmaMar stated that the concerns raised by the anonymous complainant were unsubstantiated and lacked credibility.

PharmaMar submitted that the meeting in question took place in Madrid and was organised by PharmaMar SA (Spanish headquarters). It was a meeting with a high level of scientific content and was of a promotional nature (PharmaMar was the only sponsor). The title of the meeting was 'Soft Tissue Sarcoma: Evidence and Experience'. The meeting was a forum for worldwide experts to discuss soft tissue sarcoma with 280 delegates attending (110 from Spain and 170 from various other countries, including Italy 48, Germany 45 and Nordics & Eastern Europe 15 etc). There were 11 delegates from the UK. Most delegates were from Spain and it made greater logistical sense to hold the meeting in Spain rather than in the UK. The UK delegates were invited by the UK affiliate, which also funded attendance (flights and accommodation). The flights provided to UK delegates were economy class; they flew out to Madrid on 31 March 2017 arriving in the afternoon and evening. Flight cost details were provided. During the meeting, the 11 UK delegates stayed at a 4-star hotel, chosen because of its good accessibility, its distance to the meeting venue was a 10-minute walk, and it was in line with recommendations by the Farmalndustria (Spanish) Code. The logistics for the meeting were contracted to an external provider which managed

all the hotel bookings etc for the different country delegates. As a result, PharmaMar submitted that it was not possible to provide an itemised invoice for the room cost of each delegate; however, the budget allocated for a room at the hotel was €180/night (breakfast included).

The venue for the meeting was chosen because of its transport links, conference facilities and because it could accommodate a large number of delegates in one meeting room.

The meeting began on the evening of 31 March with dinner at a named venue. PharmaMar stated that this venue was chosen for the same reason as the meeting venue: it could accommodate a large number of delegates, it had good accessibility, and it was near to the hotel and the meeting venue. The cost of the meal per head including drinks was €54.50 excluding VAT. PharmaMar provided an invoice which indicated that three hundred and fifty-seven meals were funded. PharmaMar submitted that this included staff meals. PharmaMar noted that the maximum cost per head for a meal specified in the Spanish Code was €60.

PharmaMar stated that the meeting invitation for UK delegates did not overemphasise the venue (there were no pictures of the interior or exterior and no website address was provided). PharmaMar acknowledged that the invitation seemed to imply that the meeting venue was the venue for the dinner. The actual meeting venue was noted on the meeting agenda.

The meeting began on 1 April at 8.30 and continued to 16.20. PharmaMar stated that the meeting had substantial educational content as could be seen from the agenda. Copies of the presentations were provided. Following the meeting close, for those who had flights booked for that evening, transport to the airport was provided. There were, however, no evening flights available from Madrid to the home locations of five UK delegates and they were offered an additional one-night stay and provided with an evening meal at a local restaurant. The approximate cost per head for this subsistence was €33.26 excluding VAT (the total bill being €199.55 for 6 individuals: 5 delegates plus a PharmaMar member of staff).

PharmaMar submitted that the meeting was not in breach of Clause 22.1 for the following reasons:

- The meeting contained significant scientific content;
- There were valid and cogent reasons for choosing the location;
- There was appropriate justification for choosing both the venue for the meeting and that used for accommodation;
- An additional night stay was provided to some delegates for logistical reasons; and
- The subsistence provided during the meeting was reasonable and in line with the Spanish Code.

PharmaMar further denied any breach of Clauses 9.1 or 2.

In response to a request for further information from the Panel, PharmaMar submitted that it had closed its operations in the UK. All of the UK staff that were responsible for managing UK participation at this event were no longer employed by the company. Five UK staff had attended the meeting.

PharmaMar Ltd was responsible for selecting and inviting the UK delegates. As all the personnel in charge of the local selection process had now left the company, it could not confirm the local selection criteria; it was not documented. Health professionals were contacted face to face by the local team. PharmaMar's expectation was that the selection was based on delegates' expertise and relevance for patient care. PharmaMar listed the hospitals of the UK delegates who attended.

The invitation to delegates was made face-to-face with the programme's information being used as an introduction to the event. There were no further materials in addition to the programme and welcome letter except for a letter sent to delegates who had confirmed their attendance.

One UK delegate stayed until 3 April. PharmaMar submitted that it did not know the reason for the additional night's stay, however, the delegate paid for his/her own accommodation.

The drinks at the dinner venue on 31 March included wine, beer and soft drinks before the meal and wine during the meal. All UK delegates left the venue together when the dinner finished at approximately 22:30.

PharmaMar explained that the difference between the number of delegates (280) and the number of meals invoiced (357) was due to the fact that not all invited delegates attended (eg 8 from the UK) but payment had to be given in advance to reserve the venue. In addition, the invoice included PharmaMar staff from all affiliates and headquarters as well as relevant staff from other companies with whom PharmaMar partnered in countries where it did not have direct presence. There was no agenda or presentation on the evening of 31 March. Most delegates arrived in the afternoon or evening because the event started at 8:30 the next day, and therefore dinner was offered.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the PMCPA stated that anonymous complaints would be accepted but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant could not be contacted for more information.

The Panel noted that Clause 22.1 stated that hospitality must be strictly limited to the main purpose of the event and must be secondary to the purpose of the meeting ie subsistence only. The level of subsistence offered must be appropriate and

not out of proportion to the occasion. Clause 22.1 applied to scientific meetings, promotional meetings, scientific congresses and other such meetings and training. The supplementary information stated that the impression created by the arrangements must be borne in mind. Meetings organised for groups of doctors, other health professionals and/or other relevant decision makers etc which were wholly or mainly of a social nature were unacceptable.

The Panel further noted that the supplementary information to Clause 22.1 stated that with any meetings, certain basic principles applied, *inter alia*, the meeting must have a clear educational content and the venue must be appropriate and conducive to the main purpose of the meeting; lavish, extravagant or deluxe venues must not be used.

It was an established principle under the Code that the UK company was responsible for the acts and omissions of its overseas affiliates that came within the scope of the Code.

The supplementary information to Clause 22.2 stated that the maximum of £75 plus VAT and gratuities (or local equivalent) did not apply when a meeting was held outside the UK in a European country where the national association was a member of EFPIA and thus covered by EFPIA Codes. In such circumstances the limits in the host country code would apply. The Panel noted that the cost of the meal including drinks and taxes was €59.95 per head which was marginally below the limit in the Spanish Code of €60.

The Panel considered that it was not necessarily unacceptable to offer subsistence to delegates who had arrived the day prior to the meeting – however, the arrangements had to comply with the Code. The Panel noted that the dinner invitation, provided by the complainant, referred to the dinner being held at a named venue in celebration of the second international sarcoma meeting. The Panel noted PharmaMar's submission that the meeting invitation for UK delegates (later clarified as the welcome letter) contained no pictures or website address for the dinner venue, however, the meeting invitation implied that this was the venue for the entire meeting. The Panel noted that the dinner venue was selected because it could accommodate a large number of delegates. The Panel noted that the programme referred to the meeting occurring from 31 March - 1 April. However, there was no agenda, presentations nor educational content provided on 31 March and PharmaMar provided no justification as to why all delegates needed to be together for dinner. The Panel noted, from photographs supplied by the complainant, that delegates appeared to be seated by country on separate tables. The impression from the photographs was that the dinner venue was lavish and deluxe. The Panel was aware (from an audit of PharmaMar's procedures as a result of Case AUTH/2979/9/17), that it was a 2 Michelin star restaurant*. The capacity of the dinner venue was not a justifiable reason for selecting it. The Panel considered that it was important for a company to be mindful of the impression created by its activities. Taking all the circumstances into account the Panel did not consider that the

hospitality on 31 March 2017 was secondary to the main purpose of the event ie subsistence only. The level was not appropriate and was out of proportion to the occasion. A breach of Clause 22.1 was ruled. The Panel considered that high standards had not been maintained and a breach of Clause 9.1 was ruled.

The Panel noted that the invitation to delegates was made face-to-face, with the programme being used as an introduction to the event. The complainant alleged he/she was told that new data was going to be presented on PharmaMar's product and that this was not the case and in that regard he/she felt very much misled. The Panel had no knowledge of what representatives had told health professionals about the meeting during the face-to-face invitation. The Panel noted that the complainant could not be contacted for further information. The complainant provided a copy of the programme which included the agenda item 'STS update: Latest news'. PharmaMar provided copies of the slides presented but made no submission in this regard. The Panel considered that the complainant had not proved his/her complaint on the balance of probabilities and therefore ruled no breach of Clause 9.1 in this regard.

The Panel noted that the meeting was scheduled to finish at 16:20 on Saturday, 1 April. The complainant alleged that he/she and other delegates were offered the opportunity to stay the Saturday night even though there was no meeting on Sunday, 2 April. The Panel noted PharmaMar's initial submission that there were five UK delegates for whom evening

flights were not available from Madrid to their home locations on 1 April, and these delegates were offered an additional one-night stay. No details were provided by PharmaMar about the timings of the flights. The Panel considered that, in such circumstances, it was not unreasonable for PharmaMar to offer an extra night's accommodation. The complainant had provided no evidence to support his/her allegation that the additional one night's stay offered was inappropriate. The Panel ruled no breach of Clause 22.1 on that particular point.

The Panel noted that Clause 2 was used as a sign of particular censure and reserved for such use. The Panel noted that the cost of the meal per head at the dinner venue on the Friday night was €59.95 (including taxes) and therefore just below the Spanish Code limit of €60. The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 and therefore no breach was ruled.

* Following the completion of the case, PharmaMar advised the Authority that although a 2 Michelin star restaurant was one of the facilities available at the venue, PharmaMar had not used the restaurant. Rather it had rented a room at the venue and used the venue's catering rather than that of the 2 Michelin star restaurant.

Complaint received **13 July 2018**

Case completed **18 October 2018**

EX-REPRESENTATIVE v GLAXOSMITHKLINE

Activities of GlaxoSmithKline

An ex-representative of GlaxoSmithKline complained about GlaxoSmithKline's relationship with a named practice-based pharmacist and secondly about a claim in the digital sales aids for Relvar Ellipta (fluticasone furoate, vilanterol trifenate), Anoro Ellipta (vilanterol trifenate, umeclidinium bromide) and Trelegy Ellipta (fluticasone furoate, vilanterol trifenate, umeclidinium bromide).

The detailed response from GlaxoSmithKline is given below.

1 GlaxoSmithKline's relationship with a practice-based pharmacist

The complainant alleged that a named pharmacist conducted a therapeutic review from a competitor product to Relvar and Incruse (umeclidinium bromide) without any initial input from GlaxoSmithKline. Having realised this, GlaxoSmithKline decided to use this to its advantage and initially had a 'Q and A' [question and answer] session at a national conference to show the success of what had been done.

The complainant stated that he/she attended a regional meeting along with representatives where the pharmacist in question did another 'Q and A' session and presented documents (copies provided). The complainant alleged that the objective was that representatives would ask health professionals if they needed support in carrying out a switch to a GlaxoSmithKline product. If the health professional replied yes, then the representative would email their contact details to a named senior representative who would contact the pharmacist in question who would then send over the documents to the health professionals. The senior representative in question kept a tracker of health professionals who had been contacted and submitted this higher up and had possibly received a higher rating of performance based on this piece of work. In the complainant's view this was supporting a switch/review to GlaxoSmithKline products.

The complainant stated that whilst there was no direct proof he/she queried if the pharmacist in question would have created a 'how to' document if he/she had not been contacted by GlaxoSmithKline. The complainant queried whether payments made to this pharmacist were in line with the time he/she spent for sharing his/her experience.

The Panel noted GlaxoSmithKline's submission that the pharmacist in question was contracted to speak at three internal meetings; the national sales conference in March 2017, a regional meeting in December 2017 and a respiratory leadership meeting in March 2018. The Panel noted the hourly rate and

the number of hours the pharmacist was paid for. On the basis of the information before it, the Panel considered that there was no evidence to support the complainant's allegation that payments to this pharmacist for these meetings were not in line with the time spent for speaking at meetings and no breach was ruled.

The Panel noted that the documents provided by the complainant included a protocol for inhaler changes for patients with COPD. The protocol referred to the practice pharmacist identifying all listed COPD patients on Seretide Accuhaler 500/50mcg and Spriva Capsules 18mcg and excluding from the switch those patients who were unwell or unstable as identified from their records. All the other patients would have their Seretide accuhaler changed to Relvar Ellipta 92/22 and their Spiriva inhalation capsules changed to Incruse Ellipta. The Panel considered, as acknowledged by GlaxoSmithKline, that the reference to GlaxoSmithKline in the protocol gave the impression that GlaxoSmithKline was somehow involved in the protocol and the service.

The Panel noted GlaxoSmithKline's submission that following the national conference in March 2017, the pharmacist in question offered to be contacted by interested health professionals to share his/her positive experience of medicine optimisation. The Panel noted GlaxoSmithKline's submission that it did not pay this pharmacist to speak to other practice-based pharmacists on its behalf nor did it make any payments in respect of any aspect of his/her medicines optimisation activity.

The Panel noted that in August 2017 the pharmacist in question emailed the senior representative in question informing him/her that he/she had sent information to a named individual from a named area regarding inhaler switches. The email included the information sent as attachments, which were saved as 'GSK protocol for inhaler changes in COPD', 'GSK Seretide letter', 'GSK COPD letter, Seretide and Spiriva', and 'GSK Spiriva letter' and appeared to be the same documents as those provided by the complainant. The Panel noted that whilst it had concerns with regard to the misleading impression created by the attached documents and the lack of follow up by the representative to clarify the position, it did not consider that there was evidence to suggest that GlaxoSmithKline had initiated, contributed to or funded the documents in question as implied by the allegation that the 'how to' document would not exist had GlaxoSmithKline not contacted the pharmacist in question. No breach was ruled in this regard.

The Panel was concerned to note that GlaxoSmithKline knew about the content of the documents and that the pharmacist in question

was providing these to practices following 'referrals' from GlaxoSmithKline representatives, yet it took no action other than to decline to pay for the documents. The Panel further noted GlaxoSmithKline's submission that the pharmacist in question was asked by some representatives to share copies of his/her documents with other practices. GlaxoSmithKline acknowledged that it was not appropriate for the company to endorse or encourage the activity and the representatives in question should have taken the opportunity to reinforce GlaxoSmithKline's position on switch and to clarify the nature of GlaxoSmithKline's involvement with the pharmacist in question. The Panel considered that high standards had not been maintained in this regard, as acknowledged by the company, and a breach was ruled.

The Panel noted that although the pharmacist in question was not being paid to speak to interested peers, GlaxoSmithKline representatives were actively involved in the introduction of practices to him/her. The Panel noted that communication between the GlaxoSmithKline representatives and practices, for which GlaxoSmithKline was responsible, and communication between the pharmacist in question and the practices for which GlaxoSmithKline was potentially responsible for, might lead to a change to GlaxoSmithKline's medicines. The Panel noted that the Code did not prohibit a company from promoting a switch but did prohibit switch services paid for or facilitated directly or indirectly by a pharmaceutical company whereby a patient's medicine was simply changed to another.

The Panel noted that it could be argued that the provision of documents to practices, including template letters, via referrals from GlaxoSmithKline's representatives, went beyond promoting a switch. There was a fine line between simply promoting a switch and providing so much detailed information in that regard that the information facilitated a switch.

The Panel considered that there was insufficient evidence as to whether any change of medicine was as a result of a switch service or a therapy review or that the pharmacist in question or GlaxoSmithKline had actually assisted any health professional in implementing a change to a GlaxoSmithKline medicine. GlaxoSmithKline had made no payment in relation to any service. Taking all the circumstances into account the Panel decided that on balance there was insufficient evidence to show that overall GlaxoSmithKline arrangements facilitated a switch to its medicines as prohibited by the Code. The Panel ruled no breaches of the Code accordingly.

The Panel noted that the conversations between the representatives including the completion of the senior representative's tracker, together with the presentations by the pharmacist at both the national and regional meetings, would add to the impression that GlaxoSmithKline supported and endorsed the pharmacist's views and approaches and might be seen by representatives as instructions on how the

product should be promoted. The Panel considered that the documents provided by the pharmacist in question to the 12 representatives at the regional meeting in December 2017, which could be seen as setting out GlaxoSmithKline's involvement in a switch service, in effect constituted briefing material. The Panel noted that GlaxoSmithKline made no submission with regard to any follow up with the 12 representatives confirming that it did not endorse this pharmacist's protocol or to remind the representatives of the company's position on switching. Whilst the Panel was concerned at the lack of clear guidance provided by the company, it did not consider, on the balance of probabilities, that the communications above advocated a course of action likely to be in breach of the Code and no breach was ruled.

The Panel noted that whilst GlaxoSmithKline had fallen short of the expected standards of documentation required by the Code in this instance as acknowledged by the company, the complainant had not established that this meant that there was a widespread lack of written communication and projects would disproportionately rely on verbal communication as alleged. The Panel considered that there was no evidence before it that the frequency of meetings between the pharmacist in question and GlaxoSmithKline representatives, prior to him speaking at national and regional meetings, were indicative of inappropriate verbal briefings for the meetings and no breach was ruled in this regard.

Although the Panel had some concerns about the overall arrangements and oversight by GlaxoSmithKline it did not consider that, on balance, the circumstances warranted a ruling of a breach of Clause 2, which was a sign of particular censure and reserved for such use, and ruled no breach accordingly.

2 Claim in digital sales aids for Relvar Ellipta, Anoro Ellipta and Trelegy Ellipta

The complainant stated that the digital sales aid for Relvar Ellipta, Anoro Ellipta and Trelegy Ellipta had a page that described the device as 'open, inhale and close.' This key message was contrary to the information provided in both the summary of product characteristics (SPC) and the patient information leaflet (PIL) which required more steps for the patient to benefit from the medication.

The Panel noted GlaxoSmithKline's submission that no Trelegy digital sales aids included any reference to open, inhale and close. The complainant had not provided any evidence to the contrary. The Panel, therefore, based on the very narrow allegation, ruled no breach with regard to the Trelegy sales aids.

The Panel noted that the Relvar Ellipta SPC stated under the method of administration that the step-by-step instructions should be followed. According to the Relvar SPC there were four steps.

The Panel accepted that as far as the device was concerned, it had to be opened by the patient, used for inhalation and closed by the patient. However,

to take the medicine correctly and, *inter alia*, for the dose to be effective the patient had to do more than simply open, inhale and close. The required steps were detailed in the Relvar and Incruse SPCs and PILs. It appeared from the material provided that, despite reading the PIL, some patients still made a critical error which was defined as an error most likely to result in no, or minimal, medication being inhaled.

In the Panel's view, the references to '...efficacy in 3 steps: patients simply Open Inhale Close' in the Relvar/Incruse digital sales aids (January 2018, May 2016, April 2017) and the Relvar asthma digital sales aids (May 2016, May 2017) were misleading and inconsistent with the Relvar SPC. Breaches of the Code were ruled.

On balance, the Panel considered that the Relvar Asthma digital sales aids (September 2017 and October 2017) which referred to 'With just 3 steps: patients simply Open Inhale Close' and the implication that it related to patient benefit from the medicine with just 3 steps, was misleading and inconsistent with the Relvar SPC and breaches of the Code were ruled.

The Panel noted that the current Relvar Ellipta digital sales aid (March 2018 ref UK/FFT/0004/18) did not refer to either '...efficacy in 3 steps: patients simply Open Inhale Close' or 'With just 3 steps: patients simply Open Inhale Close' as featured in previous Relvar digital sales aids. The current sales aid contained interactive Ellipta pages which referred to the mechanisms of the device rather than instructions on how patients should use the device; there were no claims regarding the number of steps required by the patient to benefit from the medicine and each page of the Interactive Ellipta section referred the user to the PIL for patient instructions. In the Panel's view, there was no evidence that the reference to open inhale close in the context of the Interactive Ellipta section was misleading or inconsistent with the SPC as alleged and no breaches were ruled.

Although there was no current digital sales aid for Anoro, previous versions (November 2016 and January 2017), used during the time-period in scope of the complaint, referred to open (with a 'click'), inhale and close beneath the statement 'delivered in a once-daily, easy-to-use Ellipta inhaler'. The Panel noted that the Anoro SPC and PIL referred to three steps when taking the medicine: first 'Prepare a dose' (including sliding the cover down until a click was heard); second 'How to inhale the medicinal product'; and third 'Close the inhaler'. Full details for how the patient was to perform each step were in the SPC and PIL. In the Panel's view, the page in question referred to the delivery of the medicine and there were no claims linking efficacy or patient benefit from the medicine to the 3 steps open, inhale and close. The Panel considered that in the circumstances and based on the narrow allegation the page in question was not misleading or inconsistent with the SPC and no breaches were ruled accordingly.

Noting its comments and rulings above, the Panel did not consider that GlaxoSmithKline had failed to maintain high standards and ruled no breach accordingly.

An ex-representative of GlaxoSmithKline complained about the activities of GlaxoSmithKline UK Limited. The complainant stated that whilst the complaint was specific in nature, there was a widespread culture within GlaxoSmithKline of 'having a conversation' as opposed to written communication. Whilst there were policies in place including 'write right', there was widespread lack of written communication and projects would disproportionately rely on verbal communication.

There were two matters raised by the complainant: the first related to GlaxoSmithKline's relationship with a practice-based pharmacist and the second related to a claim in the digital sales aids for Relvar Ellipta (fluticasone furoate, vilanterol trifenate), Anoro Ellipta (vilanterol trifenate, umeclidinium bromide) and Trelegy Ellipta (fluticasone furoate, vilanterol trifenate, umeclidinium bromide).

Anoro Ellipta, Relvar Ellipta and Trelegy Ellipta were used in adults with chronic obstructive pulmonary disease (COPD). Relvar Ellipta was also used in adults and adolescents aged 12 years and older with asthma.

1 GlaxoSmithKline's relationship with a practice-based pharmacist

COMPLAINT

The complainant alleged that a named pharmacist conducted a therapeutic review from a competitor product to Relvar and Incruse (umeclidinium bromide) without any initial input from GlaxoSmithKline. Having realised what had happened, GlaxoSmithKline decided to use this to its advantage and initially had a 'Q and A' [question and answer] session at a national conference to show the success of what had been done.

The complainant stated that these Q and A sessions were a means of allowing a free flow of information without approved slides but in fact when the customer relationship management (CRM) database was looked at it could be found as preparation of the speaker, albeit it would not be mentioned in the notes.

The complainant stated that he/she attended a regional meeting along with representatives where the pharmacist in question did another 'Q and A' session and presented documents (copies provided). The complainant alleged that the objective was that representatives would ask health professionals if they needed support in carrying out a switch to a GlaxoSmithKline product. If the health professional replied yes, then the representative would email their contact details to a named senior representative who would contact the pharmacist in question who would then send over the documents to the health professionals. The senior representative in question kept a tracker of health professionals who had been

contacted and submitted this higher up and had possibly received a higher rating of performance based on this piece of work. In the complainant's view this was supporting a switch/review to GlaxoSmithKline products.

The complainant stated that whilst there was no direct proof he/she queried if the pharmacist in question would have created the 'how to' document if he/she had not been contacted by GlaxoSmithKline. The complainant suggested looking at payments made to this pharmacist as an 'internal' speaker to see if it was in line with the time he/she spent for sharing his/her experience. The complainant alleged a breach of Clause 19 of the Code.

In response to a request from the case preparation manager, the complainant explained that the CRM system was where meetings with health professionals were recorded. GlaxoSmithKline did not allow any free text so the notes would not contain information as to the true nature of the calls/meetings. The complainant stated that if one looked at the actual meeting dates with the pharmacist in question recorded in the system, one might spot a higher frequency of meetings prior to him/her speaking at regional and national meetings. The complainant stated that this would facilitate a verbal conversation of what the main messages would be, unless there was an email trail, and this tied into GlaxoSmithKline's culture of paying a health professional for an internal meeting with limited information of what was to be discussed. So, whilst in the regional meeting it was called a 'questions and answers' session, the first part of the meeting was in fact a presentation by the pharmacist in question where the documents in question were handed out.

When writing to GlaxoSmithKline, the Authority asked it to bear in mind the requirements of Clauses 2, 9.1, 15.9, 18.1, 19.1, 19.2 and 23.1 of the Code.

RESPONSE

GlaxoSmithKline submitted that it took the complaint extremely seriously and had conducted a thorough investigation in the time available to respond. It had conducted interviews with individuals named or implicated in the complaint.

GlaxoSmithKline asserted that it was not implementing a therapy review service in COPD and GlaxoSmithKline did not pay for or facilitate a switch service.

GlaxoSmithKline's commercial strategy for the Ellipta Medicines included promoting switch for patients already receiving treatment for COPD to Ellipta medicines if appropriate. GlaxoSmithKline did not support facilitation of switch programs, nor did GlaxoSmithKline advocate for healthcare practitioners to conduct switch programs without a clinical review and legitimate clinical rationale.

Background

GlaxoSmithKline submitted that it actively marketed a number of respiratory products for asthma and

COPD. Four of those products, including Relvar and Incruse, were administered using GlaxoSmithKline's patented Ellipta inhaler. Relvar and Incruse were launched in 2014.

In 2017, a named healthcare organisation re-issued its COPD Management Plan, a set of guidelines intended to set out local recommendations for the management of COPD patients, including inhaler options available on the local formulary. These Guidelines advocated that treatment of COPD patients already established on inhaled medicines being changed (or optimised) to align to the recommended COPD treatment pathway. The Guidelines included examples of potential optimising inhalers, including Relvar.

The local Guidelines noted that the advantages of inhaler changes were optimising inhaler device, patient convenience and cost. As a result of these guidelines, clinical commissioning groups (CCGs) in the area started to adopt 'workplans' – these were plans outlining how respiratory medicines optimisation would be implemented in that CCG – for example, whether a full clinical review would be carried out or whether pharmacists, nurses or virtual technology would be deployed to identify optimisation opportunities.

Given the evolving external environment in the NHS and the increasingly important role of practice-based pharmacists with accountability for implementing medicines optimisation against aligned workplans in specific CCGs, GlaxoSmithKline sought to understand more about how optimisation was working in practice.

The NHS meaning of the word 'optimisation' was broad and was defined as looking at the value which medicines delivered, making sure they were clinically effective and cost effective, ensuring patients got the right choice of medicines, at the right time, and were engaged in the process by their clinical team.

GlaxoSmithKline understood that medicines optimisation, within the NHS, could be carried out by means of a simple switch (without clinical review). GlaxoSmithKline did not endorse this practice and prepared comprehensive briefing documents outlining that GlaxoSmithKline only supported medicines optimisation initiatives where they involved clinical review of patients.

A named CCG (which fell within the local guidelines) had a reputation for being an innovative CCG and adopting new medicines. It was therefore of interest to GlaxoSmithKline to understand how this CCG would implement these guidelines.

The pharmacist in question was working at this CCG in 2016. GlaxoSmithKline believed that he/she was self-employed and engaged on a consultancy basis by practices. He/she was engaged by the CCG Medicines Management Team to implement medicines optimisation initiatives in certain practices in the local area. GlaxoSmithKline understood that he/she implemented these initiatives in a variety of ways in consultation with the relevant practice, ranging from full clinical reviews to notes-based

reviews with follow-up support from community pharmacy.

The senior representative in question had been employed by GlaxoSmithKline for many years. This senior representative first became aware of the pharmacist in question in late 2016 during a routine call. This senior representative identified the pharmacist in question as a key emerging customer in his/her region and he/she continued to call on him/her during the ordinary course of his/her role as a representative.

A record from GlaxoSmithKline's CRM system, which showed the call log for GlaxoSmithKline's interactions with the pharmacist in question during the relevant period was provided. GlaxoSmithKline did not consider that the pattern of calls was unusual, considering this pharmacist was a key customer and strong advocate of GlaxoSmithKline medicines. GlaxoSmithKline submitted that the calls complied with the requirements of Clause 15.4 of the Code.

National Sales Conference March 2017

The objective of the annual National Sales Conference in March 2017 was to ensure that all representatives were clear on, and aligned to, GlaxoSmithKline's commercial strategy and structure for the following year. It was typical for GlaxoSmithKline sales conferences to include 'Voice of the Customer Sessions'. The pharmacist in question was identified as an appropriate customer to speak about his/her role as a practice-based pharmacist and his/her role in respiratory medicines optimisation. The session was presented as an interview style session, whereby a senior member of GlaxoSmithKline asked the pharmacist in question a series of certified questions that had been pre-agreed. The interview took place via live video link. The questions focussed on the role of a practice-based pharmacist and his/her role in medicines optimisation and not on the practical aspects of how he/she implemented optimisation.

The pharmacist in question was contracted for this activity in accordance with GlaxoSmithKline processes, with a written contract in place. Details of the hourly rate and number of hours the pharmacist was paid (including for his/her preparation time and actual presentation time) were provided.

The pharmacist in question was briefed for the meeting by a senior member of GlaxoSmithKline who was responsible for organising the 'voice of the customer' session at the conference. A copy of the hand-written briefing notes and confirmation emails as part of the briefing were provided. In the hand-written notes, the pharmacist in question's attention was drawn to the requirements of the Code, in particular the supplementary information to Clause 19.1 relating to Switch and Therapy Review Programmes.

GlaxoSmithKline submitted that clear guidance was provided at the National Conference defining the company's position on switch and what was acceptable within the Code.

Following the National Sales Conference in March, the pharmacist in question had offered to be contacted by other interested health professionals to share his/her positive experience of medicines optimisation. The senior representative in question created a tracker to support this. The pharmacist in question also made two offers for GlaxoSmithKline to commission (for a fee) a pack of the documents that he/she had used in his/her reviews that GlaxoSmithKline could share with other customers as an example of how optimisation could work. GlaxoSmithKline did not take up this offer.

Regional Sales Meeting – December 2017

The pharmacist in question was engaged by GlaxoSmithKline as a paid consultant on a second occasion to attend a regional sales meeting in December 2017. This meeting was organised by the first line sales manager and attended by 12 sales representatives from the region. It was a two-day business review meeting including an end-of-year celebration. Day 1 of the meeting included commercial strategy sessions and two 'voice of the customer' sessions. Day 2 comprised a performance review.

The pharmacist in question was engaged for an 'Ask the Expert' style session to talk about the local Guidelines on COPD management.

GlaxoSmithKline noted, with regret, that a detailed briefing for this meeting was not documented but understood that a verbal briefing was given by the senior representative in question. An account of the verbal briefing was provided. GlaxoSmithKline did not intend for any materials to be used for this session – this was supported by the pharmacist in question's contract in which it was noted that no materials were required and no audio-visual equipment was needed. However, GlaxoSmithKline understood that during the meeting the pharmacist in question produced hard copies of some of his/her medicines optimisation protocols and template letters, copies of which were provided by the complainant. GlaxoSmithKline understood that this had not been discussed or agreed with GlaxoSmithKline. During the investigation GlaxoSmithKline was told that, upon realising that these materials were being circulated to representatives, the first line sales manager collected the hard copy materials in from attendees and took them away to be destroyed. It was not clear how the complainant acquired a copy of the materials. The pharmacist in question was paid for his/her time, comprising 1 hour preparation and 1 hour speaking, based on a fair market rate (details provided).

Respiratory Leadership Team Meeting – March 2018

The pharmacist in question was engaged a third time in March 2018 to attend a Respiratory Leadership Team meeting. This was a monthly meeting which rotated around the UK and it was typical for these meetings to include a local customer for a 'voice of the customer' session. This meeting was not referenced in the complaint but for completeness GlaxoSmithKline provided the meeting agenda and a copy of the pharmacist in question's contract; he/

she was paid for his/her time, comprising 1 hour preparation and 1 hour speaking, based on a fair market rate (details provided).

Specifics of Complaint:

Clause 23.1 – Hiring of a Consultant

GlaxoSmithKline's engagement of external speakers was governed by an SOP which set out clear criteria for the selection and engagement of speakers. Representatives were trained on that policy.

GlaxoSmithKline strongly refuted the allegation that its hiring of the pharmacist in question constituted an inducement to recommend GlaxoSmithKline medicines. GlaxoSmithKline noted that:

- Payments made to this pharmacist related to legitimate services that were provided by him/her. He/she was paid a fair market value honorarium reflecting time actually spent attending and preparing for three GlaxoSmithKline internal meetings. In total over a period of 12 months he/she was paid for 6.25 hours – comprising 3.5 hours preparation and 2.75 hours speaking.
- GlaxoSmithKline did not pay this pharmacist to speak to other practice-based pharmacists on GlaxoSmithKline's behalf, or make any payments in respect of any aspect of his/her medicines optimisation activities or any other activity.
- A legitimate need for this pharmacist's services was identified in advance of requesting those services from him/her. GlaxoSmithKline noted further that on two of the three speaking engagements the pharmacist in question was not GlaxoSmithKline's first choice of speaker but in each case GlaxoSmithKline's first choice was not available. The pharmacist in question was considered to have the appropriate expertise to carry out the engagements.
- Written contracts were put in place with this pharmacist for each of his/her engagements in advance of the commencement of the services. The contracts specified the nature of the services and the basis for payment.
- A written record of GlaxoSmithKline's engagements with this pharmacist was contained in its health professional payment disclosure tracker.
- Importantly, no contracts or records existed in relation to this pharmacist's medicines optimisation activities because GlaxoSmithKline did not commission or fund those activities or the pharmacist's documents and made no payments in relation thereto.

Clause 15.9 – Detailed Briefing of Representatives

GlaxoSmithKline submitted it took training representatives very seriously and had a comprehensive training programme. The materials provided were certified.

GlaxoSmithKline referred to its SOP which set out GlaxoSmithKline's Approval Process for Promotional and Non-Promotional Material including GlaxoSmithKline's expectation that all training or briefing materials related to GlaxoSmithKline products and how they were to be promoted should be approved.

GlaxoSmithKline submitted it had comprehensive and detailed briefing documents for its representatives on promoting the Ellipta medicines. All briefing and training materials provided to representatives in connection with its commercialisation strategy for the Ellipta medicines were certified. Briefing materials drew the representatives' attention to relevant requirements of the Code and did not advocate any course of action which would be likely to lead to a breach of the Code.

GlaxoSmithKline had been asked to provide an account of all briefings related to 'the therapy review'. GlaxoSmithKline assumed this referred to the pharmacist in question's optimisation activities as GlaxoSmithKline was not conducting a therapy review service. As previously noted, this pharmacist's medicines optimisation activities did not constitute a therapy review service conceived or supported by GlaxoSmithKline. There were, therefore, no briefings (written or verbal) in relation to his/her optimisation activities.

GlaxoSmithKline noted that the complainant had provided copies of the pharmacist's documents. These documents were not produced or funded by GlaxoSmithKline and did not form part of any briefing material provided by GlaxoSmithKline to its representatives. GlaxoSmithKline's investigation ascertained that the pharmacist in question shared copies of these documents by email with a GlaxoSmithKline representative as an example of the sort of work he/she was undertaking. The names of the documents attached to this pharmacist's email contained references to GlaxoSmithKline. GlaxoSmithKline acknowledged that this created the misleading impression that the documents were created on behalf of GlaxoSmithKline. This was not so. A copy of the email was provided and GlaxoSmithKline drew attention to the final line which suggested that GlaxoSmithKline might wish to 'commission a pack for distribution'. The company's investigation found no evidence that it did so, and GlaxoSmithKline submitted that this offer validated that it was not involved in the creation of those documents.

GlaxoSmithKline ascertained that internal circulation of this pharmacist's documents were limited and the documents were not shared externally by GlaxoSmithKline.

GlaxoSmithKline acknowledged that the representatives in question should have taken the opportunity to correct and clarify the misleading impression caused by these documents and to make GlaxoSmithKline's position on switch, and the nature of GlaxoSmithKline's involvement with this pharmacist's activities, clear. GlaxoSmithKline regretted that it did not do so.

GlaxoSmithKline's investigation confirmed that this pharmacist also produced hard copies of his/her documents at the regional meeting in December 2017. GlaxoSmithKline understood that this had not been discussed or agreed with GlaxoSmithKline. During the investigation GlaxoSmithKline was told that, upon realising that these materials were being circulated to representatives, the first line sales manager collected the hard copy materials from attendees and took them away to be destroyed. It was not clear how the complainant acquired a copy.

GlaxoSmithKline asserted that it prepared detailed briefing materials which complied with the relevant requirements of the Code, in particular the certification requirements of Clause 14. GlaxoSmithKline did not believe that its briefing materials advocated any course of action which would be likely to lead to a breach of the Code. GlaxoSmithKline asserted that the pharmacist in question's documents were not training or briefing materials provided to representatives. GlaxoSmithKline therefore denied a breach of Clause 15.9.

Clause 18.1 – Prohibition on Inducements

GlaxoSmithKline strongly denied that any payments made to the pharmacist in question constituted an inducement to prescribe, supply, administer, recommend, buy or sell any GlaxoSmithKline medicine. The payments made to this pharmacist reflected a fair market value hourly rate for a *bona fide* service provided by him/her (namely speaking at internal meetings). His/her engagements met a pre-identified need as explained above.

Clause 19 – Medical and Educational Goods and Services

GlaxoSmithKline noted the requirements of the Code relating to medical education goods and services, and in particular the supplementary information relating to switch and therapy review programmes.

GlaxoSmithKline submitted it was not operating or facilitating a switch or therapy review service. The pharmacist in question's optimisation activities were carried out on behalf of the practices by whom he/she was engaged and were conceived and implemented independently of GlaxoSmithKline. GlaxoSmithKline noted that as of July 2018 it was providing a medicines goods and services COPD therapy review service that was fully compliant with the requirements of Clause 19 and was unrelated to the events outlined in the complaint.

GlaxoSmithKline submitted that its commercial strategy for the Ellipta Medicines included promoting switch from patients already receiving treatment for COPD to Ellipta Medicines if appropriate and in accordance with the requirements of the Code. GlaxoSmithKline did not support facilitation of switch programs, nor did GlaxoSmithKline advocate for health professionals to conduct switch programs without a clinical review and legitimate clinical rationale. GlaxoSmithKline had a clearly identified position on switch, which was articulated in the relevant briefing documents.

GlaxoSmithKline noted that the supplementary information relating to Clause 19.1 provided that 'it would be acceptable for a company to promote a simple switch from one product to another...' and submitted that its promotional campaign was not in breach of Clause 19.1.

GlaxoSmithKline understood that the pharmacist in question was engaged by the CCG to support the implementation of workplans in a number of practices. GlaxoSmithKline understood that this pharmacist did not adopt a 'one size fits all' approach to these activities but adapted optimisation activities to suit the requirements of the relevant practice. GlaxoSmithKline understood that a number of these included full clinical reviews and notes-based review.

GlaxoSmithKline noted the complainant's suggestion that the pharmacist in question prepared his/her protocol document, on GlaxoSmithKline's request, but the complainant had provided no evidence to support this suggestion. GlaxoSmithKline found no evidence that it commissioned or funded this pharmacist's documents.

Tracker

GlaxoSmithKline provided a copy of the tracker maintained by the senior representative in question. GlaxoSmithKline noted the complainant's assertion that the purpose of this tracker was to facilitate the sharing of documents used by the pharmacist in question in his/her optimisation programmes and stated that the complainant had not provided evidence to support this assertion.

At the relevant time, GlaxoSmithKline was working to understand and align to the NHS's focus on medicines optimisation. One element of GlaxoSmithKline's business strategy was to ask customers who had successfully carried out optimisation if they would be willing to share their positive experiences with other practices. The pharmacist in question was a strong advocate of the Ellipta medicines based on the patient outcomes he/she had seen and was keen to share his/her experiences with medicines optimisation with a network of peers.

A number of GlaxoSmithKline customers expressed an interest in engaging in this peer-to-peer dialogue. Contact details for these customers were (with their consent) passed on to the pharmacist in question and the tracker was established to record this and document any associated outcomes – such as whether other practices had implemented optimisation programmes. GlaxoSmithKline did not believe that any other representatives maintained similar trackers.

GlaxoSmithKline representatives became aware during 2017 that the pharmacist in question was sharing his/her documents with some practices who contacted him/her. GlaxoSmithKline noted, with regret, that those representatives continued to introduce practices to this pharmacist and, in some cases, the representatives asked this pharmacist to share copies of his/her documents with other practices. GlaxoSmithKline acknowledged that it

was not appropriate for GlaxoSmithKline to endorse or encourage this activity and representatives should have taken steps to reinforce GlaxoSmithKline's position on switch, and to clarify the nature of GlaxoSmithKline's involvement with the pharmacist in question.

GlaxoSmithKline submitted that it had not endorsed or briefed its representatives to partake in this activity and was taking appropriate corrective action. GlaxoSmithKline did not believe that the activities of the representatives amounted to facilitation of a switch service as contemplated by the Code.

GlaxoSmithKline noted that the supplementary information relating to Clause 19.1 provided that 'it would be acceptable for a company to promote a simple switch from one product to another but not to assist a health professional in implementing that switch, even if that such assistance was by means of a third party **such as a sponsored nurse or similar**. Such arrangements are seen as companies **in effect paying for prescriptions** and are unacceptable' (emphasis added by GlaxoSmithKline). GlaxoSmithKline noted the clear emphasis on funding of activities in the supplementary guidance.

GlaxoSmithKline also noted the Panel's consideration of similar issues in Case AUTH/2644/10/13, and the Panel's finding that there was no breach of the Code on the basis that Galen had not provided 'any service to effect or facilitate the switch. Any expense or effort ...had to be borne by the health professional or PCO [primary care organisation]'. GlaxoSmithKline further noted that the Panel's ruling was upheld by the Appeal Board.

GlaxoSmithKline submitted that it did not actively assist any health professional to switch patients or provide or fund any service to effect or facilitate a switch in the practices listed in the tracker.

GlaxoSmithKline did not believe that connecting a network of like-minded health professionals to share experiences constituted direct or indirect facilitation of switch. GlaxoSmithKline noted, with regret, that its representatives acquiesced in the sharing of the pharmacist in question's documents, which gave advice on how to switch. Whilst GlaxoSmithKline did not condone this activity, GlaxoSmithKline submitted that it did not amount to facilitation of a switch service as defined by the Code, for reasons outlined above.

New Medicines Service

GlaxoSmithKline stated that the New Medicines Service was not a GlaxoSmithKline programme. GlaxoSmithKline understood the New Medicines Service to be an NHS-led initiative in which community-based pharmacists provided support to patients starting treatment on, or switching to, new medicines for a number of conditions, including asthma, COPD, diabetes and high blood pressure. GlaxoSmithKline submitted that no materials specific to this service were provided by it.

GlaxoSmithKline did make available inexpensive patient support items and training to pharmacists

as part of GlaxoSmithKline's standard practice. Such items included placebo Ellipta devices, demonstration devices and support documents such as a leaflet instructing patients on how to use Ellipta devices. These items could be ordered by health professionals directly through GlaxoSmithKline's health professional-facing website or ordered by representatives on behalf of customers on request.

These items were made available to all customers and were not specific to, or conditional on, the provision of any switch or therapy review programme. GlaxoSmithKline representatives would have discussed the availability of these items when promoting Ellipta medicines. It would be usual practice for representatives to ensure that pharmacists known to be involved in optimisation activities had adequate supplies of these items and were trained to ensure patients were correctly shown how to use the Ellipta device. The senior representative in question was asked by the pharmacist in question to visit a local community pharmacy in this context to train the pharmacist on how to demonstrate the use of the Ellipta device in the ordinary course of his/her role.

GlaxoSmithKline submitted that these patient support items complied with the requirements of Clause 19.1 of the Code. GlaxoSmithKline acknowledged that the reference to GlaxoSmithKline's provision of these items in the pharmacist in question's documents created the misleading impression that GlaxoSmithKline was proactively involved in this pharmacist's activities, but this was not the case. GlaxoSmithKline denied any breach of Clause 19.1.

Clause 19.2

GlaxoSmithKline had not provided any grant, donation or benefit in kind to the pharmacist in question or any of the practices listed in the tracker. GlaxoSmithKline denied a breach of Clause 19.2.

Clause 9.1 – Maintaining High Standards

GlaxoSmithKline submitted that it endeavoured to maintain high standards at all times and in many cases, GlaxoSmithKline set its standards higher than the expectations of the Code.

GlaxoSmithKline noted, with regret, that the actions of a small number of its representatives in the region in question fell short of the high standards that GlaxoSmithKline expected. In particular:

- A more comprehensive written briefing relating to the regional meeting should have been kept.
- Representatives should not have encouraged the sharing of the pharmacist in question's documents and should have taken steps to reinforce GlaxoSmithKline's position on switch and clarify the nature of GlaxoSmithKline's involvement with this pharmacist's activities.

GlaxoSmithKline acknowledged, with regret, that it failed to maintain high standards pursuant to Clause 9.1 in these aspects. GlaxoSmithKline committed to taking the following steps to address these issues:

- Re-educate representatives on what constituted adequate briefing and documentation;
- Refresher Code training, with a particular emphasis on the promotion of switch and facilitation of switch services; and
- Repeat 'Write Right' training with a particular emphasis on how to catch, correct and clarify potentially misleading communications.

Communication Culture

Whilst GlaxoSmithKline noted, with regret, that it had fallen short of the expected standards of documentation required by the Code in an isolated instance identified as a result of this complaint, it strongly refuted the suggestion that this was reflective of a widespread cultural failing. GlaxoSmithKline maintained high standards of documentation, as evidenced by the materials supporting this response. The complainant referred to GlaxoSmithKline's 'Write Right' training. This was a training module given to all GlaxoSmithKline employees. Contrary to the complainant's assertion, this policy did not discourage the keeping of written records, but advocated taking care to ensure documentation was appropriate and aligned to GlaxoSmithKline values. The complete training was delivered live or by 'e-learning'.

Contrary to the complainant's assertion, this policy did not discourage the keeping of written records but advocated taking care to ensure documentation was appropriate and aligned to GlaxoSmithKline values.

GlaxoSmithKline provided a copy of the training curriculum that representatives followed and copies of relevant policies. The company drew attention to the section in which GlaxoSmithKline's expectations regarding briefing and documentation in connection with promotional meetings were set out.

GlaxoSmithKline stated it took pride in its core values of integrity, transparency, respect for people and patient focus, and encouraged employees to have regard to GlaxoSmithKline's values in all activities.

Clause 2

Based on its investigation, GlaxoSmithKline submitted that this was an isolated occurrence relating to a small group of representatives in one area and was not reflective of the high standards generally maintained by GlaxoSmithKline representatives.

GlaxoSmithKline did not accept that its activities or materials discredited or reduced confidence in the industry, compromised patient safety, constituted inducements to prescribe or involved unacceptable payments. GlaxoSmithKline noted, with regret, the shortcomings highlighted by this complaint and GlaxoSmithKline's subsequent investigation and had taken steps to reinforce that standards were maintained at all times.

GlaxoSmithKline respectfully submitted that its activities did not amount to a breach of Clause 2.

GlaxoSmithKline was disappointed to note that the complainant had chosen to raise their complaint directly with the PMCPA. GlaxoSmithKline strongly encouraged employees to raise concerns and had processes in place to provide a supportive environment in which these concerns could be raised, including anonymous 'speak up' channels. GlaxoSmithKline was extremely disappointed that the complainant chose to wait until leaving the organisation before raising his/her concerns.

In conclusion, GlaxoSmithKline denied breaches of Clauses 23.1, 15.9, 18.1, 19.1, 19.2 and Clause 2 but, as stated above, admitted a breach of Clause 9.1.

PANEL RULING

The Panel noted that Clause 23.1 stated, *inter alia*, that health professionals and other relevant decision makers may be used as consultants for services such as speaking at meetings where such participation involved remuneration and/or travel. The arrangements which covered these genuine consultancy or other services must, to the extent relevant to the particular arrangement, fulfil a number of criteria including that the hiring of the consultant to provide the relevant service must not be an inducement to prescribe, supply, administer, recommend, buy or sell any medicine and the compensation for the services must be reasonable and reflect the fair market value of the services provided. In this regard, token consultancy arrangements must not be used to justify compensating health professionals and other relevant decision makers.

Clause 18.1 stated that no gift, pecuniary advantage or benefit may be supplied, offered or promised to members of the health professions or to other relevant decision makers in connection with the promotion of medicines or as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine, subject to the provisions of Clauses 18.2 and 18.3. The supplementary information stated that any payment to an individual for an activity that was ruled in breach of Clause 23 was likely to be viewed as an unacceptable payment and thus in breach of Clause 18.1.

The Panel noted GlaxoSmithKline's submission that the pharmacist in question was contracted and paid to speak at three internal meetings; the national sales conference in March 2017, a regional meeting in December 2017 and a respiratory leadership meeting in March 2018. The Panel noted that in total over a period of 12 months the pharmacist in question was paid for 6.25 hours comprising 3.5 hours preparation and 2.75 hours speaking time (details of payments were provided). On the basis of the information before it, the Panel considered that there was no evidence to support the complainant's allegation that payments to this pharmacist for these meetings were not in line with the time spent for speaking at meetings and no breach of Clauses 23.1 and 18.1 were ruled.

The Panel noted that in 2017 some representatives would have attended two meetings where the pharmacist in question presented. The Panel noted

GlaxoSmithKline's submission that the national sales conference session in March 2017 was presented as a 30 minute interview during which the pharmacist in question was asked pre-approved questions. The output given for the session was that the audience understood the importance of the role of practice-based clinical pharmacists in medicines optimisation/switch decisions at GP level and the need for and difference Ellipta medicines could make to patients. The list of questions included advice as to how GlaxoSmithKline could add more value in its interaction with practice-based pharmacists to help further improve patient outcomes and make NHS savings, for example, through medicines optimisation/switching. Another of the prepared questions asked was 'Since you have been in role, what have you been working on in terms of medicines optimisation in respiratory? What results have you achieved and why do you think that is?'

The Panel noted that the handwritten notes by a GlaxoSmithKline representative who briefed the pharmacist in question stated that the purpose of the session was the role of the practice-based pharmacist in respiratory medicine optimisation at GP practice level (including switching). The handwritten briefing further stated, 'Code on Switch/ page 29'. The Panel also noted GlaxoSmithKline's submission that clear guidance was provided at the conference defining its position on switch and what was acceptable within the Code. The 'GlaxoSmithKline believes that...' document (ref UK/RESP/0048/17a) defined switch as a change in preferred treatment options within a class of medicines, in appropriate patients, following clinical review. It stated that the Code allowed it to promote switching, where appropriate. However, it was not allowed to be involved in implementing a patient switch.

The Panel noted GlaxoSmithKline's submission that at the regional meeting in December 2017, the pharmacist in question provided hard copies of some of his/her medicines optimisation protocols and template letters to the 12 representatives attending the meeting without GlaxoSmithKline's permission. Copies of those documents were included in the complaint. GlaxoSmithKline further submitted that upon realising these materials were being circulated, the documents were collected by the first line sales manager to be destroyed. It was not clear to GlaxoSmithKline how the complainant acquired a copy of the materials. It was not clear to the Panel how long the attendees had the documents in their possession.

The Panel noted that the documents provided by the complainant included a protocol for inhaler changes for patients with COPD. The protocol referred to the practice pharmacist identifying all listed COPD patients on Seretide Accuhaler 500/50mcg and Spriva Capsules 18mcg and excluding from the switch those patients who were unwell or unstable as identified from their records. All the other patients would have their Seretide accuhaler changed to Relvar Ellipta 92/22 and their Spiriva inhalation capsules changed to Incruse Ellipta. The protocol stated that inhalation technique for all three devices

was very similar so face-to-face training was not mandatory; the practice pharmacist would make the change on an electronic patient record system and the new inhaler(s) would be issued when the patient next requested a repeat of their former inhalers. The patient would be sent a letter informing them of the change, a GlaxoSmithKline leaflet explaining how to use the new Ellipta inhaler and a re-order form highlighting the new inhalers. The local community pharmacist would be asked to offer the new medicine service (NMS) to explain to patients how to use their new inhaler and to follow them up over the phone during the first month. The protocol further stated that 'GlaxoSmithKline will provide the community pharmacy with placebo devices and information leaflets and training to support the NMS intervention'. The protocol included sections headed 'Advantages for patients' and 'Advantages for the Practice'. The complainant also provided template letters to be sent to the patients and reports of switches in COPD patients at named medical centres. The Panel considered, as acknowledged by GlaxoSmithKline, that the reference to GlaxoSmithKline in the protocol gave the impression that GlaxoSmithKline was somehow involved in the protocol and the service. The Panel noted GlaxoSmithKline's submission that this was not so and the documents gave a misleading impression in that regard. GlaxoSmithKline acknowledged that it provided training to pharmacists and had patient support items which could be ordered by any health professional; it was not conditional on the provision of any switch or therapy review programme.

The Panel noted the requirements of Clause 19 and the supplementary information to Clause 19.1, Switch and Therapy Review Programmes which stated that Clauses 18.1 and 19.1 prohibited switch services paid for or facilitated directly or indirectly by a pharmaceutical company whereby a company's medicine was simply changed to another without any clinical assessment. It was acceptable for a company to promote a simple switch from one product to another but not to assist the health professional in implementing that switch even if assistance was by means of a third party such as a sponsored nurse or similar. A therapeutic review was different to a switch service: it aimed to ensure that patients received optimal treatment following a clinical assessment and was a legitimate activity for a pharmaceutical company to support and/or assist. Clause 19.2 stated that medical and educational goods and services in the form of donations, grants and benefits in kind to institutions, organisations and associations that were comprised of health professionals and/or, *inter alia*, provided healthcare were only allowed if they complied with Clause 19.1, were documented and kept on record by the company and did not constitute an inducement to, *inter alia*, prescribe.

The complainant alleged that GlaxoSmithKline was supporting a switch to GlaxoSmithKline medicines because at the Q and A session at the regional meeting in December 2017, the pharmacist in question presented the documents referred to above, the objective being that representatives would ask health professionals if they needed support in

carrying out a switch to a GlaxoSmithKline product. If the answer was yes, the representative would email the health professional's contact details to the senior representative in question who would pass them to the pharmacist in question to send the documents. The senior representative in question kept a tracker of which health professionals had been contacted.

The Panel noted GlaxoSmithKline's submission that following the national conference in March 2017, the pharmacist in question offered to be contacted by interested health professionals to share his/her positive experience of medicine optimisation. The Panel noted GlaxoSmithKline's submission that it did not pay this pharmacist to speak to other practice-based pharmacists on its behalf nor did it make any payments in respect of any aspect of his/her medicines optimisation activity. The Panel noted GlaxoSmithKline's submission that one element of its business strategy was to ask customers who had successfully carried out optimisation if they would be willing to share their positive experiences with other practices.

The Panel noted that in August 2017 the pharmacist in question emailed the senior representative in question informing him/her that he/she had sent information to a named individual from a named area regarding inhaler switches. The email further stated 'Attached is the info I am sending to practices for your information...'. The names of the documents attached were 'GSK protocol for inhaler changes in COPD', 'GSK Seretide letter', 'GSK COPD letter, Seretide and Spiriva' and 'GSK Spiriva letter' and appeared to be the same as those documents provided by the complainant. The Panel considered that this created the misleading impression that the documents were created on behalf of GlaxoSmithKline, as acknowledged by the company, which submitted that it had declined to commission a pack of the documents for use. The Panel noted that whilst it had concerns with regard to the misleading impression created by the documents and the lack of follow up by the representative to clarify the position, it did not consider that there was evidence to suggest that GlaxoSmithKline had initiated, contributed to or funded the documents in question as implied by the allegation that the 'how to' document would not exist had GlaxoSmithKline not contacted the pharmacist in question. No breach of Clause 9.1 was ruled in this regard.

The Panel was concerned to note that GlaxoSmithKline knew about the content of the documents and that the pharmacist in question was providing these to practices following 'referrals' from GlaxoSmithKline representatives, yet it took no action other than to decline to pay for the documents. The Panel further noted GlaxoSmithKline's submission that the pharmacist in question was asked by some representatives to share copies of his/her documents with other practices. GlaxoSmithKline acknowledged that it was not appropriate for the company to endorse or encourage the activity and the representatives in question should have taken the opportunity to reinforce GlaxoSmithKline's position on switch

and to clarify the nature of GlaxoSmithKline's involvement with the pharmacist in question. The Panel considered that high standards had not been maintained in this regard, as acknowledged by the company, and a breach of Clause 9.1 was ruled.

The Panel recognised that NHS colleagues would talk to each other but was, nonetheless, concerned that contact details of health professionals had been provided to the pharmacist in question by GlaxoSmithKline representatives. Follow-up of his/her interaction with those health professionals and outcomes were also tracked by the company. The tracker listed the GlaxoSmithKline representatives, the account interested, the date the contact was passed on, whether contact had been made with the pharmacist in question, Seretide numbers, 'Tio' numbers and 'relevant' information. It appeared from the tracker that in one practice, Tiotropium was changed to Incruse after a practice-based pharmacist ran 'lists' and 'letters' were sent out by the practice manager. The tracker did not specifically record any contact by the pharmacist in question with this practice in relation to this change, however, the Panel noted GlaxoSmithKline's submission that the tracker in question was established to record details of customers contacts passed on to this pharmacist and any associated outcomes such as whether practices had implemented optimisation programmes. A different practice listed on the tracker featured a note that contact was made with the pharmacist in question and it led to the practice employing a practice-based pharmacist to look at COPD and asthma and the pharmacist was currently being trained for optimisation.

The Panel noted that although the pharmacist in question was not being paid to speak to interested peers, GlaxoSmithKline representatives were actively involved in the introduction of practices to him/her. The Panel noted that communication between the GlaxoSmithKline representatives and practices, for which GlaxoSmithKline was responsible, and communication between the pharmacist in question and the practices for which GlaxoSmithKline was potentially responsible for, might lead to a change to GlaxoSmithKline's medicines. The Panel noted that the Code did not prohibit a company from promoting a switch but did prohibit switch services paid for or facilitated directly or indirectly by a pharmaceutical company whereby a patient's medicine was simply changed to another.

The Panel noted that it could be argued that the provision of the pharmacist in question's documents to practices, including template letters, via referrals from GlaxoSmithKline's representatives, went beyond promoting a switch. There was a fine line between simply promoting a switch and providing so much detailed information in that regard that the information facilitated a switch.

The Panel considered that there was insufficient evidence as to whether any change of medicine was as a result of a switch service or a therapy review or that the pharmacist in question or GlaxoSmithKline had actually assisted any health professional in implementing a change to a GlaxoSmithKline

medicine. GlaxoSmithKline had made no payment in relation to any service. Taking all the circumstances into account the Panel decided that on balance there was insufficient evidence to show that overall GlaxoSmithKline arrangements facilitated a switch to its medicines as prohibited by Clause 19.1. The Panel ruled no breach of Clause 19.1 and thus no breach of Clause 18.1. In addition, the Panel did not consider that there was an allegation of a breach of Clause 19.2 and no breach was ruled accordingly.

The Panel noted that Clause 15.9 required, *inter alia*, that companies must prepare detailed briefing material for medical representatives on the technical aspects of each medicine which they will promote. The supplementary information referred to both the training material and instructions about how a product should be promoted. Briefing material must comply with the relevant requirements of the Code and, in particular, was subject to the certification requirements of Clause 14 and must not advocate, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code.

The Panel noted that the conversations between the representatives including the completion of the senior representative's tracker, together with the presentations by the pharmacist in question at both the national and regional meetings, would add to the impression that GlaxoSmithKline supported and endorsed this pharmacist's views and approaches and might be seen by representatives as instructions on how the product should be promoted. The Panel considered that the documents provided by the pharmacist in question to the 12 representatives at the regional meeting in December 2017, which could be seen as setting out GlaxoSmithKline's involvement in a switch service, in effect constituted briefing material. The Panel noted that GlaxoSmithKline made no submission with regard to any follow up with the 12 representatives confirming that it did not endorse this pharmacist's protocol or to remind the representatives of the company's position on switching. Whilst the Panel was concerned at the lack of clear guidance provided by the company, it did not consider, on the balance of probabilities, that the communications above advocated a course of action likely to be in breach of the Code. No breach of Clause 15.9 was ruled.

The Panel noted that whilst GlaxoSmithKline had fallen short of the expected standards of documentation required by the Code in this instance as acknowledged by the company, the complainant had not established that this meant that there was a widespread lack of written communication and projects would disproportionately rely on verbal communication as alleged. The Panel considered that there was no evidence before it that the frequency of meetings between the pharmacist in question and GlaxoSmithKline representatives, prior to him speaking at national and regional meetings, were indicative of inappropriate verbal briefings for the meetings and no breach of Clause 9.1 was ruled in this regard.

Although the Panel had some concerns about the overall arrangements and oversight by

GlaxoSmithKline, noting its ruling of a breach of Clause 9.1 above, it did not consider that, on balance, the circumstances warranted a ruling of a breach of Clause 2, which was a sign of particular censure and reserved for such use, and ruled no breach accordingly.

2 Claim in digital sales aids for Relvar Ellipta, Anoro Ellipta and Trelegy Ellipta

COMPLAINT

The complainant stated that the digital sales aid that representatives used for Relvar Ellipta, Anoro Ellipta and Trelegy Ellipta had a page that described the device as 'open, inhale and close.' This was a key message for the Ellipta portfolio and had been since 2016. The complainant stated that this was contrary to the information provided in both the summary of product characteristics (SPC) and the patient information leaflet (PIL) which required more steps for the patient to benefit from the medication.

When writing to GlaxoSmithKline, the Authority asked it to bear in mind the requirements of Clauses 3.2, 7.2 and 9.1 of the Code.

RESPONSE

GlaxoSmithKline submitted that digital detail aids were amended and re-certified as promotional campaigns developed over time. GlaxoSmithKline stated that the time point in question was not clear from the complainant, so it had reviewed the digital sales aids which the therapy representatives currently used for two of the three products. There was no current Anoro digital sales aid as representatives no longer actively promoted it.

For the Trelegy digital sales aid, the statement 'Open, Inhale and close' was not used at all. Similarly, the Relvar digital sales aid did not have a page which described the device as open, inhale and close as alleged by the complainant. However, there was a digitally interactive section of the digital sales aid headed 'Interactive Ellipta' which was designed for therapy representatives to initiate discussions concerning the mechanism and internal workings of the device. At the bottom of the screen in this section there were four digital 'buttons' labelled: open, look inside, inhale and close. These were not claims regarding the Ellipta device but functional digital 'buttons' which when touched allowed the health professional to show these four specific features of the device. The button labelled, 'Look inside' showed the internal structure of the device, something not normally visible to the health professional unless they actively dismantled it and so allowed them to view the mechanistic details of the device in more detail.

The interactive digital section of the digital sales aid also allowed the health professional to look at the device in a 3D setting as by placing their finger on the digital image they were able to move it in all directions and rotate the model accordingly. The briefing instructions to the therapy representatives for this section of the interactive digital sales aid

even stated that, 'If appropriate you may wish to give your iPad to the HCP to allow them to use the interactive Ellipta Device'.

This interactive section of the digital sales aid also had the following statement at the bottom of the screen: 'For patient Instructions, refer to the Patient Information leaflet' so as to ensure that there was no confusion between the mechanistic workings of the device and the instructions for patient use of the device. In addition, GlaxoSmithKline also provided a tear-off pad for representatives to use with health professionals which gave detailed instructions as to how to use the Ellipta device as well as a photograph of the Ellipta device demonstration kit which health professionals might use with their patients on an individual basis enabling them to be able to competently demonstrate these GlaxoSmithKline medicines.

This interactive section of the digital sales aid was only 4 of 9 pages, all of which had in the heading 'After reading the PIL' (Patient Information Leaflet).

In summary, GlaxoSmithKline denied any breach of the Code.

In response to a request for further information, GlaxoSmithKline noted that Trelegy was only promoted after it received a marketing authorisation in November 2017 and submitted that no digital sales aid used since that date included any reference to 'open, inhale and close'.

With respect to Relvar and Anoro, GlaxoSmithKline had ascertained that certain versions of its digital sales aids as used by the representatives from 2016 to date contained references to 'open, inhale and close' (copies of relevant pages provided).

GlaxoSmithKline submitted it made certain core claims in relation to its Ellipta medicines. One of those core claims related to ease of use of the device, as had been clinically evaluated in patients with both asthma and COPD. The Ellipta device was a single-step breath-activated inhaler featuring a cover that was opened by the patient to simultaneously reveal the mouthpiece and automatically load a single dose of medication (Collison *et al* 2018). This distinguished the inhaler from other devices, in which an additional loading step was required, in that simply opening the inhaler rendered it ready for use. Grant *et al* (2015) stated that 'There are three principal operating steps to administer a dose: open, inhale, close'. In addition, Grant stated 'The inhaler is operated through three simple steps: 1) opening the mouthpiece cover fully; 2) inhaling the dose; and 3) closing the mouthpiece cover'. Additional evidence to support the claim was reported by Svedsater *et al* (2013) in an ease of use study. Several participants spontaneously reported on the straightforwardness and intuitiveness of the use of the dry powder inhaler (DPI), describing the few steps required eg 'open and inhale, that's it: not much to it'.

GlaxoSmithKline noted that the Panel had previously considered a claim that the Ellipta device was

'straightforward to use' and found that the claim was not misleading and was substantiable (Case AUTH/2701/2/14).

The pages of the materials that include references to 'Open, Inhale, Close' were included under the heading 'Ease of Use' in each of the relevant materials.

GlaxoSmithKline noted that the 'open, inhale, close' language was reviewed by the PMCPA in Case AUTH/2933/2/17 which concerned Chiesi's use of the 'open, inhale, close' claim in relation to Fostair NEXThaler and the Panel ruled a breach of the Code because the claim was inconsistent with the SPC and the PIL for Fostair. This was on the basis that the SPC and PIL for Fostair in fact included four steps. GlaxoSmithKline asserted that this case could be distinguished from Case AUTH/2933/17 in that the SPCs and PILs for each of the relevant GlaxoSmithKline Ellipta products contained only three steps. The SPCs for all three Ellipta products presented the step-by-step instructions on how to use the inhaler under distinct headings. Each heading then had more detail below it. The same was true of the PILs for each of the Ellipta products. There were three substantive steps for use of the Ellipta inhaler on a daily basis. The first step was headed 'Prepare a dose' the second 'Inhale your medicine' and the third 'Close the inhaler'. Under the first heading 'Prepare a dose', the only instruction was 'slide down the cover until you hear a click. Your medicine is now ready to be inhaled'. In other words, the only step to preparing the device is to open it. GlaxoSmithKline acknowledged that in the 'Instructions for Use' section of the SPC for Relvar and Trelegy, these three steps were in fact labelled steps 2, 3 and 4. This was because step 1 was an instruction to the patient to read all the following information before commencing. This was to avoid patients opening and closing the device without inhaling the medicine, as by doing so the dose would be lost. GlaxoSmithKline did not consider that this cautionary note constituted an additional step to using the device on a day to day basis, and therefore did not believe that this created an inconsistency with the materials.

GlaxoSmithKline noted that the materials in question were intended for use with health professionals and were not intended to provide instructions to patients on how to use the Ellipta device. GlaxoSmithKline made available a number of patient support materials, including a tear-off pad for representatives to use with health professionals which gave detailed instructions as to how to use the Ellipta device as well as an Ellipta device demonstration kit which a health professional might use with their patients on an individual basis enabling them to be able to competently demonstrate the medicines. GlaxoSmithKline therefore submitted that the claim was not inconsistent with the licences for the Ellipta medicines and so not in breach of Clause 3. The claim was accurate and unambiguous and therefore not in breach of Clause 7.2. GlaxoSmithKline submitted it had therefore maintained high standards in the promotion of its medicines and was not in breach of Clause 9.1.

PANEL RULING

The Panel noted the allegation that the Relvar, Anoro and Trelegy digital sales aids contained a page that described the device as 'open, inhale and close', which had been a key message for the Ellipta portfolio since 2016 and was contrary to the SPC and patient information leaflet (PIL) which described more steps in order for the patient to benefit from the medication.

The Panel noted GlaxoSmithKline's initial submission that the time point in question was not clear from the complaint and therefore it provided the currently used Relvar and Trelegy digital sales aids; there was no current sales aid for Anoro as it was no longer promoted.

The Panel noted GlaxoSmithKline's submission that the current Trelegy digital sales aid did not use the statement 'open, inhale and close'. The current Relvar digital sales aid, however, featured an 'Interactive Ellipta' section which contained four digital buttons labelled: open, look inside, inhale and close, which GlaxoSmithKline submitted were not claims regarding the device, but functional buttons to show specific features of the device.

In the Panel's view, it was clear that the complaint covered material used from 2016 onwards. The Panel was concerned that it was only after a request for further information that GlaxoSmithKline submitted that certain versions of its Anoro and Relvar digital sales aids since 2016 had contained references to open, inhale and close and subsequently provided the relevant pages.

The Panel noted GlaxoSmithKline's submission that no Trelegy digital sales aids included any reference to open, inhale and close. The complainant had not provided any evidence to the contrary. The Panel, therefore, based on the very narrow allegation, ruled no breach of Clauses 3.2 and 7.2 with regard to the Trelegy sales aids used since the product received a marketing authorisation in November 2017.

The Panel noted that the Relvar Ellipta SPC stated under the method of administration that the step-by-step instructions should be followed. According to the Relvar SPC, the first step required the patient to read the information on how to use the device to avoid losing a dose by opening and closing the inhaler without inhaling. The second step was about how to prepare a dose and involved opening the cover and sliding it down until a click was heard. The third step covered how to inhale the medicine and stated that before inhaling, the patient should hold the inhaler away from their mouth and breathe out as far as comfortable. The patient was warned not to block the air-vents with their fingers and to take a long, steady, deep breath in holding the breath for as long as possible (at least 3-4 seconds) and then remove the inhaler from the mouth and breathe out slowly and gently. The fourth step involved closing the inhaler and rinsing the mouth to reduce the risk of developing a sore mouth or throat as a side-effect.

The Panel noted that the Relvar/Incruse January 2018 digital sales aid stated 'Incruse & Relvar delivers

24 hours of continuous efficacy in 3 steps: patients simply Open Inhale Close'. The May 2016 and April 2017 Relvar/Incruse digital sales aids stated 'Incruse in combination with Relvar delivers 24 hours of continuous efficacy in 3 steps: patients simply Open Inhale Close'. The Relvar Asthma digital sales aids (May 2016 and May 2017) stated 'Relvar delivers 24 hours of continuous efficacy in 3 steps: patients simply Open Inhale Close'. The Panel accepted that as far as the device was concerned, it had to be opened by the patient, used for inhalation and closed by the patient. However, to take the medicine correctly and, *inter alia*, for the dose to be effective the patient had to do more than simply open, inhale and close. The required steps were detailed in the Relvar and Incruse SPCs and PILs. It appeared from the material provided that, despite reading the PIL, some patients still made a critical error which was defined as an error most likely to result in no, or minimal, medication being inhaled. In the Panel's view it was important that the step-by-step instructions were followed, and this was highlighted in the Relvar SPC, to obtain the full benefit of the medicine.

In the Panel's view, the references to '...efficacy in 3 steps: patients simply Open Inhale Close' in the Relvar/Incruse digital sales aids (January 2018, May 2016, April 2017) and the Relvar asthma digital sales aids (May 2016, May 2017) were misleading and inconsistent with the Relvar SPC. A breach of Clauses 3.2 and 7.2 were ruled.

The Relvar Asthma digital sales aids (September 2017 and October 2017) stated 'With just 3 steps: patients simply Open Inhale Close' which appeared on a page titled 'The Ellipta inhaler is easy-to-use'. The Panel noted that there was no reference to 'efficacy in 3 steps'. The Panel considered that the reference to 'With just 3 steps: patients simply Open Inhale Close' in the context of a further claim on the page which stated 'Fewer patients using Ellipta made a critical error compared with other commonly used inhalers after reading the patient information leaflet...' where a critical error was defined as an error most likely to result in no, or minimal, medication being inhaled, implied that the page was referring to the patient needing to perform 3 steps to receive benefit from the medicine. As noted above, the Relvar SPC featured four steps and each of the steps had a number of instructions. The 'How to inhale the medicine' section included an instruction to hold the inhaler away from your mouth and breathe out as far as was comfortable and another to take one long, steady, deep breath in and hold it for as long as possible (at least 3-4 seconds) before removing the inhaler from the mouth and breathing out slowly and gently.

The Panel accepted that as far as the device was concerned, it had to be opened by the patient, used for inhalation and closed by the patient. However, to take the medicine correctly and, *inter alia*, for the dose to be effective, the patient had to do more than simply open, inhale and close.

On balance, the Panel considered that the Relvar Asthma digital sales aids (September 2017 and October 2017) which referred to 'With just 3

steps: patients simply Open Inhale Close’ and the implication that it related to patient benefit from the medicine with just 3 steps, was misleading and inconsistent with the Relvar SPC and a breach of Clauses 3.2 and 7.2 were ruled.

The Panel noted that the current Relvar Ellipta digital sales aid (March 2018 ref UK/FFT/0004/18) had been adapted from previous versions and did not refer to either ‘...efficacy in 3 steps: patients simply Open Inhale Close’ or ‘With just 3 steps: patients simply Open Inhale Close’ as featured in previous Relvar digital sales aids. The current sales aid contained a section headed ‘Interactive Ellipta’ which GlaxoSmithKline submitted was designed to initiate discussions concerning the mechanism and internal workings of the device. The Panel noted that this page contained four interactive tabs labelled ‘Open’, ‘Look inside’, ‘Inhale’ and ‘Close’; each linked to an image of the device at that stage. Below the tabs was the statement ‘For patient instructions, refer to the Patient Information Leaflet’ and the Panel noted GlaxoSmithKline’s submission that this statement was to prevent confusion between the mechanistic workings of the device and the instructions for patient use of the device. The Panel noted that some pages in the digital sales aid contained the claim ‘easy to use’ with a link to the Interactive Ellipta pages. The accompanying briefing document stated that the objective of the interactive pages in question was to show the health professional how the Ellipta device was used. The briefing further stated, ‘if appropriate you may wish to give your iPad to the HCP to allow them to use the interactive Ellipta device’ and to use this as an opportunity to offer, *inter alia*, placebo devices. The briefing gave a proposed probing question which asked ‘How do you think the Ellipta inhaler device compares to others you currently prescribe?’. The Panel noted GlaxoSmithKline’s submission that there was a separate leaflet which gave detailed instructions on patient use of the device. In the Panel’s view, the interactive Ellipta pages, which could be accessed via pages citing ‘easy to use’ constituted product claims regarding the device. The Panel considered that the pages in question referred to the mechanisms of the device rather than instructions on how

patients should use the device; there were no claims regarding the number of steps required by the patient to benefit from the medicine and each page of the Interactive Ellipta section referred the user to the PIL for patient instructions. In the Panel’s view, there was no evidence that the reference to open inhale close in the context of the Interactive Ellipta section was misleading or inconsistent with the SPC as alleged and no breach of Clauses 3.2 and 7.2 were ruled.

Although there was no current digital sales aid for Anoro, previous versions (November 2016 and January 2017), used during the time-period in scope of the complaint, referred to open (with a ‘click’), inhale and close beneath the statement ‘delivered in a once-daily, easy-to-use Ellipta inhaler’. The Panel had requested that GlaxoSmithKline provide the sections of the digital sales aids which referred to open, inhale, close. The Panel was provided with a single page and therefore reviewed the page in isolation and not within the context of the entire digital sales aid. The Panel noted that the Anoro SPC and PIL referred to three steps when taking the medicine: first ‘Prepare a dose’ (including sliding the cover down until a click was heard); second ‘How to inhale the medicinal product’; and third ‘Close the inhaler’. Full details for how the patient was to perform each step were in the SPC and PIL. In the Panel’s view, the page in question referred to the delivery of the medicine and there were no claims linking efficacy or patient benefit from the medicine to the 3 steps open, inhale and close. The Panel considered that in the circumstances and based on the narrow allegation the page in question was not misleading or inconsistent with the SPC and no breach of Clauses 7.2 and 3.2 were ruled accordingly.

Noting its comments and rulings above, the Panel did not consider that GlaxoSmithKline had failed to maintain high standards and ruled no breach of Clause 9.1.

Complaint received	31 July 2018
Case completed	11 March 2019

CLINICAL COMMISSIONING GROUP EMPLOYEE v NOVO NORDISK

Conduct of a representative

The head of prescribing and medicines management at a clinical commissioning group (CCG), complained about the promotion of Victoza (liraglutide) by a named Novo Nordisk representative. Victoza was used in adults with insufficiently controlled type 2 diabetes.

The complainant alleged that the representative asked a receptionist to write a note on promotional information for Victoza to inform GPs that the product could be used in estimated glomerular filtration rate (eGFR) <15 and told the receptionist that he/she could not write this him/herself. The complainant provided a scanned copy of the handwritten note and alleged that the statement in question was outside the product's licence.

The detailed response from Novo Nordisk is given below.

The Panel noted the representative denied that he/she had asked the receptionist to write the note. The Panel noted that the parties' accounts differed. The Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was often impossible in such circumstances to determine precisely what had happened. A complainant had the burden of proving his/her complaint on the balance of probabilities. The Panel noted, however, that a high degree of dissatisfaction was usually required before an individual was moved to submit a formal complaint.

The Panel noted that section 4.2 of the Victoza Summary of Product Characteristics (SPC) included:

'Renal impairment

No dose adjustment is required for patients with mild, moderate or severe renal impairment. There is no therapeutic experience in patients with end-stage renal disease, and Victoza is therefore not recommended for use in these patients (see sections 5.1 and 5.2).'

The Panel noted that the Victoza SPC did not specifically define severe renal impairment or end-stage renal disease in terms of eGFR parameters. There was mention of creatine clearance in relation to renal impairment. The Panel noted Novo Nordisk's submission that severe renal impairment was characterised by an eGFR of 15-29 ml/min/1.73m² and that it did not advocate the use of Victoza in patients with end-stage renal disease which it stated was an eGFR <15.

The Panel noted that the handwritten note stated, 'can be used in eGFR 15' and not that Victoza could

be used in eGFR <15, as alleged. In the Panel's view, an eGFR of 15 was likely to be considered the lower limit of severe renal impairment.

The Panel was concerned to note that when responding to the initial complaint Novo Nordisk had discovered that slides from a training course had referred to Victoza being used in patients with a eGFR down to less than 15 in error. Novo Nordisk explained that the slides were not read out verbatim but were used as a basis for a role play exercise and the presenters were very clear that Victoza could be used in patients with renal impairment down to an eGFR of 15ml/min/1.73m². It appeared that the slides were sent to the sales managers. It was not clear whether the slides had been circulated to the representatives. The Panel further noted Novo Nordisk's submission that this error was not reflected in other materials. According to Novo Nordisk the representative in question did not attend this training and his/her manager confirmed that he/she was very clear regarding eGFR and the use of Victoza.

Turning to the materials provided by the complainant, the Panel considered that the statement 'can be used in eGFR 15' was a product claim. It was not acceptable for a representative to handwrite claims on materials for health professionals or to instruct a receptionist to do so on his/her behalf. The Panel considered that the handwritten note did not appear to be inconsistent with the Victoza SPC. It was unlikely something would have been written on the Novo Nordisk materials without any discussion or prompt. However, the Panel did not consider that the complainant had proved on the balance of probabilities that the representative had asked the receptionist to write the note in question. The Panel therefore ruled no breach of the Code including Clause 2 based on the narrow allegation.

The head of prescribing and medicines management at a clinical commissioning group (CCG), complained about the promotion of Victoza (liraglutide) by a named Novo Nordisk representative. Victoza was used in adults with insufficiently controlled type 2 diabetes.

The scanned material provided by the complainant appeared to show four separate pieces of material placed on top of one another. There appeared to be an A4 sized Victoza leavepiece, on top of which was an A5 sized Tresiba (insulin degludec) leavepiece. On top of the Tresiba leavepiece was the business card of the representative in question. Below the business card, and also over the Tresiba leavepiece,

appeared a blank piece of material, the same size as the business card, with a handwritten note that stated, 'can be used in eGFR 15'. A handwritten arrow pointed to the statement with the text 'Added by receptionist on direction of rep'. Below the statement was further handwriting by the practice pharmacist, which stated 'Got receptionist to write this [date and centre name]'

COMPLAINT

The complainant alleged that a named Novo Nordisk representative was observed on 8 August asking a receptionist to write a note on promotional information for Victoza to inform GPs that the product could be used in estimated glomerular filtration rate (eGFR) <15 and was heard telling the receptionist that he/she could not write this him/herself. The complainant noted that the statement in question was outside the product's licence. The complainant provided a scanned copy of the documents with additional notes added by one of the CCG's team of pharmacists.

When writing to Novo Nordisk, the Authority asked it to consider the requirements of Clauses 2, 3.2, 9.1 and 15.2 of the Code.

RESPONSE

Novo Nordisk submitted that the representative in question worked within primary care, promoting Victoza and Tresiba. The representative had passed the ABPI medical representatives examination, had completed all relevant training since joining the company and had been trained and validated on product knowledge before making calls on health professionals. Novo Nordisk stated that the representative denied the complainant's allegations and had confirmed that he/she did not ask a receptionist to write a note.

Novo Nordisk provided a summary of the face-to-face interview by a senior member of Novo Nordisk with the representative to ascertain the events of the date in question. The representative was told that a complaint had been made but was not told the details before the meeting. During the investigation the representative was shown the email from the complainant, after he/she had given his/her initial account of the day and the visit in question. The representative recounted that it was a speculative visit to confirm the name of the diabetes specialist nurse with the aim of booking an appointment at a later date. The representative recalled that on entering the practice there were two receptionists at the desk and two patients; he/she waited until the patients had been dealt with before approaching the desk. The representative spoke to one of the receptionists; the other receptionist and the patients had moved away, and he/she was not aware of anyone nearby or within earshot of his/her conversation with the receptionist. The representative asked the receptionist the name of the diabetes specialist nurse and if he/she could make an appointment. The representative was told that the centre did not make appointments to see representatives. The representative left the

promotional literature and his/her business card and told the receptionist to ask the nurse to call him/her if he/she had any questions.

When shown the details of the complaint, the representative denied the allegation and stated that it would be inappropriate to ask a receptionist to write notes. The representative stated that he/she would only give such specific, product related information to a health professional in a promotional call.

During the interview, the representative was asked about discussions he/she might have had about the use of Victoza in patients with renal impairment. The representative responded that if having such discussions, he/she would usually use the terminology 'severe' renal impairment; when asked what that meant he/she stated this was 'eGFR 15'.

Novo Nordisk argued that the note on the photocopy provided by the complainant stated 'can be used in eGFR 15'; it did not state eGFR <15 as alleged. The summary of product characteristics (SPC) for Victoza stated:

4.2 Posology and method of administration

Special populations

Renal impairment

No dose adjustment is required for patients with mild, moderate or severe renal impairment. There is no therapeutic experience in patients with end-stage renal disease, and Victoza is therefore not recommended for use in these patients (see sections 5.1 and 5.2).'

Novo Nordisk noted that severe renal impairment (chronic kidney disease stage G4) was characterised by an eGFR of 15-29 ml/min/1.73m².

Novo Nordisk submitted that based on the representative's testimony and considering his/her experience and training, it could not substantiate that the conversation between the representative and the receptionist took place as alleged. Novo Nordisk was confident that the representative had maintained high compliance standards and denied breaches of Clauses 2, 3.2, 9.1 and 15.2.

In response to a request for further information, Novo Nordisk submitted that a verbal briefing was given via teleconference to the diabetes sales representatives for the leavepiece UK/VT/0418/0186. Novo Nordisk further submitted that the SPC for Victoza was updated in July 2017 and included a change to section 4.2, special populations, to include wording regarding severe renal impairment. A member of the Novo Nordisk medical department briefed the Victoza representatives regarding all the changes to the SPC, including the update to section 4.2 about use in patients with renal impairment, over a web-based teleconference in August 2017. The presentation stated that there was no therapeutic experience in patients with end-stage renal disease and Victoza was therefore not recommended for use in those patients.

Novo Nordisk stated that in their initial training course (ITC) new representatives were trained on the diabetes therapy area, Novo Nordisk products and the focus that they would have as a sales person. During the ITC, representatives were trained on the relevant clinical data for Victoza which included a slide on use in patients with renal impairment. Training was delivered by a medical advisor who trained on the use of Victoza in patients with renal impairment as specified in the SPC and the eGFR and creatine clearance rates. In addition, during the ITC, new representatives were trained on the entire Victoza SPC in a workshop format and key sections of the SPC were analysed, including section 4.2, use of Victoza in special populations. There was a written validation following the training and one of the questions tested the representatives' knowledge about the use of Victoza in patients with renal impairment. Novo Nordisk confirmed that the representative in question had passed the validation.

Novo Nordisk explained that at a training course in July 2018 for, *inter alia*, the primary care sales force, a presentation regarding the strategy and campaign for Victoza (UK/VT/0618/0311), was delivered. The presentation included two profiles of patients who might benefit from Victoza. The focus was patients whose HbA1c levels were not on target with their current treatments. During the presentation, the presenters demonstrated how a sales call might be conducted using the patient profiles as examples. One of the profiles focused on a patient who might have renal impairment. Novo Nordisk submitted that whilst responding as above it discovered that the presentation in question had a typographical error. The slide stated 'Victoza offers not only reductions in HbA1c and weight and can be used in patients with a eGFR down to less than 15...'. Novo Nordisk submitted that the sentence did not make sense and was an unfortunate error that was not reflected in the other materials. Novo Nordisk explained that the slides for the role play were not read out verbatim by the two presenters but instead were used as a basis for the role play and the presenters were very clear during the role play that Victoza could be used in patients with renal impairment down to an eGFR of 15ml/min/1.73m². Novo Nordisk further explained that the representative in question did not attend this training. His/her manager had confirmed that the representative was very clear regarding the parameters of eGFR and the use of Victoza. Novo Nordisk stated that this aligned with the interview it carried out with the representative.

Novo Nordisk submitted that following the discovery of the typographical error, for the avoidance of doubt, a briefing document was prepared in August 2018 and sent to the sales teams to ensure that there was absolute clarity regarding the use of Victoza in patients with renal impairment.

Novo Nordisk concluded by stating that it did not advocate the use of Victoza in patients with end stage renal disease (eGFR <15) and all relevant staff had been trained and were clear on the use of Victoza in patients with renal impairment.

PANEL RULING

The Panel noted the complainant's allegation that a named Novo Nordisk representative asked a receptionist to write a note on promotional information for Victoza to inform GPs that the product could be used in eGFR<15 which was outside the product's licence. Novo Nordisk stated that the representative denied the allegations and confirmed that he/she had not asked the receptionist to write the note. The Panel noted that the parties' accounts differed. The Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was often impossible in such circumstances to determine precisely what had happened. The introduction to the Constitution and Procedure stated that a complainant had the burden of proving their complaint on the balance of probabilities. The Panel noted, however, that a high degree of dissatisfaction was usually required before an individual was moved to submit a formal complaint.

The Panel considered from the scanned material provided by the complainant whether the handwritten note 'can be used in EGFR 15' was in relation to Victoza or Tresiba. The complainant referred to Victoza and therefore the Panel considered the statement in relation to Victoza.

The Panel noted that the Victoza SPC stated in section 4.2, under the sub-heading special populations:

'Renal impairment

No dose adjustment is required for patients with mild, moderate or severe renal impairment. There is no therapeutic experience in patients with end-stage renal disease, and Victoza is therefore not recommended for use in these patients (see sections 5.1 and 5.2).'

The Panel noted that the Victoza SPC did not specifically define severe renal impairment or end-stage renal disease in terms of eGFR parameters. There was mention of creatine clearance in relation to renal impairment. The Panel noted Novo Nordisk's submission that severe renal impairment was characterised by an eGFR of 15-29 ml/min/1.73m² and that it did not advocate the use of Victoza in patients with end-stage renal disease which it stated was an eGFR less than 15.

The Panel noted that the handwritten note stated, 'can be used in eGFR 15'. It did not state that the product could be used in eGFR less than 15, as alleged. In the Panel's view, an eGFR of 15 was likely to be considered the lower limit of severe renal impairment.

The Panel was concerned to note that Novo Nordisk discovered that slides from a training course held in July 2018 contained an error. One slide stated 'Victoza offers not only reductions in HbA1c and weight and can be used in patients with a eGFR down to less than 15 ...'. Novo Nordisk explained that the slides were not read out verbatim but instead were used as a basis for a role play exercise and the presenters were very clear during the role

play that Victoza could be used in patients with renal impairment down to an eGFR of 15ml/min/1.73m². It appeared that the slides were sent to the sales managers. It was not clear whether the slides had been circulated to the representatives. The Panel further noted Novo Nordisk's submission that this error was not reflected in other materials. According to Novo Nordisk the representative in question did not attend the July 2018 training and his/her manager confirmed that he/she was very clear regarding the parameters of eGFR and the use of Victoza.

Turning to the materials provided by the complainant, the Panel considered that the statement 'can be used in eGFR 15' was a product claim. It was not acceptable for a representative to handwrite claims on materials for health professionals or to

instruct a receptionist to do so on his/her behalf. The Panel considered that the handwritten note did not appear to be inconsistent with the Victoza SPC. The Panel noted that it was unlikely something would have been written on the Novo Nordisk materials without any discussion or prompt. However, the Panel did not consider that the complainant had proved on the balance of probabilities that the representative had asked the receptionist to write the note in question. The Panel therefore ruled no breach of Clauses 15.2, 3.2, 9.1 and 2 based on the narrow allegation.

Complaint received **15 August 2018**

Case completed **16 October 2018**

PHARMACISTS v PROVECA

Letter regarding the supply of unlicensed and off-label glycopyrronium

Two prescribing team pharmacists from a clinical commissioning group (CCG) (Case AUTH/3058/8/18) and a community pharmacist (Case AUTH/3060/8/18) complained about a letter sent in August 2018 by Proveca about the supply of unlicensed and off-label glycopyrronium bromide. Proveca marketed Sialanar (glycopyrronium bromide) for the symptomatic treatment of severe sialorrhoea in children aged 3-17 years. The letter at issue was copied to the Medicines and Healthcare products Regulatory Agency (MHRA).

Case AUTH/3058/8/18

The complainants noted that the letter was sent to at least two GP surgeries within the CCG and alleged that Proveca had taken a very aggressive marketing approach since it launched Sialanar and appeared to be communicating with surgeries and provider trusts in a similar intimidating vein. One of the complainants stated that he/she had previously received a similar letter in his/her capacity as a hospital pharmacist approximately three months ago.

The complainants explained that one key distinction between glycopyrronium 'specials' and Sialanar was the concentration of glycopyrronium bromide; the branded product was 2mg/5ml whereas the concentration historically used as a 'special' was 5mg/5ml. Hence, the two products were not of an equivalent strength. A switch from a 'special' to Sialanar might be appropriate in some instances but it meant that the liquid volume to be given to a child with severe drooling would be increased 2.5 – fold. There might be valid reasons why a special product had to be used. The last sentence of the letter ('It is only failing all of the above, and lack of importation of an approved medicinal product, that a 'special' may be supplied') recognised that there might be exceptions to the general guidance of using a special, although the first sentence of the same paragraph ('Therefore, not only is it not allowed to dispense an unlicensed drug where there is a licensed alternative, but a licensed product should be the preferred option for other indications outside of its authorization, given that it has already been assessed for safety and efficacy') seemed to claim that it was not permissible to dispense an unlicensed medicine.

The complainants alleged that although the letter described the relevant national guidance on the prescribing of 'specials' – from the MHRA and General Medical Council (GMC) – the way the letter was written and some of the wording was in breach of the Code.

The style of the letter was explicitly aggressive and threatening. The second paragraph referred to a 'breach of the law'. The sentence '.... officially putting you on notice for illegitimate dispensing practices ...' was clearly designed to scare staff. Likewise, the request that surgeries confirmed that they had ceased these activities back to the company was totally unnecessary and a scare tactic.

Although addressed to the surgery, the letter referred to 'your pharmacy' and implied that there might have been commercial and financial damage to Proveca. Pharmacies, or even dispensaries in surgeries, dispensed what was prescribed on the GP prescription and their actions should not be disparaged for doing so. Further, the letter seemed to suggest that specials were used on cost grounds ('Dispensing off-label on cost grounds where a licensed product is available and will meet the same therapeutic need is not acceptable...'). The complainants stated that the 'special' had been used for many years and any move away from the special to Sialanar needed careful consideration because of the different concentration. If the switch did not happen quickly enough for Proveca then it was likely to be because this was not a simple switch.

The letter referred to the Medicines and Healthcare products Regulatory Agency (MHRA) and a copy had supposedly been sent to the MHRA. The complainants queried whether this was a copy of every single letter or just a copy of the master letter and whether the MHRA had given the permission required to include reference to it in the letter.

The detailed response from Proveca is set out below.

The Panel noted that according to Proveca the letter at issue was sent to around 16,000 pharmacies, primarily consisting of community pharmacists and hospital outpatients. The letter urged pharmacies to refrain from dispensing glycopyrronium bromide 'specials', and off-license preparations for children with chronic drooling and ensure that Sialanar was dispensed.

The Panel noted that the letter in question was promotional and bore prescribing information. It was not necessarily unacceptable to draw the attention of prescribers to the prescribing legal framework, however such material had to comply with the Code. In the Panel's view there was a difference between writing to all pharmacists as opposed to those whose dispensing was the subject of Proveca's concern. The Panel noted the company's submission that it was not possible for

the company to know which pharmacists were dispensing glycopyrronium bromide.

The Panel noted that another letter which the complainant referred to briefly as a similar letter had been sent by Proveca's Medical Director in March 2018. That letter, which was not the subject of complaint, gave the licensed indication of Sialanar and stated that it had come to Proveca's attention that many pharmacists were continuing to supply unlicensed and off-label glycopyrronium bromide products even when the prescription was for a child with chronic drooling. The letter further stated that unless specifically requested by the prescribing physician, the licensed product should be dispensed as per the National Pharmacy Association (NPA) guidance on the supply of unlicensed medicines, and an extract of the guidance was included at the bottom of the letter. The Panel noted that the letter sent in March 2018 was very different to that sent in August 2018.

Turning to the letter at issue, sent in August 2018, the Panel noted the complainant's concern that pharmacies and dispensaries in surgeries were being disparaged for dispensing what was prescribed by GPs. Paragraph 2.2 of the MHRA guidance on 'The supply of unlicensed medicinal products ("specials")' allowed a doctor, dentist, nurse independent prescriber, pharmacist independent prescriber or other prescriber to decide whether an unlicensed medicine should be supplied in preference to a licensed medicine where the licensed product could not meet an individual patient's special needs. The Panel noted that the letter at issue highlighted that any pharmacy continuing to dispense unlicensed and off-label preparations for children was in breach of the pharmaceutical legal framework. The Panel noted the complainant's allegation that the letter implied that supplying a special in preference to the use of Sialanar was illegal. The Panel noted the company's response that if there was a *bona fide* reason for the prescription of an unlicensed product then it was the prerogative of the prescriber and Proveca was not suggesting that it was not dispensed. The Panel noted Proveca's submission that it might be suitable to prescribe an unlicensed product instead of Sialanar when the concentration of Sialanar (2mg/5ml) was too low and a much lower volume of product would be required. However, the Panel considered that the letter misleadingly implied that the activity was illegal by stating that if a pharmacy was supplying unlicensed or off-label preparations of glycopyrronium bromide for the indication of chronic drooling in paediatric patients then it should consider the letter as officially putting it on notice for illegitimate dispensing practices which might be a contravention of legally established rights and have caused Proveca significant commercial and financial damage. The Panel noted, as acknowledged by Proveca, that the supply of an unlicensed medicine was legally permissible in certain circumstances where there was a patient with a 'special need'. The Panel considered that the letter in question queried a health professional's decision to prescribe a special and the pharmacist's action of dispensing against a prescription, without

any knowledge of the clinical circumstances, which in the Panel's view might potentially put patient safety at risk. The letter stated that such a decision was inconsistent with MHRA Guidance and law and implied that serious consequences could ensue. The Panel further noted the negative responses received from at least six recipients of the letter. It appeared that the recipients considered that the content of the letter was such that it questioned the reader's professional judgement. In the Panel's view, the content and tone of the letter was such that it disparaged the professional opinion of health professionals and a breach was ruled.

The letter stated that Proveca had brought the disparaging practice at issue to the attention of the MHRA which was copied into the letter.

In the Panel's view, the implication was that the MHRA approved or otherwise endorsed the content of the letter. The Panel noted that it appeared that the MHRA had not asked to be copied into the letter. The Panel did not consider that Proveca's account of a conversation with the MHRA meant that the wording in the promotional letter in question was specifically required by the MHRA and thus a breach was ruled.

The Panel noted its comments and rulings above and ruled that Proveca had failed to maintain high standards.

The Panel considered that the letter in question queried a health professional's decision to prescribe a special and the pharmacist's action of dispensing against a prescription, without any knowledge of the clinical circumstances which in the Panel's view might potentially put patient safety at risk. The letter stated that such a decision was inconsistent with MHRA Guidance and law and implied that serious consequences could ensue if the letter was not adhered to. The Panel was very concerned about the content and tone of the letter and noted its comments and rulings above. In the Panel's view, pharmacists who had received the letter would be very concerned by the misleading implication that his/her dispensing practices were potentially illegal and that legal consequences including an implication that a claim for financial damages might ensue. The Panel noted that not all recipients of the letter would have dispensed glycopyrronium bromide. The tone of the promotional letter could be seen as threatening and, in the Panel's view, brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

Proveca appealed all the Panel's rulings of breaches of the Code. The Appeal Board upheld all the rulings of breaches of the Code.

Case AUTH/3060/8/18

The complainant stated that the crux of his/her complaint was that the tone of the letter was quite threatening; it had been copied to the MHRA and alleged that illegitimate dispensing practices were being followed.

The complainant had had a discussion with colleagues at a local surgery about the issues surrounding the letter to remedy any issues following clinical review from a local GP.

The complainant alleged that the letter was unnecessarily threatening towards the pharmacy and making the switch would pose an additional cost burden on the NHS. An additional concern was that the original prescriptions were initiated in secondary care so there might be clinical reasons for prescribing the original unlicensed special. The complainant had sought clarification from a local primary care clinician who would hopefully feedback at the appropriate time.

The detailed response from Proveca is given below.

The Panel noted that the letter urged pharmacies to refrain from dispensing glycopyrronium bromide 'specials', and off-license preparations for children with chronic drooling and ensure that Sialanar was dispensed.

The Panel noted that the letter in question was promotional and bore prescribing information. The Panel noted that it was not necessarily unacceptable to draw the attention of prescribers to the prescribing legal framework, however such material had to comply with the Code. In the Panel's view there was a difference between writing to all pharmacists as opposed to those whose dispensing was the subject of Proveca's concern. The Panel noted the company's submission that it was not possible for the company to know which pharmacists were dispensing glycopyrronium bromide.

The Panel noted the complainant's submission that the original prescriptions were initiated in secondary care so there might be clinical reasons for prescribing the original unlicensed special.

The Panel noted Proveca's submission that it might be suitable to prescribe an unlicensed product instead of Sialanar when the concentration of Sialanar (2mg/5ml) was too low and a much lower volume of product would be required (provided by a higher concentration of special eg 5mg/5ml). However, the Panel considered that the letter in question misleadingly implied that the activity was illegal by stating that if a pharmacy was supplying unlicensed or off-label preparations of glycopyrronium bromide for the indication of chronic drooling in paediatric patients then it should consider the letter as officially putting it on notice for illegitimate dispensing practices which might be a contravention of legally established rights and have caused Proveca significant commercial and financial damage. The Panel noted, as acknowledged by Proveca, that the supply of an unlicensed medicine was legally permissible in certain circumstances where there was a patient with a 'special need'. The Panel considered that the letter in question queried the health professional's decision to prescribe a special and the pharmacist's action of dispensing against a prescription, without any knowledge of the clinical circumstances, stating that such a decision was inconsistent with MHRA Guidance and law and implying that serious consequences could ensue.

The Panel noted that the letter in question stated that Proveca had brought the dispensing practice at issue to the attention of the MHRA which was copied into the letter. In the Panel's view the implication was that the MHRA approved of or otherwise endorsed the content of the letter which was not so. The Panel further noted the negative responses received from at least six recipients of the letter at issue. It appeared that the recipients considered that the content of the letter was such that it was threatening and questioned the reader's professional judgement. In the Panel's view Proveca had failed to maintain high standards and a breach was ruled.

The Panel considered that the letter in question queried a health professional's decision to prescribe a special and the pharmacist's action of dispensing against a prescription, without any knowledge of the clinical circumstances which in the Panel's view might potentially put patient safety at risk. The letter stated that such a decision was inconsistent with MHRA Guidance and law and implied that serious consequences could ensue if the letter was not adhered to. The Panel was very concerned about the content and tone of the letter and noted its comments and rulings above. In the Panel's view, pharmacists who had received the letter would be very concerned by the misleading implication that his/her dispensing practices were potentially illegal and that legal consequences including an implication that a claim for financial damages might ensue. The Panel noted that not all recipients of the letter would have dispensed glycopyrronium bromide. The tone of the promotional letter could be seen as threatening and, in the Panel's view, brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

Proveca appealed all the Panel's rulings of breaches of the Code. The Appeal Board upheld all the rulings of breaches of the Code.

Two prescribing team pharmacists from a clinical commissioning group (CCG) (Case AUTH/3058/8/18) and a community pharmacist (Case AUTH/3060/8/18) complained about a letter (ref Sia/Legal/01) sent in August 2018 by Proveca Ltd about the supply of unlicensed and off-label glycopyrronium bromide. Proveca marketed Sialanar (glycopyrronium bromide) for the symptomatic treatment of severe sialorrhoea in children aged 3-17 years. The letter at issue was copied to the Medicines and Healthcare products Regulatory Agency (MHRA).

Case AUTH/3058/8/18

COMPLAINT

The complainants noted that the letter was sent to at least two GP surgeries within the CCG and alleged that Proveca had taken a very aggressive marketing approach since it launched Sialanar and appeared to be communicating with surgeries and provider trusts in a similar intimidating vein. One of the complainants noted that he/she had previously received a similar letter in his/her capacity as a hospital pharmacist approximately three months ago.

The complainants explained that one key distinction between glycopyrronium 'specials' and Sialanar was the concentration of glycopyrronium bromide; the branded product was 2mg/5ml whereas the concentration historically used as a 'special' was 5mg/5ml. Hence, the two products were not of an equivalent strength. A switch from a 'special' to Sialanar might be appropriate in some instances but it meant that the liquid volume to be given to a child with severe drooling would be increased 2.5 – fold. There might be valid reasons why a specials product had to be used. The last sentence in paragraph 3 on page 2 of the letter ('It is only failing all of the above, and lack of importation of an approved medicinal product, that a 'special' may be supplied') recognised that there might be exceptions to the general guidance of using a special, although the first sentence of the same paragraph ('Therefore, not only is it not allowed to dispense an unlicensed drug where there is a licensed alternative, but a licensed product should be the preferred option for other indications outside of its authorization, given that it has already been assessed for safety and efficacy') seemed to claim that it was not permissible to dispense an unlicensed medicine.

The complainants submitted that although the letter described the relevant national guidance on the prescribing of 'specials' – from the MHRA and General Medical Council (GMC) - they considered that the way the letter was written and some of the wording was in breach of the Code. In particular:

Clause 2 – Discredit to, and reduction of confidence in, the industry. The style of the letter was explicitly aggressive and threatening. The second paragraph referred to a 'breach of the law'. The final sentence commencing at the bottom of page 2, '.... officially putting you on notice for illegitimate dispensing practices...' was clearly designed to scare staff at the surgery. Likewise, the request that surgeries confirmed that they had ceased these activities back to the company was totally unnecessary and a scare tactic.

Clause 8.2 The health professions and the clinical and scientific opinions of health professionals must not be disparaged. Although addressed to the surgery, the letter referred to 'your pharmacy' and implied that there might have been commercial and financial damage to Proveca. Pharmacies, or even dispensaries in surgeries, dispensed what was prescribed on the GP prescription and their actions should not be disparaged for doing so. Further, the letter seemed to suggest that specials were used on cost grounds ('Dispensing off-label on cost grounds where a licensed product is available and will meet the same therapeutic need is not acceptable...'). The complainants submitted that the 'special' had been used for many, many years and any move away from the special to Sialanar needed careful consideration because of the different concentration. If the switch did not happen quickly enough for Proveca then it was likely to be because this was not a simple switch.

Clause 9.5 Promotional material must not include any reference to the Commission on Human

Medicines, the Medicines and Healthcare products Regulatory Agency or the licensing authority, unless this is specifically required by the licensing authority. The letter referred to the MHRA and a copy had supposedly been sent to the Agency. The complainants queried whether this was a copy of every single letter that had gone to each and every surgery or just a copy of the master letter and whether the MHRA had given the permission required to include reference to it in the letter.

When writing to Proveca, the Authority asked it to consider the requirements of Clause 9.1 in addition to Clauses 8.2, 9.5 and 2 as cited by the complainant.

RESPONSE

Proveca submitted that it was a small pharmaceutical company which specialised in the development and licensing of off-patent medicines through the paediatric – use marketing authorization (PUMA) regulatory route. The law and guidelines from the MHRA were very clear as to when an off-licence medicine could be dispensed to patients. It was not the prerogative of the pharmacists (with the exception of pharmacist independent prescribers) to choose an unlicensed medicine where a licensed alternative existed. It was the prerogative of the health practitioner in accordance with the law. Proveca stated that it had noted this in an earlier letter of March 2018 which resulted in very little change in practice. Rather than considering legal action, the company thus sent the letter in question to reiterate the position as a courtesy to the pharmacists.

The letter was sent to 16,154 pharmacies across the UK, primarily consisting of community pharmacists and hospital outpatients.

The letter at issue was intended to inform all pharmacists of the licensed status of Sialanar and the legal requirement for the dispensing and supply of unlicensed products. Proveca stated that it consulted with the MHRA which agreed with its proposal to write to pharmacists to remind them of their legal obligations with a 'cease and desist' letter. If this was not successful, the MHRA suggested that the company get back in touch to see how the Agency might be further involved. Despite the March 2018 letter informing pharmacists that there was now a licensed product available, significant off-label and unlicensed dispensing of glycopyrronium bromide continued to be widespread for children with chronic drooling. Proveca took legal advice to ensure its communications were aligned with UK law and sent the letter at issue to remind pharmacists of their obligations around supply of unlicensed medicines.

Proveca explained that it was only by a narrowly drawn exemption expressed in Article 5(1) of Directive 2001/83/EC, implemented in Regulation 167 of the Human Medicines Regulations 2012 (SI/2012/1916), that the supply of an unlicensed drug was legally permissible. This was where a patient had a 'special need' namely where there was no other available licensed medicine and a company received a *bona fide* unsolicited request from a

prescriber for a specific individual patient. Proveca noted that where there was a prescription for an unlicensed product it had not suggested that it was not dispensed; if there was a *bona fide* reason for the prescription this was the prescriber's prerogative.

Proveca submitted that several pharmacists had emailed the company following receipt of the letter. In total 65 emails had been received; 59 confirmed receipt of the letter, advising the company of actions taken and/or thanking it for the information; 6 expressed some level of concern at the letter but acknowledged its content. Proveca had met with or called everyone who contacted it. The overwhelming response to the calls was that, now they were aware of their obligations, the pharmacist was keen to comply with the law and move away from dispensing specials in situations where their use was not warranted, justified or prescribed by a health professional. Some pharmacists stated that the communication had been helpful in allowing them to ensure good governance.

Proveca denied a breach of Clause 2.

Proveca stated that it had not been its intention to disparage the clinical and scientific opinions of health professionals and it did not consider that the letter at issue did so. The letter was sent to all pharmacists as it was not possible for the company to know which pharmacists were dispensing glycopyrronium bromide and, in any event, it was never suggested that any 'Specials' dispensing was intentionally contravening legal requirements.

Proveca noted that it had communicated the licensed status and the requirement for licensed dispensing in its letter in March. Despite that, off-label and unlicensed dispensing continued to be widespread for children. The company consulted with the MHRA and took legal advice and as a result had sent the letter at issue which intended to clarify the legal position with respect to the continued dispensing of off-label and unlicensed glycopyrronium bromide where a licensed product existed. The letter was sent on the assumption that pharmacists were not deliberately breaching the law but simply did not know about the law applicable to 'Specials' and/or the fact that Sialanar had been authorised for use in paediatrics. This was also indicated in the company's recommendation to 'Specials' manufacturers that they contact any unaware prescribers placing the order accordingly, to ensure proper observance of the rules that health professionals were bound to follow. Proveca referred to the narrow exemption in the regulations stated above.

Proveca submitted that health professionals remained free to prescribe whatever they considered was suitable for their patients. However, if they prescribed a product off-label then they bore the product liability. Pharmacists were obliged to supply the product prescribed by the health professional and 'specials' could only be prescribed and supplied in accordance with the law as explained in the letter. Proveca further submitted that unlicensed product should only be prescribed and supplied in instances

where there was an unmet patient need which could not be met by the licensed product. Only under these circumstances could an unlicensed medicine be dispensed. Sialanar was the only glycopyrronium bromide licensed for children and had been designed specifically for the paediatric population. Examples of when it would be unsuitable would include allergy to one of the ingredients or the child being unable to take a liquid. Proveca had not suggested that, in such circumstances, an unlicensed product might not be the appropriate choice, and as such had not questioned any professional knowledge and decision making.

With regard to high standards, Proveca submitted that the letter at issue was professionally written and courteous. It provided in a clear and comprehensive manner, the legal position which it appreciated pharmacists might not be familiar with. The company denied a breach of Clause 9.1.

With regard to Clause 9.5, Proveca stated that it referred to the MHRA as it was copied into the letter and it had sought advice from the Agency previously. The company submitted that to this end, omission of such a reference would have been misleading and it denied a breach of Clause 9.5.

FURTHER INFORMATION FROM PROVECA

In response to a request for further information Proveca provided details of a telephone call with the MHRA on 11 September 2017 which consisted of a short discussion around the extent of the MHRA's involvement in cease and desist letters sent by companies. The MHRA explained that whilst the MHRA was not involved in the issue or drafting of cease and desist letters (and therefore had no templates or examples to share), it was aware of this practice by companies sending such letters referring to MHRA Guidance Note 14. Proveca suggested drafting a letter along these lines and the MHRA agreed. Proveca considered reference to the relevant guidance crucial for informing the recipients of the applicable rules and their obligations by reference to national guidance, instead of risking being perceived as suggesting its own rules and interpretation of the applicable framework. Proveca considered this an objective and factual reference to the applicable national rules and in line with the informative tone that it sought to adopt.

According to Proveca, the MHRA suggested that once Proveca had taken a number of steps, including a cease and desist letter, to remedy the situation it considered wrong, it could then contact the MHRA explaining the position and the steps that Proveca had taken, so that the MHRA could then take a view on whether there was scope for the Agency's involvement.

Proveca submitted that, it was therefore clear that Proveca could not have consulted the MHRA more specifically about the letter, seeking any pre-approval, and Proveca did not consider it appropriate to take up the Agency's time considering that they did not issue such letters. Proveca submitted, however, that it did promptly send copies of the

finalised letter to the MHRA. No comments or correspondence were received from the MHRA in response to the letter.

The MHRA responded to a pharmacist who complained about the letter that this was not an enforcement matter and it would be handled by either the regulatory affairs or customer services teams, if appropriate.

Whilst the MHRA suggested that Proveca contact the Agency if its approach was unsuccessful, Proveca wished to exhaust all possible avenues of informing the concerned parties of the illegitimacy of the specials dispensing practice without justification, before involving the Agency. Given the recency of the letters sent by Proveca, it wanted to wait for an appropriate time to elapse in order to assess the success of its effort to inform pharmacists.

Proveca provided anonymised copies of the 6 emails from health professionals setting out concerns following receipt of the letter at issue. Proveca also provided a copy of the letter that it sent to pharmacists in March 2018 informing them of the existence of a licensed product. No responses to this letter were provided.

Proveca considered that it might be suitable to prescribe an unlicensed product instead of Sialanar when:

- the concentration of Sialanar was too low and a much lower volume of product would be required (provided by a higher concentration of special eg 5mg/5ml). This would be unusual but there could be the rare occasion.
- the child had an allergy to one of the excipients of Sialanar, where a special might exclude the excipient. Again, this would be highly unlikely since Sialanar contained very few ingredients. The lack of such ingredient would need to be assured in the special formulation.

PANEL RULING

The Panel noted that according to Proveca the letter at issue was sent to 16,154 pharmacies across the UK, primarily consisting of community pharmacists and hospital outpatients. The letter urged pharmacies to refrain from dispensing glycopyrronium bromide 'specials', and off-license preparations for children with chronic drooling and ensure that Sialanar was dispensed. The letter in question stated Sialanar's licensed indication in the second paragraph on the first page, namely that it was the only product licensed in the UK for the symptomatic treatment of severe drooling in the paediatric population (children aged 3-17 years).

The Panel noted that the letter in question was promotional and bore prescribing information. The Panel noted that it was not necessarily unacceptable to draw the attention of prescribers to the prescribing legal framework, however such material had to comply with the Code. In the Panel's view there was a difference between writing to all pharmacists as opposed to those whose dispensing was the subject of Proveca's concern. The Panel

noted the company's submission that it was not possible for the company to know which pharmacists were dispensing glycopyrronium bromide.

The Panel noted that another letter which the complainant referred to briefly as a similar letter had been sent by Proveca's Medical Director in March 2018. That letter, which was not the subject of complaint, gave the licensed indication of Sialanar and stated that it had come to Proveca's attention that many pharmacists were continuing to supply unlicensed and off-label glycopyrronium bromide products even when the prescription was for a child with chronic drooling. The letter further stated that unless specifically requested by the prescribing physician, the licensed product should be dispensed as per the National Pharmacy Association (NPA) guidance on the supply of unlicensed medicines, and an extract of the guidance was included at the bottom of the letter. The Panel noted that the letter sent in March 2018 was very different to that sent in August 2018.

Turning to the letter at issue, sent in August 2018, the Panel noted the complainant's concern that pharmacies and dispensaries in surgeries were being disparaged for dispensing what was prescribed by GPs. The Panel noted that Clause 8.2 stated that health professions and the clinical and scientific opinions of health professionals must not be disparaged. Paragraph 2.2 of the MHRA guidance on 'The supply of unlicensed medicinal products ("specials")' allowed a doctor, dentist, nurse independent prescriber, pharmacist independent prescriber or other prescriber to decide whether an unlicensed medicine should be supplied in preference to a licensed medicine where the licensed product could not meet an individual patient's special needs. The Panel noted that the letter at issue highlighted that any pharmacy continuing to dispense unlicensed and off-label preparations for children was in breach of the pharmaceutical legal framework. The Panel noted the complainant's allegation that the letter implied that supplying a special in preference to the use of Sialanar was illegal. The Panel noted the company's response that if there was a *bona fide* reason for the prescription of an unlicensed product then it was the prerogative of the prescriber and Proveca was not suggesting that it was not dispensed. The Panel noted Proveca's submission that it might be suitable to prescribe an unlicensed product instead of Sialanar when the concentration of Sialanar (2mg/5ml) was too low and a much lower volume of product would be required. However, the Panel considered that the letter misleadingly implied that the activity was illegal by stating that if a pharmacy was supplying unlicensed or off-label preparations of glycopyrronium bromide for the indication of chronic drooling in paediatric patients then it should consider the letter as officially putting it on notice for illegitimate dispensing practices which might be a contravention of legally established rights and have caused Proveca significant commercial and financial damage. The Panel noted, as acknowledged by Proveca, that the supply of an unlicensed medicine was legally permissible in certain circumstances where there was a patient with a 'special need'. The Panel considered that the letter in question queried a health professional's decision to prescribe

a special and the pharmacist's action of dispensing against a prescription, without any knowledge of the clinical circumstances, which in the Panel's view might potentially put patient safety at risk. The letter stated that such a decision was inconsistent with MHRA Guidance and law and implied that serious consequences could ensue. The Panel further noted the negative responses received from at least six recipients of the letter at issue. It appeared that the recipients considered that the content of the letter at issue was such that it questioned the reader's professional judgement. In the Panel's view, the content and tone of the letter was such that it disparaged the professional opinion of health professionals and a breach of Clause 8.2 was ruled.

The Panel noted that Clause 9.5 stated that promotional material must not include any reference to, *inter alia*, the Medicines and Healthcare products Regulatory Agency, unless this was specifically required by the licensing authority. The exception in the relevant supplementary information in relation to factual safety information and the MHRA Drug Safety Update did not apply to the letter at issue. The Panel noted that the letter in question referred to the MHRA's Guidance Note 14 on the supply of unlicensed medicinal products (specials) and the hierarchy for the use of unlicensed medicines, an appendix to this guidance note. The letter in question stated that Proveca had brought the dispensing practice at issue to the attention of the MHRA which was copied into the letter. In the Panel's view, the implication was that the MHRA approved or otherwise endorsed the content of the letter. The Panel noted that it appeared that the MHRA had not asked to be copied into the letter. The Panel noted that the impression was supported by Proveca's initial submission that it had consulted with the MHRA which agreed with its proposal to write to pharmacists to remind them of their legal obligations with a 'cease and desist letter' and suggested that Proveca get back in touch with the MHRA to see how it might be further involved should the letter be unsuccessful. The Panel noted Proveca's further submission, following a request from the Panel for further information, regarding the telephone conversation the MHRA in September 2017 around the extent of the MHRA's involvement in cease and desist letters sent by companies. According to Proveca the MHRA explained that whilst it was not involved in the issue or drafting of cease and desist letters (and therefore had no templates or examples to share), it was aware of the practice by companies sending such letters referring to MHRA Guidance Note 14. According to Proveca, the MHRA apparently agreed with Proveca's suggestion of drafting such a letter and suggested that Proveca contact the MHRA explaining Proveca's position and the steps it had taken, including a cease and desist letter, to remedy the situation it considered wrong, so that the MHRA could then take a view on whether there was scope for its involvement. There was no written follow up of this conversation. The Panel did not consider that Proveca's account of the conversation meant that the wording in the promotional letter in question was specifically required by the MHRA as stated in Clause 9.5 and thus a breach of Clause 9.5 was ruled.

The Panel noted its comments and rulings above and considered that Proveca had failed to maintain high standards and a breach of Clause 9.1 was ruled. The Panel considered that the letter in question queried a health professional's decision to prescribe a special and the pharmacist's action of dispensing against a prescription, without any knowledge of the clinical circumstances which in the Panel's view might potentially put patient safety at risk. The letter stated that such a decision was inconsistent with MHRA Guidance and law and implied that serious consequences could ensue if the letter was not adhered to. The Panel was very concerned about the content and tone of the letter and noted its comments and rulings above. In the Panel's view, pharmacists who had received the letter would be very concerned by the misleading implication that his/her dispensing practices were potentially illegal and that legal consequences including an implication that a claim for financial damages might ensue. The Panel noted that not all recipients of the letter would have dispensed glycopyrronium bromide. The tone of the promotional letter could be seen as threatening and, in the Panel's view, brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel noted its ruling of a breach of Clause 2 which would mean that brief details of the case would be the subject of an advertisement. The Panel therefore decided on balance taking all the circumstances into account not to report Proveca to the Appeal Board for it to consider in accordance with Paragraph 8.2 of the Constitution and Procedure.

APPEAL BY PROVECA

Proveca submitted that the Panel misunderstood and mischaracterised what the letter in question was saying, to whom it was addressed and why; in doing so it had erroneously ruled that Proveca was in breach of Clauses 2, 8.2, 9.1 and 9.5.

Proveca submitted that firstly, the letter in question concerned the application and operation of the applicable legal framework concerning Specials as well as off-label products. It was informative in nature and aimed to enable the pharmacists and manufacturers of Specials to assess whether they were in compliance, and at no point did it discuss or challenge the clinical assessment or scientific opinion conducted by a health professional about the treatment of a patient. Secondly, the letter in question was addressed to dispensers and not prescribers. The clinical judgement of the recipient was never at stake, as the Panel opined; on the contrary, the letter clearly stated that prescribers could decide to prescribe a Special or off-label product to a particular patient if the health professional considered that there was a special need. Thirdly, the parallel drawn with Case AUTH/2971/8/17 was inappropriate, as the present case differed on a number of significant grounds, such as that (a) the MHRA was not the competent authority and its involvement was entirely mischaracterised in Case AUTH/2971/8/17,

as opposed to the present case in which the MHRA were consulted by Proveca about the general situation and (b) in Case AUTH/2971/8/17 the letter at issue misled the recipient about the licensed indication.

Proveca submitted that it had micro SME status, and was engaged in the development and licensing of medicinal products for the paediatric population with chronic and life-limiting conditions. Sialanar was the only oral glycopyrronium product licensed for children on the UK market and the only one licensed for severe chronic drooling. Sialanar was first launched in the UK in February 2017, and prior to its approval, the needs of the market were fulfilled by off-label and unlicensed glycopyrronium bromide products within the 'Special' legal framework. By December 2017, Sialanar's market penetration was very limited and accounted less than 5% of the paediatric market compared to unlicensed and off-label oral glycopyrronium bromide.

Proveca noted that it had become aware of a disproportionately high supply of off-label and unlicensed products compared to its own licensed product, due to its limited market share. This discrepancy could neither be justified nor explained on medical or clinical grounds for preferring unlicensed products in the vast majority of cases. This would only be the case where Sialanar was contraindicated as a result of its excipients or where a significantly different concentration leading to a much lower volume was required. Currently there was no evidence of a gap on the market in respect of glycopyrronium bromide for the licensed indication in children. Considering that there was no shortage of supply of Sialanar, it was obvious that at least some of the off-label and unlicensed product was dispensed outside of the strict conditions established by the legal framework applicable to the supply of Specials.

Upon becoming aware of the extent of the widespread supply of off-label and unlicensed glycopyrronium bromide products, Proveca submitted in the first instance it had sought to discuss this with the MHRA on a general basis. The MHRA agreed with Proveca approaching the potentially infringing parties to explain the rules around off-label and unlicensed supply and to inform them that there was now a licensed glycopyrronium bromide product available to treat severe sialorrhoea in the paediatric population. Proveca was told by the MHRA that if the approach was unsuccessful, it should contact the MHRA again and it would assess whether it should take action.

The issue that Proveca wanted to raise was in the event where the prescription did not specify the product from and/or strength, in which case it was up to the pharmacist to determine what to dispense in order to fulfil the prescription. The legal framework imposed on the pharmacist the obligation to dispense the licensed product, unless there were evidenced medical grounds to dispense a Special or off-label product. With variability in the preparation of unlicensed products and the specific warning in the off-label products that they should not be used in

children, there were potential serious public health concerns. Such concerns were what had led to the established legal framework. This was precisely what Proveca wanted to ensure was brought to the pharmacists' and specials manufacturers' attention.

Therefore, Proveca wrote to pharmacists and manufacturers alike to inform them that a licensed product was now available and reminding them about the legal framework applicable to Specials, in a balanced and proportionate manner.

Proveca now addressed the breaches in turn.

Clause 8.2

Proveca noted that the Panel had ruled that the letter in question was disparaging of the health profession and clinical and scientific opinions of health professionals because it '... highlighted that any pharmacy continuing to dispense unlicensed and off-label preparations for children was in **breach** of the pharmaceutical legal framework' and '**implied** that supplying a special in preference to the use of Sialanar was illegal.'

The Panel further stated '... the letter in question **queried the health professional's decision to prescribe a special** and the pharmacist's action of dispensing against a prescription, **without any knowledge of the clinical circumstances**, stating that such a decision was inconsistent with MHRA Guidelines and law and **implying** that serious consequences could ensue.' (emphasis added by Proveca).

Proveca submitted that these two extracts clearly showed that the Panel misunderstood and misinterpreted the letter. Indeed, not only had Proveca not challenged the clinical or scientific opinion of a health professional, but on the contrary made it very clear that it was for the health professional to make the clinical decision to provide a Special or an off-label product to a patient and this decision must fulfil the legal conditions under which a Special could be provided. The applicable framework was formed of the laws, the guidance issued by the MHRA and jurisdiction of the European Court of Justice, allowing Specials where (i) 'there was a patient 'special need', namely where there was no other available licensed medicinal product; or (ii) 'when there is no authorised equivalent on the national market or which is unavailable on that market' or (iii) 'where there are strong therapeutic arguments in favour of [not supplying the licensed medicinal product and preferring other products not licensed for the specific indication].

Proveca submitted that the letter ensured that pharmacists and Special manufacturers were aware of the legal framework under which they must operate and could assess their compliance under legal, rather than scientific or clinical principles. Therefore, it was incorrect to claim that Proveca had at any point challenged the health professional's opinion or disparaged the health profession.

In addition, Proveca submitted that it had explicitly explained in its letter that an unlicensed product might be supplied '...if there was a *bona fide* unsolicited request from a health professional', ie prescriber, for an individual patient for the indication of excessive sialorrhoea. This was clearly stated without ambiguity in the letter. So, it was incorrect of the Panel, and highly inaccurate, to ignore the clear wording of the letter in its full context and instead to erroneously conclude that Proveca claimed that '...any pharmacy continuing to dispense unlicensed and off-label preparations for children was in breach of the pharmaceutical legal framework'. (emphasis added by Proveca).

Proveca submitted that its argument had always been that in the absence of an identified patient need by a health professional then the applicable legislation, the MHRA guidance and jurisprudence made clear that the dispensing of unlicensed products was not permissible. Proveca had accepted from the onset that a health professional's prescription for a Special or off-label product because of a special need was to be respected as a valid ground for such supply. In further correspondence with the Panel in Case AUTH/3060/8/18, Proveca set out a detailed set of examples and reasons for when it might be suitable for an unlicensed product to be provided. Proveca never questioned a health professional's ability or authority to prescribe a special or off-label product, but merely drew the addressed pharmacists attention to the fact that there must be such a prescription evidencing the patient's special need, as required by the law. Therefore, Proveca was concerned that the Panel's ruling was reached on the wrong grounds, considering that the facts relied on by the Panel were mischaracterised, as illustrated in the above-referenced excerpts from the Panel's letter.

Proveca submitted that all the statements that it had made about the appropriateness of Sialanar for paediatric patients with excessive sialorrhoea were accurate, balanced fair and capable of substantiation. Proveca provided all the relevant references so that the pharmacists and Specials manufacturers would be able to confirm the validity of the information and determine whether their supply practice of Specials was compliant with the applicable legal framework.

Proveca submitted that moreover, the analogy with Case AUTH/2971/8/17 drawn by the Panel was not applicable in the present case. Proveca did not write to either clinicians or prescribers but rather to dispensers who must act upon a prescription. The two should not be confused; there was a difference between a clinician writing a prescription and a pharmacist making a dispensing decision. Therefore, it could not be stated that Proveca disparaged the view or clinical decision of health professional's when simply drawing the dispenser's attention to the need for prescriptions evidencing a special need in order to depart from the licensed product. Furthermore, the Panel noted the additional six complaints received by Proveca and concluded that, implying illegality, putting the recipients on notice and requesting that the recipients would confirm that they would cease this practice, questioned

the reader's professional judgement. Again, Proveca submitted that there was no reference to the professional judgement of the addressees of the letter, which aimed to seek confirmation from the addressee that this information had been read and understood and that any supply of off-label or unlicensed glycopyrronium bromide was in accordance with the law.

Proveca submitted that the benefit of this correspondence rather than resolving to take immediate legal action was illustrated by the positive responses that Proveca received from some recipients of the letters, thanking Proveca for bringing this information to its attention (provided). These confirmed that Proveca, rather than assuming wrongdoing or misjudgement by the recipient, instead helped the recipient to ensure that their dispensing activities were in accordance with the law.

Further, Proveca submitted that in this context, it was also important to note that the content of the letter was in line with the views publicly expressed by the ABPI and of the European Federation of Pharmaceutical Industries and Associations (EFPIA) on the matters of prescription of products without a license in respect of the intended indication.

Proveca submitted that the ABPI's position regarding the use of unlicensed medicines was set out in a press release that it issued in May 2012. The press release stated that the '... health and safety of UK patients should always be paramount, and all other considerations, including cost, must be secondary'. In the statement, the ABPI reiterated that use of unlicensed medicines put patients at risk and should be strictly limited to those occasions where there was no licensed alternatives. Proveca's position as expressed in the letter supported and reiterated this point.

In addition, in March 2017 EFPIA made some statements on off-label supply, which applied equally and directly to the supply of unlicensed products beyond the special needs' exemption. Commenting on the European Commission's study report on off-label use, EFPIA stated that:

'Indeed, pharmaceutical companies may be less ready to invest in costly and lengthy clinical development and authorisation processes for a given indication if public authorities promote the use of cheaper off-label medicines that have not been subject to the same stringent safety and efficacy assessments as existing on-label medicines, for financial reasons.'

Proveca submitted that these public positions indicated that the industry and trade association bodies considered that supply of a medicine for an indication for which it was not licensed, contained many risks, ranging from public health to reduction in investment and compromise of the regulatory system, resulting in uncertainties and the undermining of the pharmaceutical industry. These considerations were present in and directly applicable to the situation that Proveca had been

facing and in line with the approach Proveca had taken to engage with the potential involuntary infringer by restating the law applicable to off-label and unlicensed medicines and informing them of the fact that there was now a licensed product available to treat those medical conditions in the paediatric population.

Proveca submitted that in the same way that the ABPI's and EFPIA's statement did not disparage the medical profession but rather sought to protect it, Proveca's letter had been aimed at ensuring the safe and lawful operation of supply of medicines. It was not fair for a company to be criticised in trying to ensure that the law was rightly implemented, especially when seeking to discourage the potentially unjustified use of a medicine that had not been subject to the regulatory approval and use for an indication. This undermined the regulatory legal system applicable to medicinal products. Indeed, the use of Specials was a *de facto* circumvention of the pharmaceutical system, only allowed in exceptional circumstances when there was an evidenced patient need identified by a health professional. In the absence of such an identified patient need, the law had established that only authorised medicinal products should be used.

Clause 9.5

Proveca submitted that the Panel noted that the letter, by mentioning the MHRA, implied that it had approved or endorsed the content of the letter, while in fact there was no written follow up with the MHRA and the conversation was nothing beyond a single, general, short, non-product specific telephone conversation.

Firstly, Proveca submitted that the Panel had placed significant weight on its view that the letter was promotional. Proveca did not accept this characterisation, as the letter was factual and informative in nature as could be seen from all the parts of the letter with an objective characterisation of the applicable regulatory legal framework. The Code permitted dissemination of informational or educational materials, under Clause 9.7. The letter was informational and educational which was obviously 'inexpensive, directly relevant to the practice of medicine or pharmacy and directly beneficial to the care of patients'. The letter set out the legal framework and explained the difference between the licensed and off label or unlicensed products. As such, it was permissible material under the Code. The informative tone of letter could be corroborated by correspondence that Proveca received from dispensers thanking Proveca for this informative content.

Proveca submitted that the letter aimed to educate the recipients about the legal framework applicable to off-label and unlicensed medicines, with verbatim citations of the guidance by the MHRA, including the quotation that licensed products should be preferred over unlicensed products even when provided off-label. The MHRA was in copy as this exchange of correspondence was the first step undertaken by Proveca to try to resolve this apparent potential breach of the law. The second step was to get

back to the MHRA for them to take action. It was therefore essential to copy the MHRA to the letter so that it could see the content and enforce the correct application of the law and the circumvention of the protection afforded to Proveca's product. The third option was to bring a case before the court in order to enforce the protection afforded to the product under the terms of its marketing authorisation and PUMA designation. Therefore, copying the MHRA was for consistency with Proveca's communications and for Proveca to reserve its right to seek damages against offenders at court, being able to transparently show all the relevant steps it took before legal action.

Secondly, Proveca wished to distinguish the present set of circumstances from the ruling in Case AUTH/2971/8/17. In Case AUTH/2971/8/17, the letter at issue implied that the MHRA had endorsed this approach and would take action against recipients and the Panel had taken a similar interpretation on Proveca's letter. However, in Case AUTH/2971/8/17 the letter misleadingly implied that the MHRA would take action against the recipient of the letter, a food supplement distributor which in fact was outside the remit of the MHRA. On the contrary, human medicinal products such as in the present case fell within the remit of the MHRA's jurisdiction. Proveca only sent the letters after contacting the MHRA about the situation and never implied that the MHRA reviewed, approved or endorsed the letters, which besides was something that the MHRA explicitly never did so this would not be possible in any event. Rather, the letter was a courtesy note before Proveca could report this practice and related pharmacies to the MHRA and offer them the opportunity to revisit any potential illegitimate dispensing practices. The MHRA had been consulted about the intended use of 'cease and desist letters' and agreed with the appropriateness of such an approach.

Clause 9.1

Proveca submitted that it disagreed with the Panel's ruling, which was regrettable given the professional way in which Proveca attempted to address a potential serious breach of the law by courteously informing the recipients of the letter of the legal framework applicable to off-label and unlicensed medicines and the existence of a licensed product instead of engaging in contentious practices.

Proveca submitted that the letter was targeted specifically at pharmacists and dispensers of medicinal products, who were presumed to have a certain level of knowledge and expertise in the rules of what products to dispense. The letters were never aimed at or provided to the general public. Therefore, anyone receiving the letter would understand the basis of Proveca's information, rather than, as the Panel held, have felt 'threatened', which might be arguable for a member of the general public with no understanding of the applicable rule and its obligations. The content and tone of the letter was informative, with references to EU and UK legislation, jurisprudence and guidance in order to convey an accurate and complete picture of the applicable framework.

Proveca submitted that the letter addressed professional, sophisticated readers and addressed them in an appropriate tone, without any attempt of concealed promotion or with a 'threatening' manner. It was important to explain the consequences of non-compliance with the law. A company striving to uphold the law, as established by the authorities and the courts, was one which aimed to maintain the high standards of the industry and did not accept their compromise resulting from the uncontrolled supply of unlicensed product, which was the case when there was no specific request for a Special or off-label product by a health professional who had identified a patient need. This was also supported by ABPI and EFPIA, the pharmaceutical industry bodies. Under all circumstances Proveca's conduct was in accordance with the industry's expected high standards, in order to ensure that these very standards were observed by all parties.

Clause 2

Proveca noted that the Panel was '... very concerned about the content and tone of the letter ...', which, in the Panel's view, was threatening. The Panel noted that the misleading implication that patients could be switched without any consideration of their clinical circumstances might potentially prejudice patient safety. The Panel was particularly concerned that a health professional '... who had received the letter would be very concerned by the misleading implication that his/her **prescribing decision** was potentially illegal. The tone of the promotional letter could be seen as threatening and, in the Panel's view, brought discredit upon, and reduced confidence in, the pharmaceutical industry'.

Proveca disputed the Panel's rulings and submitted that the factual basis was incorrect. The letter was not directed or addressed to prescribers but to pharmacists and manufacturers of Specials. As already explained the letter neither stated that dispensing Specials was *per se* an illegitimate practice nor did it seek to threaten the recipient. Instead, and as explained above in further detail, Proveca stated the law and in particular the conditions under which a Special might be dispensed and explained to the Panel when a patient need might arise.

Proveca submitted that the letter was informational in tone and regretted the fact that it had been perceived by a few recipients as 'threatening'. On the contrary, most of the correspondence that Proveca received following its letter was positive or neutral, with many recipients thanking Proveca for bringing this information to their attention. The overwhelmingly higher number of such positive/neutral responses 67, compared to the six negative responses and the two complaints, indicated that the communication was perceived by the majority as intended, namely as informational in nature. The attempt by a commercial entity to seek to settle a disagreement by way of correspondence, especially when the disagreement concerned potentially illegal action before resorting to other means, was an honourable practice and not one which could be seen as bringing discredit upon the pharmaceutical industry.

Moreover, Proveca submitted that a recipient who only supplied and/or dispensed unlicensed glycopyrronium bromide when supported by a health professional's unsolicited request for a Special or off-label product in respect of a specific patient need would have no reason to feel threatened upon reading the letter. The letter explicitly stated that a prescription specifically written for an off-label or unlicensed product (where there was a legitimate patient special need) was recognised as a valid reason for providing an off-label or unlicensed medicine instead of the licensed product (e.g. Sialanar). Proveca did not see how a letter setting out the applicable legal framework in a factual and objective manner brought discredit upon and reduced confidence in the industry, especially having regard to the correspondence received by Proveca expressing gratitude for this crucial information. Once a pharmacist was fully informed of the applicable legal framework, he/she could decide whether his/her practice was in line with the applicable rules. It seemed that engaging in a dialogue with potential infringers was the appropriate approach which, to restate, was only undertaken after speaking with the MHRA.

Proveca did not agree with the Panel's rulings that the '... misleading implication that patients could be switched without any consideration of their clinical circumstances might potentially prejudice patient safety'. Firstly, this was a mischaracterisation of Proveca's position by the Panel. Proveca never argued in favour of switching, but only provided information in the event that a pharmacist did not prescribe a licensed product in response to a generic prescription not specifying concentration, formulation or a special need. In the event of uncertainty, the pharmacist was under an obligation to communicate with the prescriber to identify his/her concern and clarify the subject matter of the prescription. This was vastly different from 'switching'.

Proveca submitted that its product was the only approved product for this indication, with a *per se* established safety profile and the only one which might be lawfully dispensed, unless the prescriber requested otherwise, and this would only arise, in very limited cases, on grounds of patient needs. The concern that Sialanar was less safe than unlicensed preparations was never raised by any complainant and did not make sense considering the licensed nature of Sialanar for the age group and indication. In fact, as evidenced in Case AUTH/3060/8/18, one of the complainant's primary concerns was that '... making the switch would pose **an additional cost burden** on the NHS', without any reference to the switch impacting on patient safety. So, the primary and unique concern expressed by the complainant altered to be financial rather than a safety issue. In fact, refusing to provide the licensed product on costs grounds was both an irrelevant consideration to the present matter and had been explicitly held by the European Court in *Commission v Poland* and by the MHRA in its Guidance Note 14 and by the ABPI itself (as set out above) not to be a valid reason for providing Specials. Once there was a prescription for glycopyrronium bromide, the NHS would pay the standard price cited in the formulary;

the precise profit margin for a dispenser would then depend on the price of the product actually supplied. This should not influence what product was supplied, especially if tilting the position in favour of unlicensed products, in the absence of a clinical need. This confirmed the exact concern that was raised in Proveca's letter in order to inform any recipients who might not be aware of this legal consideration. On the contrary, Proveca stated in its letter that providing Specials instead of Sialanar was acceptable on clinical grounds only; therefore, the Panel's statement that Proveca argued in favour of 'switching without any consideration of the [patients'] clinical circumstances' was simply incorrect.

Proveca did not see how bringing all this information to the recipients' attention brought discredit to the profession, when in fact it had the effect of enabling them to understand the legal limitations and ensure that the supply of medicinal product was conducted in accordance with the applicable legislation. The reference to the decision in Case AUTH/2971/8/17 was inappropriate as in that case the letter misled the recipient about the licensed indications, whereas in the current case Proveca referred specifically to the target indication (excessive sialorrhoea) and patient population (paediatric population) covered by Sialanar's licence. No particular special need for providing unlicensed glycopyrronium bromide on such a wide scale had been evidenced in the case of Proveca.

Overarching reasons to uphold the appeal against the Panel's decision

Proveca submitted that in addition to all the above it was also concerned that the Panel's ruling, had a potential detrimental effect on the patient's safety and clearly undermined the appropriate application of the pharmaceutical legal framework.

Proveca submitted that the Panel did not refer anywhere to the fact that the guidance cited by Proveca was all factually accurate. The letter did not promote Sialanar and all the information was an accurate and objective characterisation of the legal framework. In addition, it was obvious that despite and after Proveca's letter setting out the law, the complainant still thought that it should be entitled to disregard the law for financial considerations (eg, cost burden on the NHS). The direct result of penalising a company for bringing potential breaches of the law to the attention of the other party, was a blatant misapplication of the existing legal framework, which was established to protect public health and safeguard the proprietary rights of the pharmaceutical industry. Within this context, the Panel had not given due consideration to the surrounding circumstances, which had resulted in an unjust ruling, both for Proveca and for the pharmaceutical industry which was rendered incapable of taking action to safeguard its rights in a non-invasive, non-contentious manner. The detailed provisions in the Code aimed to ensure that pharmaceutical companies operated in a responsible, ethical and professional manner and the promotion of medicines to health professionals

and other relevant decision makers was carried out within a robust framework to support high quality patient care. In addition, Clause 1.1 of the Constitution and Procedure stated that the Panel was also responsible for arranging for conciliation between companies when requested to do so.

Proveca stated that in its letter, abided by these principles, aimed peacefully to resolve its disagreement of a practice in order to ensure that off-label and unlicensed products were not provided without a justification, thus possibly compromising the high patient care standards afforded by the marketing authorisation procedure. Observance of the established rules in fact increased confidence in the pharmaceutical industry that the law would be observed and that members of the industry would be monitoring compliance and identifying any possible deviations from the rules.

Proveca submitted that the Panel's ruling as it stood was perverse and provided no recourse outside of litigation or referral to the regulatory authorities to a company which had invested in research and development in getting its medicine approved, especially when it was the only such product on the market and approved for the paediatric population. This decision left no recourse to members of the pharmaceutical industry wishing to safeguard their proprietary rights. Letters, informative in tone, sent to the impacted parties, as discussed with the MHRA before formally reporting suspected wrongdoing to the MHRA, for further action where appropriate, were the most straightforward way for a company to ensure that the applicable rules were observed without involving an enforcement authority. The Panel's ruling effectively deprived pharmaceutical companies of ways to ensure that the legal rules in place to protect their investment in R&D were observed. Moreover, this ruling appeared to support pharmacists and Specials manufacturers which would be infringing the legal framework with impunity.

For the reasons expressed above, Proveca vigorously refuted the Panel's ruling that the content of the letter was in breach of Clauses 2, 8.2, 9.1 and 9.5 of the Code nor did Proveca agree that the message had any other effect beyond informing the recipient of a potentially illegitimate practice.

RESPONSE FROM THE COMPLAINANT

The complainants alleged that the tone and sentiment of this issue of supply of an unlicensed and off-label medicine as expressed in the appeal was more in keeping with how they would have wished it to be communicated, as opposed to the way it was actually written in the letter at issue.

Though the complainants did not have the data they alleged that it was not pharmacists and their prerogative that resulted in an unlicensed medicine being chosen, rather the dispenser was responding to a prescription for a liquid formulation that was of a different strength or formulation to Sialanar. Hence if there was little change in Sialanar prescribing since the March 2018, then Proveca should have

concentrated on communicating with prescribers rather than being aggressive with dispensers.

Though Proveca stated the letter was sent to pharmacies, the complainants alleged that they knew that it was also sent to dispensing doctors and so would have been seen by prescribers and not just dispensing pharmacists or dispensers.

The complainants repeated the initial complaint regarding the relevant clauses in that the letter did read 'Therefore, the provision of unlicensed glycopyrronium bromide preparations for children with chronic drooling when Sialanar is the only available, authorised medicinal product in the UK for that paediatric population is in breach of the law.' and 'We respectfully request that you cease these activities immediately ...'.

The complainants disagreed with the appeal that the letter was professionally written and courteous when it also stated '... please consider this letter as officially putting you on notice for illegitimate dispensing practices...' the complainants alleged this was threatening especially as the remainder of that sentence referred to '... significant commercial and financial damage to Proveca'.

The complainant alleged that the appeal was not warranted.

APPEAL BOARD RULING

The Appeal Board noted that prior to the launch of Sialanar in the UK in February 2017, paediatric patients with chronic pathological drooling due to chronic neurological disorders were treated with off-label glycopyrronium bromide products or specials. The Appeal Board noted Proveca's submission that by December 2017, Sialanar's market share of the glycopyrronium bromide paediatric market was only 5% and the company considered that this was due to pharmacists continuing to dispense off label glycopyrronium bromide or specials. The Appeal Board noted that pharmacists would be dispensing prescriptions written by GPs, hospital doctors etc. What was dispensed would depend on what was written on the prescription. It noted the company's position that most of the prescribing was written for the generic medicine and unless features were specified that were not met by Sialanar, such as a different strength or formulation, then Sialanar should be dispensed.

The Appeal Board noted Proveca's submission about its telephone conversation with the MHRA in September 2017. According to Proveca, the MHRA confirmed that although it did not get involved in cease and desist letters, it knew that companies had sent them, reference was made to the MHRA guidance note 14 and it was agreed that a cease and desist letter would be the first step. Consequently, Proveca sent a letter to pharmacists in March 2018 which set out the legal framework for prescribing in relation to Sialanar and unlicensed and off-label glycopyrronium bromide products. Proveca submitted that this letter had had no effect and so the company sent a second letter, the letter at issue,

on 10 August. The MHRA was sent one copy of the letter at issue on 17 August. The Appeal Board noted that the content and tone of the second letter was markedly different to the letter sent in March.

The Appeal Board noted that the letter at issue was sent to 16,154 UK pharmacies, primarily consisting of community pharmacists and hospital outpatients pharmacists. The Appeal Board noted from the Proveca representatives at the appeal that the letters were sent in envelopes which were personally addressed to named individuals whose details were obtained from a database. Each letter started 'Dear Sir/Madam' and included 'Copy sent to the Medicines Healthcare products Regulatory Authority'. In the Appeal Board's view as the letters were sent to named individuals, recipients would probably assume that their individual letter had been specifically highlighted to the MHRA. There was no indication to the recipient that the letter at issue had been sent to over 16,000 pharmacies.

The Appeal Board noted that recipients were asked to confirm via email to Proveca that they had ceased such activities.

The Appeal Board noted the content of the letter including the references to breaching the pharmaceutical legal framework and breaches of the law. In the Appeal Board's view, there was also an implication that a claim for damages might ensue.

The Appeal Board was concerned about the tone of the letter in question and, in that regard, it noted that the complainant and five of the six negative responses from recipients to the letter in question, provided by Proveca, stated that they found it to be threatening.

The Appeal Board noted that there was a difference between writing to all pharmacies as opposed to those whose dispensing was the subject of Proveca's concern. The Appeal Board noted the company's submission that it had chosen to send the letter to all pharmacies as it did not consider that it was possible for the company to identify which were dispensing glycopyrronium bromide off-licence or as specials. The Appeal Board questioned if this was an acceptable approach. This was compounded by the fact that the treatment of chronic pathological drooling in paediatric patients with chronic neurological disorders was likely to be a niche area and the majority of pharmacists on the mailing list would not be dispensing glycopyrronium bromide products for paediatric use.

The Appeal Board noted that it was not necessarily unacceptable to draw the attention of pharmacists to the legal framework, however, such material had to comply with the Code. The Appeal Board queried the company's submission at the appeal that the letter in question was an essential step if it wished to pursue court action. In the Appeal Board's view, a *bona fide* letter before action would be sent solely to those individuals whose dispensing was the subject of concern and would certainly not bear prescribing information. The Appeal Board, therefore, did not accept Proveca's submission that upholding

the Panel's decisions would have dangerous consequences and prevent companies from enforcing the law and protecting their rights. The Appeal Board understood the company's position. It was the content and tone of the letter that was the issue for consideration not the principle that a letter had been written to address the commercial situation.

The Appeal Board considered that the letter in question which bore prescribing information was clearly promotional and it queried how Proveca could consider it to be anything else.

The Appeal Board noted the complainant's concern that pharmacies and dispensaries in surgeries were being disparaged for dispensing what was prescribed by other health professionals such as GPs hospital doctors etc. The Appeal Board noted that whilst the letter in question did deal with some of the exceptions, overall the letter implied that supplying off label glycopyrronium bromide or a special rather than Sialanar would always be in breach of UK law which was not so. The Appeal Board noted, as acknowledged by Proveca, that the supply of an unlicensed medicine was legally permissible in certain circumstances where there was a patient with a 'special need'.

The Appeal Board considered that the letter in question implied that pharmacists did not know the legal requirements regarding the dispensing of specials. The Appeal Board further noted the negative responses received from at least six recipients of the letter at issue. It appeared that the recipients considered that the content of the letter at issue was such that it questioned the reader's professional judgement. In the Appeal Board's view, the content and tone of the letter was such that it disparaged the professional opinion of health professionals and it upheld the Panel's ruling of a breach of Clause 8.2. The appeal on this point was unsuccessful.

The Appeal Board noted that Clause 9.5 stated that promotional material must not include any reference to, *inter alia*, the Medicines and Healthcare products Regulatory Agency, unless this was specifically required by the licensing authority. The exception in the relevant supplementary information in relation to factual safety information and the MHRA Drug Safety Update did not apply to the letter at issue. The Appeal Board noted that the letter in question referred to the MHRA's Guidance Note 14 on the supply of unlicensed medicinal products (specials) and the hierarchy for the use of unlicensed medicines, an appendix to this guidance note. The letter in question stated that Proveca had brought the dispensing practices at issue to the attention of the MHRA which was copied into the letter, albeit 7 days after it had been sent. In the Appeal Board's view, the implication was that the MHRA approved or otherwise endorsed the content of the letter. The Appeal Board did not consider that Proveca's account of the conversation between it and the MHRA in September 2017 meant that the wording in the letter in question was specifically required by the MHRA as stated in Clause 9.5 and thus it upheld the Panel's

ruling of a breach of that Clause. The appeal on this point was unsuccessful.

The Appeal Board noted its comments and rulings above and considered that Proveca had failed to maintain high standards and it upheld the Panel's ruling of a breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board considered that pharmacists who had received the letter would be very concerned by the misleading implication that his/her dispensing practices were potentially illegal and that legal consequences including an implication that a claim for financial damages might ensue. The Appeal Board noted that the majority of the recipients of the letter would not have dispensed glycopyrronium bromide. The tone of the promotional letter could be seen as threatening and, in the Appeal Board's view, brought discredit upon, and reduced confidence in, the pharmaceutical industry. The Appeal Board upheld the Panel's ruling of a breach of Clause 2. The appeal on this point was unsuccessful.

Case AUTH/3060/8/18

COMPLAINT

The complainant stated that he/she had received a letter from Proveca asking that the dispensing of an unlicensed product should cease when there was a licensed alternative available. The prescription originated from a secondary care consultant and was a historic one. The complainant stated that the crux of his/her complaint was that the tone of the letter was quite threatening; it had been copied to the MHRA and alleged that illegitimate dispensing practices were being followed.

The complainant had had a discussion with colleagues at a local surgery about the issues surrounding the letter to remedy any issues following clinical review from a local GP. The complainant alleged that the letter was unnecessarily threatening towards the pharmacy and making the switch would pose an additional cost burden on the NHS. An additional concern was that the original prescriptions were initiated in secondary care so there might be clinical reasons for prescribing the original unlicensed special. The complainant had sought clarification from a local primary care clinician who would hopefully feedback at the appropriate time.

When writing to Proveca, the Authority asked it to consider the requirements of Clauses 9.1 and 2.

RESPONSE

Proveca submitted that it was a small independent pharmaceutical company which specialised in the development and licensing of off-patent medicines through the paediatric – use marketing authorization (PUMA) regulatory route. The law and guidelines from the MHRA were very clear as to when an off-licensed medicine could be dispensed to patients. It was not the prerogative of the pharmacists to choose an unlicensed medicine where a licensed alternative

existed. It was the prerogative of the health practitioner in accordance with the law. Proveca stated that it had noted this in an earlier letter of March 2018 which resulted in very little change in practice. Rather than considering legal action, the company thus sent the letter in question to reiterate the position as a courtesy to the pharmacists.

Proveca noted that the complainant considered the letter in question to be threatening in tone. Proveca submitted that the letter at issue was intended to inform all pharmacists of the licensed status of Sialanar and the legal requirement for the dispensing and supply of unlicensed products. Proveca stated that the MHRA agreed with its proposal to write to pharmacists to remind them of their legal obligations with a 'cease and desist' letter. If this was not successful, the MHRA suggested that the company get back in touch to see how the Agency might be further involved. Despite the March 2018 letter informing pharmacists that there was now a licensed product available, significant off-label and unlicensed dispensing of glycopyrronium bromide continued to be widespread for children with chronic drooling. Proveca took legal advice to ensure its communications were aligned with UK law and sent the letter at issue to remind pharmacists of their obligations around supply of unlicensed medicines.

Proveca explained that it was only by a narrowly drawn exemption expressed in Article 5(1) of Directive 2001/83/EC, implemented in the UK Regulation 167 of the Human Medicines Regulations 2012 (SI/2012/1916), that the supply of an unlicensed drug was legally permissible. This was where a patient had a 'special need' ie where there was no other available licensed medicine and a company received a *bona fide* unsolicited request from a prescriber for a specific individual patient.

Proveca noted that where there was a prescription for an unlicensed product it had not suggested that it was not dispensed; if there was a *bona fide* reason for the prescription this was the prescriber's prerogative.

Proveca submitted that several pharmacists had emailed the company following receipt of the letter. In total 65 emails had been received; 59 confirmed receipt of the letter, advising the company of actions taken and/or thanking it for the information; 6 expressed some level of concern at the letter but acknowledged its content. Proveca had met with or called everyone who contacted it. The overwhelming response to the calls was that, now they were aware of their obligations, the pharmacist was keen to comply with the law and move away from dispensing specials in situations where their use was not warranted, justified or prescribed by a health professional. Some pharmacists stated that the communication had been helpful in allowing them to ensure good governance. Proveca denied a breach of Clause 2.

With regard to high standards, Proveca submitted that the letter at issue was professionally written and courteous. It provided, in a clear and comprehensive manner, the legal position which it appreciated

pharmacists might not be familiar with. The company denied a breach of Clause 9.1.

FURTHER INFORMATION FROM PROVECA

In response to a request for further information Proveca provided details of a telephone call with the MHRA in September 2017, which consisted of a short discussion around the extent of the MHRA's involvement in cease and desist letters sent by companies. The MHRA explained that whilst the MHRA was not involved in the issue or drafting of cease and desist letters (and therefore had no templates or examples to share), it was aware of this practice by companies sending such letters referring to MHRA Guidance Note 14. Proveca suggested drafting a letter along these lines and the MHRA agreed. Proveca considered reference to the relevant guidance crucial for informing the recipients of the applicable rules and their obligations by reference to national guidance, instead of risking being perceived as suggesting its own rules and interpretation of the applicable framework. Proveca considered this an objective and factual reference to the applicable national rules and in line with the informative tone that it sought to adopt.

According to Proveca, the MHRA suggested that once Proveca had taken a number of steps, including a cease and desist letter, to remedy the situation it considered wrong, it could then contact the MHRA explaining the position and the steps that Proveca had taken, so that the MHRA could then take a view on whether there was scope for the Agency's involvement.

Proveca submitted that it was clear that it could not have consulted the MHRA more specifically about the letter, seeking any pre-approval, and Proveca did not consider it appropriate to take up the Agency's time considering that they did not issue such letters. Proveca submitted, however, that it did promptly send copies of the finalised letter to the MHRA. No comments or correspondence were received from the MHRA in response to the letter.

The MHRA responded to a pharmacist who complained about the letter that it was not an enforcement matter and it would be handled by either the regulatory affairs or customer services teams, if appropriate.

Whilst the MHRA suggested that Proveca contact the Agency if its approach was unsuccessful, Proveca wished to exhaust all possible avenues of informing the concerned parties of the illegitimacy of the specials dispensing practice without justification, before involving the Agency. Given the recency of the letters sent by Proveca, Proveca wanted to wait for an appropriate time to elapse in order to assess the success of its effort to inform pharmacists.

Proveca provided anonymised copies of the 6 emails setting out concerns following receipt of the letter at issue. Proveca also provided a copy of the letter that it sent to pharmacists in March 2018 informing them of the existence of a licensed product. No responses to this letter were provided.

Proveca considered that it might be suitable to prescribe an unlicensed product instead of Sialanar when:

- the concentration of Sialanar was too low and a much lower volume of product would be required (provided by a higher concentration of special eg 5mg/5ml). This would be unusual but there could be the rare occasion.
- The child had an allergy to one of the excipients of Sialanar, where a special might exclude the excipient. Again, this would be highly unlikely since Sialanar contained very few ingredients. The lack of such ingredient would need to be assured in the special formulation.

PANEL RULING

The Panel noted that the letter urged pharmacies to refrain from dispensing glycopyrronium bromide 'specials', and off-license preparations for children with chronic drooling and ensure that Sialanar was dispensed. The letter in question stated Sialanar's licensed indication in the second paragraph on the first page, namely that it was the only product licensed in the UK for the symptomatic treatment of severe drooling in the paediatric population (children aged 3 - 17 years).

The Panel noted that the letter in question was promotional and bore prescribing information. The Panel noted that it was not necessarily unacceptable to draw the attention of prescribers to the prescribing legal framework, however such material had to comply with the Code. In the Panel's view there was a difference between writing to all pharmacists as opposed to those whose dispensing was the subject of Proveca's concern. The Panel noted the company's submission that it was not possible for the company to know which pharmacists were dispensing glycopyrronium bromide.

The Panel noted the complainant's submission that the original prescriptions were initiated in secondary care so there might be clinical reasons for prescribing the original unlicensed special.

The Panel noted that Clause 8.2 stated that health professions and the clinical and scientific opinions of health professionals must not be disparaged. Paragraph 2.2 of the MHRA guidance on 'The supply of unlicensed medicinal products ("specials")' allowed a doctor, dentist, nurse independent prescriber, pharmacist independent prescriber or other prescriber to decide whether an unlicensed medicine should be supplied in preference to a licensed medicine where the licensed product could not meet an individual patient's special needs. The Panel noted that the letter highlighted that any pharmacy continuing to dispense unlicensed and off-label preparations for children was in breach of the pharmaceutical legal framework. The Panel noted Proveca's response that if there was a *bona fide* reason for the prescription of an unlicensed product then it was the prerogative of the prescriber and Proveca was not suggesting that it was not dispensed.

The Panel noted Proveca's submission that it might be suitable to prescribe an unlicensed product instead of Sialanar when the concentration of Sialanar (2mg/5ml) was too low and a much lower volume of product would be required (provided by a higher concentration of special eg 5mg/5ml). However, the Panel considered that the letter in question misleadingly implied that the activity was illegal by stating that if a pharmacy was supplying unlicensed or off-label preparations of glycopyrronium bromide for the indication of chronic drooling in paediatric patients then it should consider the letter as officially putting it on notice for illegitimate dispensing practices which might be a contravention of legally established rights and have caused Proveca significant commercial and financial damage. The Panel noted, as acknowledged by Proveca, that the supply of an unlicensed medicine was legally permissible in certain circumstances where there was a patient with a 'special need'. The Panel considered that the letter in question queried the health professional's decision to prescribe a special and the pharmacist's action of dispensing against a prescription, without any knowledge of the clinical circumstances, stating that such a decision was inconsistent with MHRA Guidance and law and implying that serious consequences could ensue. The Panel noted that the letter in question stated that Proveca had brought the dispensing practice at issue to the attention of the MHRA which was copied into the letter. In the Panel's view the implication was that the MHRA approved of or otherwise endorsed the content of the letter which was not so. The Panel further noted the negative responses received from at least six recipients of the letter at issue. It appeared that the recipients considered that the content of the letter was such that it was threatening and questioned the reader's professional judgement. In the Panel's view Proveca had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel considered that the letter in question queried a health professional's decision to prescribe a special and the pharmacist's action of dispensing against a prescription, without any knowledge of the clinical circumstances which in the Panel's view might potentially put patient safety at risk. The letter stated that such a decision was inconsistent with MHRA Guidance and law and implied that serious consequences could ensue if the letter was not adhered to. The Panel was very concerned about the content and tone of the letter and noted its comments and rulings above. In the Panel's view, pharmacists who had received the letter would be very concerned by the misleading implication that his/her dispensing practices were potentially illegal and that legal consequences including an implication that a claim for financial damages might ensue. The Panel noted that not all recipients of the letter would have dispensed glycopyrronium bromide. The tone of the promotional letter could be seen as threatening and, in the Panel's view, brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel noted its ruling of a breach of Clause 2 which would mean that brief details of the case would be the subject of an advertisement. The

Panel therefore decided on balance taking all the circumstances into account not to report Proveca to the Appeal Board for it to consider in accordance with Paragraph 8.2 of the Constitution and Procedure.

During its consideration of these cases, the Panel noted that the promotional letter at issue stated that not only is it not allowed to dispense an unlicensed medicine where there is a licensed alternative, but a licensed product should be the preferred option for other indications outside of its marketing authorization given it had already been assessed for safety and efficacy. The Panel queried whether this was in line with Clause 3.2 and asked that Proveca be advised of its concerns.

APPEAL BY PROVECA

Proveca submitted that the Panel had misunderstood and mischaracterised what the letter in question was saying, to whom it was addressed and why; in doing so it has erroneously concluded that Proveca was in breach of Clause 2 and 9.1.

Proveca submitted that firstly, the letter in question concerned the application and operation of the applicable legal framework concerning Specials and off-label products. It was informative in nature and aimed to enable the pharmacists and manufacturers of Specials to assess whether they were in compliance when dispensing a product without an identified special need in the prescription. At no point did the letter either 'queried a health professional's decision to prescribe a special and the pharmacist's action of dispensing against a prescription ...' or that any supply of off-label or unlicensed products was illegal as the Panel mistakenly stated. Secondly, Proveca submitted that the letter was addressed to dispensers and not prescribers. Proveca did not discuss, let alone challenge the clinical assessment or scientific opinion conducted by a health professional about the treatment of a patient. The clinical judgment of the recipient was never at stake; on the contrary, the letter clearly stated that prescribers could decide to prescribe a Special (or off-label product) to a particular patient if the health professional considered that there was a specific patient need. Thirdly, Proveca submitted that the parallel drawn with Case AUTH/2971/8/17 was inappropriate, as the present case differed on a number of significant grounds, such as that (a) the MHRA was not the competent authority and its involvement was entirely mischaracterised in Case AUTH/2971/8/17, as opposed to the present case in which the MHRA were consulted by Proveca about the general situation and (b) in Case AUTH/2971/8/17 the letter at issue misled the recipient about the licensed indication.

Proveca submitted that it was an innovative company with micro SME status that was engaged in the development and licensing of medicinal products for the paediatric population with chronic and life-limiting conditions. Proveca's product, Sialanar, was the only oral glycopyrronium product licensed for children on the UK market and the only one

licensed for severe chronic drooling. Sialanar was first launched in the UK in February 2017, and prior to its approval, the needs of the market were fulfilled by off-label and unlicensed glycopyrronium bromide products within the 'Specials' legal framework. By December 2017, Sialanar's market penetration was very limited and accounted for less than 5% of the paediatric market compared to unlicensed and off-label oral glycopyrronium bromide.

Proveca noted that it had become aware of a disproportionately high supply of off-label and unlicensed products compared to its own licensed product, due to its limited market share. This discrepancy could neither be justified nor explained on medical or clinical grounds for preferring unlicensed products in the vast majority of cases. This would only be the case where Sialanar was contraindicated as a result of its excipients or where a significantly different concentration leading to a much lower volume was required. Currently there was no evidence of a patient need on the market in respect of glycopyrronium bromide for the licensed indication in children. Considering that there was no shortage of supply of Sialanar, it was obvious that at least some of the off-label and unlicensed products were dispensed outside of the strict conditions established by the applicable legal framework; including the legal framework applicable to the dispensing and supply of Specials.

Upon becoming aware of the extent of the widespread supply of off-label and unlicensed glycopyrronium bromide products, Proveca in the first instance sought to discuss this with the MHRA on a general basis. The MHRA agreed with Proveca approaching the potentially infringing specials manufacturers and pharmacists to explain the rules around off-label and unlicensed supply and to inform them that there was now a licensed glycopyrronium bromide product available to treat severe sialorrhoea in the paediatric population. Proveca was told by the MHRA that if the recommended approach was unsuccessful, it should contact the MHRA again and it would assess whether Proveca should take action.

The issue that Proveca wanted to raise was in the event where the prescription did not specify the product form and/or strength, in which case it was up to the pharmacist to determine what to dispense in order to fulfil the prescription. The legal framework imposed on the pharmacist the obligation to dispense the licensed product, unless there were evidenced medical grounds to dispense an unlicensed or off-label product. With variability in the preparation of Specials and the lack of any regulatory oversight on unlicensed products, there were serious public health concerns that had led to the established legal framework. This was precisely what Proveca wanted to ensure was brought to the pharmacists' and specials manufacturers' attention. Therefore, Proveca submitted that it had written to pharmacists and specials manufacturers alike to inform them that a licensed product was now available and reminding them about the legal framework applicable to Specials, in a balanced and proportionate manner.

Clause 9.1

Proveca submitted that it disagreed with the Panel's finding, which was regrettable given the professional way in which Proveca attempted to address a potential serious breach of the law by courteously informing the recipients of the letter of the legal framework applicable to off-label and unlicensed medicines and the existence of a licensed product instead of engaging in contentious practices. The letter ensured that pharmacists and Specials manufacturers were aware of the legal framework under which they must operate and could assess their compliance under legal, rather than scientific or clinical principles.

All the statements that Proveca had made about the appropriateness of Sialanar for paediatric patients with excessive sialorrhoea were accurate, balanced, fair and capable of substantiation. Proveca provided all the relevant references so that the pharmacists and Specials manufacturers would be able to confirm the validity of the information and determine whether their supply practice of Specials was compliant with the applicable legal framework. The benefit of this correspondence rather than resolving to take immediate legal action was illustrated by the positive responses that Proveca received from some recipients of the letters, thanking Proveca for bringing this information to their attention. A selection of the correspondence was quoted. Those confirmed that Proveca helped the recipients to ensure that their dispensing activities were in accordance with the law.

Further, Proveca submitted that in this context, it was also important to note that the content of the letter was in line with the views publicly expressed by the ABPI and EFPIA on the matters of prescription of products without a licence in respect of the intended indication.

Proveca submitted that the ABPI's position regarding the use of unlicensed medicines was set out in a press release that it issued in May 2012. The press release stated that the '... health and safety of UK patients should always be paramount, and all other considerations, including cost, must be secondary'. In the statement, the ABPI reiterated that use of unlicensed medicines put patients at risk and should be strictly limited to those occasions where there was no licensed alternative. Proveca's position as expressed in the letter supported and reiterated this point.

In addition, in March 2017 EFPIA made some statements on off-label supply, which applied equally and directly to the supply of unlicensed products beyond the special needs' exemption. Commenting on the European Commission's study report on off-label use, EFPIA stated that:

'Indeed, pharmaceutical companies may be less ready to invest in costly and lengthy clinical development and authorisation processes for a given indication if public authorities promote the use of cheaper off-label medicines that have not been subject to the same stringent safety and efficacy assessments as existing on-label medicines, for financial reasons.'

Proveca submitted that these public positions indicated that the ABPI and EFPIA considered that supply of a medicine for an indication for which it was not licensed, contained many risks, ranging from public health to reduction in investment and compromise of the regulatory system, resulting in uncertainties and the undermining of the pharmaceutical industry. These considerations were present in and directly applicable to the situation that Proveca had been facing and in line with the approach Proveca had taken to engage with the potential involuntary infringer by restating the law applicable to off-label and unlicensed medicines and informing them of the fact that there was now a licensed product available to treat those medical conditions in the paediatric population.

Proveca submitted that the letter was targeted specifically at pharmacists and dispensers of medicinal products, who were presumed to have a certain level of knowledge and expertise in the rules of what products to dispense. The letters were never aimed at or provided to the general public. Therefore, anyone receiving the letter would understand the basis of Proveca's information, rather than, as the Panel held, have felt 'threatened', which might be arguable for a member of the general public with no understanding of the applicable rule and its obligations. The content and tone of the letter was informative, with references to EU and UK legislation, jurisprudence and guidance in order to convey an accurate and complete picture of the applicable framework.

Proveca submitted that the letter addressed professional, sophisticated readers and addressed them in an appropriate tone, without any attempt of concealed promotion or with a 'threatening' manner. It was important to explain the consequences of non-compliance with the law. A company striving to uphold the law, as established by the authorities and the courts, was one which aimed to maintain the high standards of the industry and did not accept their compromise resulting from the uncontrolled supply of unlicensed product, which was the case when there was no specific request for a Special or off-label product by a health professional who had identified a patient need. This was also supported by ABPI and EFPIA. Under all circumstances Proveca's conduct was in accordance with the industry's expected high standards, in order to ensure that these very standards were observed by all parties.

Clause 2

Proveca noted that the Panel was '... very concerned about the content and tone of the letter ...', which in the Panel's view was threatening. The Panel noted that the misleading implication that patients could be switched without any consideration of their clinical circumstances might potentially prejudice patient safety. The Panel was particularly concerned that a health professional '... who had received the letter would be very concerned by the misleading implication that his/her prescribing decision was potentially illegal. The tone of the promotional letter could be seen as threatening and, in the Panel's view, brought discredit upon, and reduced confidence in, the pharmaceutical industry'.

Proveca disputed the Panel's ruling and submitted that the factual basis was incorrect. The letter was not directed or addressed to 'prescribers' but to pharmacists and manufactures of Specials. As already explained the letter neither stated that dispensing off-label or unlicensed medicines was *per se* an illegitimate practice nor did it seek to threaten the recipient. Instead, and as explained above in further detail, Proveca stated the law and in particular the conditions under which an off-label or unlicensed product might be dispensed and explained to the Panel when a patient need might arise.

Proveca submitted that the letter was informational in tone and regretted the fact that it had been perceived by a few recipients as 'threatening'. On the contrary, most of the correspondence that Proveca received following its letter was positive or neutral, with many recipients thanking Proveca for bringing this information to their attention. The overwhelmingly higher number of such positive/neutral responses, 67 compared to the 6 negative responses and the two complaints, indicated that the communication was perceived by the majority as intended, namely as informational in nature. The attempt by a commercial entity to seek to settle a disagreement by way of correspondence, especially when the disagreement concerned potentially illegal action before resorting to other means, was an honourable practice and not one which could be seen as bringing discredit upon the pharmaceutical industry.

Moreover, a recipient who only supplied and/or dispensed unlicensed glycopyrronium bromide when supported by a health professional's unsolicited request for a Special or off-label product in respect of a specific patient need would have no reason to feel threatened upon reading the letter. The letter explicitly stated that a prescription specifically written for an off-label or unlicensed product (where there was a legitimate patient special need) was recognised as a valid reason for providing an off-label or unlicensed medicine instead of the licensed product (e.g. Sialanar). Proveca did not see how a letter setting out the applicable legal framework in a factual and objective manner brought discredit and reduced confidence in the industry, especially having regard to the correspondence received by Proveca expressing gratitude for this crucial information. Once a pharmacist was fully informed of the applicable legal framework, he/she could decide whether his/her practice was in line with the applicable rules. It seemed that engaging in a dialogue with potential infringers was the appropriate approach which, to restate, was only undertaken after speaking with the MHRA. Proveca did not agree with the Panel's ruling that the '... misleading implication that patients could be switched without any consideration of their clinical circumstances might potentially prejudice patient safety'. Firstly, this was a mischaracterisation of Proveca's position by the Panel. Proveca never argued in favour of switching, but only provided information in the event that a pharmacist did not prescribe a licensed product in response to a generic prescription not specifying concentration,

formulation or a special need. In the event of uncertainty, the pharmacist was under an obligation to communicate with the prescriber to identify his/her concern and clarify the subject matter of the prescription. This was vastly different from 'switching'.

Proveca stated that its product was the only approved product for this indication, with a *per se* established safety profile and the only one which might be lawfully dispensed, unless the prescriber requested otherwise, and this would only arise, in very limited cases, on grounds of patient needs. The concern that Sialanar was less safe than unlicensed preparations was never raised by any complainant and was legally unsound considering licensed nature of Sialanar for the age group and indication. In fact, as evidenced in Case AUTH/3060/8/18, one of the complainant's primary concerns was that making the switch would pose **an additional cost burden** on the NHS, without any reference to the switch impacting on patient safety. So, the primary and unique concern expressed by the complainant seems to be financial rather than a safety issue. In fact, refusing to provide the licensed product on costs grounds was both an irrelevant consideration to the present matter and had been explicitly held by the European Court in *Commission v Poland* and by the MHRA in its Guidance Note 14 and by the ABPI itself (as set out above) not to be a valid reason for dispensing and supplying Specials. Once there was a prescription for glycopyrronium bromide, the NHS would pay the standard price cited in the formulary; the precise profit margin for a dispenser would then depend on the price of the product actually supplied. This should not influence what product was supplied, especially if tilting the position in favour of unlicensed products, in the absence of a clinical need. This confirmed the exact concern that was raised in Proveca's letter in order to inform any recipients who might not be aware of this legal consideration. On the contrary, Proveca stated in its letter that providing off-label and unlicensed glycopyrronium instead of Sialanar was acceptable on clinical grounds only; therefore, the Panel's statement that Proveca argued in favour of dispensing '... without any consideration of the [patients'] clinical circumstances' was simply incorrect.

Proveca did not see how bringing all this information to the recipients' attention brought discredit to the profession, when in fact it had the effect of enabling them to understand the legal limitations and ensure that the supply of medicinal product was conducted in accordance with the applicable legislation. The reference to Case AUTH/2971/8/17 was inappropriate as in that case the letter misled the recipient about the licensed indications, whereas Proveca referred specifically to the target indication (excessive sialorrhoea) and patient population (paediatric population) covered by Sialanar's licence. No particular special need for providing unlicensed glycopyrronium bromide on such a wide scale had been evidenced in the case of Proveca.

Overarching reasons to uphold the appeal against the Panel's decision

Proveca submitted that in addition to all the above it was also concerned that the Panel's ruling, had a potential detrimental effect on the patient's safety and clearly undermined the appropriate application of the pharmaceutical legal framework.

Proveca submitted that the Panel did not refer anywhere to the fact that the guidance cited by Proveca was all factually accurate. The letter did not promote Sialanar and all the information was an accurate and objective characterisation of the legal framework. In addition, it was obvious that despite and after Proveca's letter setting out the law, the complainant still thought that it should be entitled to disregard the law for financial considerations (e.g. cost burden on the NHS). The direct result of penalising a company for bringing potential breaches of the law to the attention of the other party was a blatant misapplication of the existing legal framework, which was established to protect public health and safeguard the proprietary rights of the pharmaceutical industry. Within this context, the Panel had not given due consideration to the surrounding circumstances, which had resulted in an unjust ruling, both for Proveca and for the pharmaceutical industry which was rendered incapable of taking action to safeguard its rights in a non-invasive, non-contentious manner.

The detailed provisions in the Code aimed to ensure that pharmaceutical companies operate in a responsible, ethical and professional manner and the promotion of medicines to health professionals and other relevant decision makers was carried out within a robust framework to support high quality patient care. In addition, Clause 1.1 of the Constitution and Procedure stated that the Panel was also responsible for arranging for conciliation between companies when requested to do so.

Proveca submitted that its letter, abided by these principles, aimed peacefully to resolve its disagreement of a practice in order to ensure that off-label and unlicensed products were not provided without a justification, thus possibly compromising the high patient care standards afforded by the marketing authorisation procedure. Observance of the established rules in fact increased confidence in the pharmaceutical industry that the law would be observed and that members of the industry would be monitoring compliance and identifying any possible deviations.

Proveca submitted that the Panel's ruling as it stood was perverse and provided no recourse outside of litigation or referral to the regulatory authorities to a company which had invested in research and development in getting its medicinal product approved, especially when it was the only such product on the market and approved for the paediatric population. This decision left no recourse to members of the pharmaceutical industry wishing to safeguard their proprietary rights. Letters, informative in tone, sent to the impacted parties, as discussed with the MHRA before formally reporting suspected wrongdoing to the MHRA, for further action, where appropriate, were the most straightforward way for a company to ensure that the

applicable rules were observed without involving an enforcement authority. The Panel's ruling effectively deprived pharmaceutical companies of ways to ensure that the legal rules in place to protect their investment in R&D were observed. Moreover, this ruling appeared to support pharmacists and Specials manufacturers who would be infringing the legal framework with impunity.

For the reasons expressed above, Proveca vigorously refuted the Panel's ruling that the content of the letter was in breach of Clauses 2 and 9.1 of the Code, as the letter's message had no other effect beyond informing the recipient of a potentially illegitimate practice.

RESPONSE FROM THE COMPLAINANT

The complainant had no comments on the appeal.

APPEAL BOARD RULING

The Appeal Board noted that prior to the launch of Sialanar in the UK in February 2017, paediatric patients with chronic pathological drooling due to chronic neurological disorders were treated with off-label glycopyrronium bromide products or specials. The Appeal Board noted Proveca's submission that by December 2017, Sialanar's market share of the glycopyrronium bromide paediatric market was only 5% and the company considered that this was due to pharmacists continuing to dispense off label glycopyrronium bromide or specials. The Appeal Board noted that pharmacists would be dispensing prescriptions written by GPs, hospital doctors etc. What was dispensed would depend on what was written on the prescription. It noted the company's position that most of the prescribing was written for the generic medicine and unless features were specified that were not met by Sialanar, such as a different strength or formulation, then Sialanar should be dispensed.

The Appeal Board noted Proveca's submission about its telephone conversation with the MHRA in September 2017. According to Proveca, the MHRA confirmed that although it did not get involved in cease and desist letters, it knew that companies had sent them, reference was made to the MHRA guidance note 14 and it was agreed that a cease and desist letter would be the first step. Consequently, Proveca sent a letter to pharmacists in March 2018 which set out the legal framework for prescribing in relation to Sialanar and unlicensed and off-label glycopyrronium bromide products. Proveca submitted that this letter had had no effect and so the company sent a second letter, the letter at issue, on 10 August. The MHRA was sent one copy of the letter at issue on 17 August. The Appeal Board noted that the content and tone of the second letter was markedly different to the letter sent in March. The Appeal Board noted that the letter at issue was sent to 16,154 UK pharmacies, primarily consisting of community pharmacists and hospital outpatients pharmacists. The Appeal Board noted from the Proveca representatives at the appeal that the letters were sent in envelopes which were personally addressed to named individuals whose

details were obtained from a database. Each letter started 'Dear Sir/Madam' and included 'Copy sent to the Medicines Healthcare products Regulatory Authority'. In the Appeal Board's view as the letters were sent to named individuals, recipients would probably assume that their individual letter had been specifically highlighted to the MHRA. There was no indication to the recipient that the letter at issue had been sent to over 16,000 pharmacies.

The Appeal Board noted that recipients were asked to confirm via email to Proveca that they had ceased such activities.

The Appeal Board noted the content of the letter including the references to breaching the pharmaceutical legal framework and breaches of the law. In the Appeal Board's view, there was also an implication that a claim for damages might ensue.

The Appeal Board was concerned about the tone of the letter in question and, in that regard, it noted that the complainant and five of the six negative responses from recipients to the letter in question, provided by Proveca, stated that they found it to be threatening.

The Appeal Board noted that there was a difference between writing to all pharmacies as opposed to those whose dispensing was the subject of Proveca's concern. The Appeal Board noted the company's submission that it had chosen to send the letter to all pharmacies as it did not consider that it was possible for the company to identify which were dispensing glycopyrronium bromide off-licence or as specials. The Appeal Board questioned if this was an acceptable approach. This was compounded by the fact that the treatment of chronic pathological drooling in paediatric patients with chronic neurological disorders was likely to be a niche area and the majority of pharmacists on the mailing list would not be dispensing glycopyrronium bromide products for paediatric use.

The Appeal Board noted that it was not necessarily unacceptable to draw the attention of pharmacists to the legal framework, however, such material had to comply with the Code. The Appeal Board queried the company's submission at the appeal that the letter in question was an essential step if it wished to pursue court action. In the Appeal Board's view, a *bona fide* letter before action would be sent solely to those individuals whose dispensing was the subject of concern and would certainly not bear prescribing information. The Appeal Board, therefore, did not accept Proveca's submission that upholding the Panel's decisions would have dangerous consequences and prevent companies from enforcing the law and protecting their rights. The Appeal Board understood the company's position.

It was the content and tone of the letter that was the issue for consideration not the principle that a letter had been written to address the commercial situation.

The Appeal Board considered that the letter in question which bore prescribing information was clearly promotional and it queried how Proveca could consider it to be anything else.

The Appeal Board noted the complainant's concern that pharmacies and dispensaries in surgeries were being disparaged for dispensing what was prescribed by other health professionals such as GPs hospital doctors etc. The Appeal Board noted that whilst the letter in question did deal with some of the exceptions, overall the letter implied that supplying off label glycopyrronium bromide or a special rather than Sialanar would always be in breach of UK law which was not so. The Appeal Board noted, as acknowledged by Proveca, that the supply of an unlicensed medicine was legally permissible in certain circumstances where there was a patient with a 'special need'.

The Appeal Board considered that the letter in question implied that pharmacists did not know the legal requirements regarding the dispensing of specials.

In the Appeal Board's view, the implication was that the MHRA approved or otherwise endorsed the content of the letter in question and that was not so.

The Appeal Board noted its comments above and considered that Proveca had failed to maintain high standards and it upheld the Panel's ruling of a breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board considered that pharmacists who had received the letter would be very concerned by the misleading implication that his/her dispensing practices were potentially illegal and that legal consequences including an implication that a claim for financial damages might ensue. The Appeal Board noted that the majority of the recipients of the letter would not have dispensed glycopyrronium bromide. The tone of the promotional letter could be seen as threatening and, in the Appeal Board's view, brought discredit upon, and reduced confidence in, the pharmaceutical industry. The Appeal Board upheld the Panel's ruling of a breach of Clause 2. The appeal on this point was unsuccessful.

Complaint received **21 August 2018**

Case completed **11 December 2018**

ANONYMOUS, NON-CONTACTABLE v LUNDBECK

Company webpage and certification of promotional material

An anonymous, non-contactable complainant, who appeared to be a Lundbeck employee, complained about the product section of the Lundbeck website and the certification of promotional materials under a co-promotion agreement with Otsuka. Lundbeck and Otsuka co-promoted Abilify Maintena (aripiprazole prolonged-release suspension for injection) which was indicated for maintenance treatment of schizophrenia in adult patients stabilised with oral aripiprazole.

The complainant alleged that the product section of the company webpage was available to all and constituted promotion to the public. Both the brand and generic names were stated and the complainant queried whether the prescribing information should have been provided. The complainant further queried what additional information had been provided to consumers to 'encourage correct usage'.

The complainant further alleged that a member of the Lundbeck medical department was responsible for Lundbeck not certifying materials correctly for the product it co-promoted with Otsuka; he/she had not realised that two signatories were required to certify items under co-promotion agreements and most of Lundbeck's promotional material since this individual was appointed had not been certified correctly and was in breach of the Code.

The detailed response from Lundbeck is given below.

The Panel noted Lundbeck's submission that the aim of the webpage in question was to provide the public with correct information about its products, including the doses where relevant, and their licensed indication. The Panel noted that the webpage in question included the medicines' brand names, non-proprietary names, dosages, formulations and indications in a tabular format. Beneath the table was a link to the electronic medicines compendium (eMC) website homepage.

The Panel considered that given the combination of the medicine's name and indication and the fact that members of the public looking for information on a particular product would see such information for all Lundbeck's products meant that the webpage advertised prescription only medicines to the public and on the balance of probabilities might encourage members of the public to ask their health professional to prescribe a specific prescription only medicine and breaches of the Code were ruled.

The Panel noted that the supplementary information to the Code stated, *inter alia*, that under co-promotion arrangements the companies concerned could agree to have only one final signatory to

certify on behalf of all the companies, however, this must be agreed beforehand and the MHRA and PMCPA must be informed in advance who the signatory would be.

The Panel considered that the time period within the scope of the complaint was from February 2017 onwards and noted that during this time a number of promotional items were certified by only one company without prior notification to the MHRA and PMCPA as required by the Code. Other promotional material, which was signed by a registered medical practitioner or a pharmacist registered in the UK from one company and a commercial person from the other, was also ruled in breach of the Code. The commercial person was no longer recognised as a final signatory under the Code and the relevant material had therefore only been certified by one company without prior notification to the MHRA and PMCPA. Consequently, the materials had not been certified in accordance with the Code and breaches were ruled.

An anonymous, non-contactable complainant, who appeared to be a Lundbeck employee, complained about the product section of the Lundbeck website and the certification of promotional materials under a co-promotion agreement with Otsuka. Lundbeck and Otsuka co-promoted Abilify Maintena (aripiprazole prolonged-release suspension for injection) which was indicated for maintenance treatment of schizophrenia in adult patients stabilised with oral aripiprazole.

1 Company webpage

COMPLAINT

The complainant alleged that the company webpage <http://www.lundbeck.com/uk/our-products/our-products> which stated 'Here you will find information that is provided to consumers on each of our Lundbeck distributed products to encourage correct usage' was available to all and constituted promotion to the general public. Both the brand and generic names were stated and the complainant queried whether the prescribing information should have been provided. The complainant further queried what additional information had been provided to consumers to 'encourage correct usage'.

When writing to Lundbeck, the Authority asked it to consider the requirements of Clauses 26.1, 26.2 and 28.3 of the Code.

RESPONSE

Lundbeck submitted that the webpage in question was compliant with Clauses 26.1 and 26.2. The

intended audience was members of the public and Lundbeck refuted the allegation that the webpage promoted to the public. Lundbeck submitted that the website provided factual and balanced information about its products. The only information provided was the brand names, any associated black triangles, the generic names, the doses and formulations, and the licensed indications. Under the product list was information about reporting of adverse events and where readers could find the summary of product characteristics (SPC) and patient information leaflets (PIL) through the electronic medicines compendium (eMC) website. Lundbeck submitted that prescribing information was not required as the purpose of the webpage was to simply inform the public and not to promote to them; as such prescribing information was neither indicated nor appropriate for the webpage in question.

Lundbeck re-iterated that its intention was to simply inform the public of correct information about its products including the doses (where relevant) and their licensed indication. Lundbeck submitted that by complying with Clause 26.2 it was also in compliance with Clause 28.3 and, furthermore, its intention was also to comply with Clause 28.5 and its supplementary information on MHRA guidance.

In response to a request for further information, Lundbeck was not able to provide the certificate and job bag summary for the webpage in question as it did not go through certification when it was last updated in 2015. Furthermore, Lundbeck submitted that a discrepancy between the company webpage and the SPCs on the eMC website for Cipramil (citalopram) and Ebixa (memantine) was due to the fact that the webpage was last updated prior to the SPC updates in 2016. Lundbeck stated that this was an unintentional error. Unfortunately, due to unexpectedly high workload and recent internal resource limitations, it was regrettable that errors had been made. Lundbeck stated that it took this very seriously and was instituting a corrective and preventative action plan and had immediately suspended its Lundbeck UK website. In the meantime, there was a holding page containing obligatory medical information and pharmacovigilance contacts and reporting details. The website would undergo review, update, amendment and certification (where appropriate eg where products were mentioned) urgently.

Lundbeck had taken steps to address its resource limitations within its medical department.

PANEL RULING

The Panel noted that Clause 26.1 prohibited the promotion of prescription only medicines to the public. Clause 26.2 permitted information about prescription only medicines to be supplied directly or indirectly to the public but such information must be factual, presented in a balanced way, must not raise unfounded hopes of successful treatment and must not encourage members of the public to ask their health professional to prescribe a specific prescription only medicine. The Panel noted that the supplementary information to Clause 26.2 required

reference information, if provided, to be, *inter alia*, up-to-date and Clause 28.3 required information on the internet covered by Clauses 28.1 and 28.2 which was intended for members of the public, to comply with Clause 26.2.

The Panel noted Lundbeck's submission that the aim of the webpage in question was to provide the public with correct information about its products, including the doses where relevant, and their licensed indication. The Panel noted that the webpage in question included the medicines' brand names, non-proprietary names, dosages, formulations and indications in a tabular format. Above the table were the statements: 'Here you will find information that is provided to consumers on each of our Lundbeck distributed products to encourage correct usage' and 'N.B The following products are licensed for the indicated treatments in the UK only'. The Panel noted that beneath the table listing Lundbeck's products was the statement 'For summary of product characteristics and patient information leaflets click here for the eMC (electronic Medicines Compendium) website'. The link took readers to the eMC homepage. In the Panel's view a patient was unlikely to be familiar with navigating the eMC website.

The Panel noted that the webpage in question listed the product names and indications for Lundbeck's prescription only medicines in one table. The Panel considered that given the combination of the medicine's name and indication and the fact that members of the public looking for information on a particular product would see such information for all Lundbeck's products meant that the webpage advertised prescription only medicines to the public and a breach of Clause 26.1 was ruled. The Panel considered that on the balance of probabilities the information might encourage members of the public to ask their health professional to prescribe a specific prescription only medicine and ruled a breach of Clause 26.2.

The Panel noted that Clause 28.3 required that information about medicines on the internet which was intended for members of the public must comply with Clause 26.2. The Panel noted its comments and rulings above and consequently ruled a breach of Clause 28.3.

2 Certification of promotional material

COMPLAINT

The complainant alleged that a member of the Lundbeck medical department applied the Code as it suited him/her and at times was 'incredibly strict' and at other times not. The complainant stated that the individual in question was responsible for Lundbeck not certifying materials correctly for the product it co-promoted with Otsuka and this information was well known throughout the organisation. The individual had not realised that two signatories were required to certify items under co-promotion agreements. The complainant alleged that most of Lundbeck's promotional material since

this individual was appointed was in breach of the Code (not certified correctly). The complainant stated that senior executives at Lundbeck were aware of the situation but did not voluntarily admit a breach to the PMCPA.

When writing to Lundbeck, the Authority asked it to consider the requirements of Clauses 14.1, 14.3 and 14.4 of the Code.

RESPONSE

Lundbeck stated that the names of its UK medical signatories who were registered with the General Medical Council (GMC) with licence to practice were provided to the PMCPA and MHRA before signatory duties were undertaken. Lundbeck submitted that the position for current material that required certification as per Clause 14.3 for the product co-promoted with Otsuka Pharmaceuticals UK was that one medical signatory from each company reviewed and certified the material in its final form prior to issue, ie two medical signatories' signatures on the certificate. Lundbeck hoped that it was evident from the information above that it was compliant with Clauses 14.1, 14.3 and 14.4. Lundbeck attached an example of a piece of current material (UK/AM/0817/0050c(2)) which had been certified by one medical signatory from Otsuka and one medical signatory from Lundbeck, which it submitted was evidence of its compliance.

In response to a request for further information from the Panel, Lundbeck submitted that the certification process for Abilify Maintena materials had undergone several changes since February 2017 due to changes in personnel within both Lundbeck and Otsuka. In April 2017, Otsuka and Lundbeck met and agreed to change the approval process to comply with the 2016 Code. The change in approval process agreed was that central and joint materials required certification from both companies' medical signatories. Internal training/briefing materials and local meeting materials (small representative meetings) organised and executed by one company required certification from one medical signatory from that respective company. In December 2017, the companies agreed to seek clarification from the PMCPA regarding whether local meetings' materials by a single company required dual company sign-off. In January 2018, a member of the Otsuka medical department confirmed verbally to Lundbeck, after consulting with the PMCPA, that all materials to be certified required certification by medical signatories from both companies. In June 2018, a memorandum of understanding for working practices between Otsuka and Lundbeck was finalised, which outlined the approval process above. Lundbeck provided a list of Abilify Maintena materials that were certified between 1 February 2017 and 17 August 2018.

Lundbeck submitted that Otsuka and Lundbeck UK operated jointly as an Alliance. Work on the memorandum of understanding on the working practices between the two companies in the UK started in January 2018 and was finalised in June 2018 and signed by a senior executive from each company. The previous Alliance joint approvals SOP

was dated 2014. Both Lundbeck and Otsuka had agreed that the 2014 SOP was not in compliance with the 2016 Code and a new approval process was agreed via email between senior executives of both companies and was implemented and operational whilst a formal SOP was drafted. The SOP was delayed due to a change of personnel in Otsuka. An amended approval process was implemented and operational from mid-December 2017. The current approvals process and procedures were covered in the memorandum of understanding, June 2018.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the PMCPA stated that anonymous complaints would be accepted but like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities.

The Panel noted that the case preparation manager raised Clause 14.3. In the Panel's view, the complaint only referred to promotional material and therefore it made no ruling with regard to Clause 14.3.

The Panel noted Lundbeck's submission that the current position with regard to certification of Abilify Maintena materials was that one medical signatory from each company in the Alliance must certify all materials that required certification under the Code.

The Panel noted the complainant's allegation that a member of the Lundbeck medical department had not realised that two signatories were required to certify items under co-promotion agreements and that most of Lundbeck's promotional material since this person was appointed was not certified correctly and was therefore in breach of the Code. The Panel noted Lundbeck's submission that the individual in question was notified to the PMCPA and MHRA as a signatory at the end of January 2017. The Panel therefore considered that the time-period within the scope of the complaint was from February 2017 onwards.

The Panel noted Lundbeck's review of its copy approval systems from February 2017 to August 2018, excluding jobs that were either: cancelled, waiting for upload, currently undergoing review or which were never used, which gave a final list of 790 Abilify Maintena materials/activities.

The Panel noted that Lundbeck provided four separate spreadsheets; 2018 Alliance job bags; 2017 Alliance job bags which included joint/central activities that Lundbeck and Otsuka had agreed required medical signatory certification by both companies; 2017 Lundbeck only job bags which included materials for local meetings or single company training sessions/briefings initiated for use by a single company and certified by one company as agreed between Lundbeck and Otsuka; and the 2017 and 2018 Lundbeck only Veeva MLR job bags.

The Panel noted that the list of Alliance 2017 job bags included 60 promotional job bags that had

been certified by only one company (only one final signatory or was certified by a commercial and medical signatory from the same company) and 18 promotional job bags that had been certified by a medical signatory from one company and a commercial signatory from the other. The Panel noted that 78 job bags were listed on the 2017 Lundbeck only Zinc job bag list and 93 job bags on the 2017 and 2018 Lundbeck only Veeva MLR job bag list. The Panel noted that the job bags in the two latter lists had only been certified by Lundbeck.

The Panel noted that in February 2017 the SOP in place with regard to Abilify materials and copy approval procedure (ref OPUK-LUN-JWP-003 V 1.0, effective from 11 February 2014) required that under co-promotion agreements, each company should certify the promotional material involved as they would be held jointly responsible for it under the Code. The SOP further stated, in a section headed final certification, that promotional materials must be certified by one Otsuka signatory and one Lundbeck signatory. In general, if the material owner was from Lundbeck then the commercial signatory should be Lundbeck and the medical Otsuka. The reverse was true if the material owner was from Otsuka.

The Panel noted that under the 2016 Code, which came into operation on 1 January 2016, Clause 14.1 stated that the person certifying material on behalf of a company must be a registered medical practitioner or a pharmacist registered in the UK. In the Panel's view, regardless of the fact that Abilify Maintena materials were being certified by a medical signatory from one company and a commercial signatory from the other, commercial signatories were no longer recognised as final signatories in Clause 14.1 of the 2016 Code and in effect materials signed off in this manner had effectively only been certified by one medical signatory and therefore one company.

The Panel noted that the supplementary information to Clause 14.1 stated, *inter alia*, that under co-promotion arrangements the companies concerned could agree to have only one final signatory to certify on behalf of all the companies, however, this must be agreed beforehand and the MHRA and PMCPA must be informed in advance who the signatory would be.

The Panel noted that Clause 14.4 required that, *inter alia*, the names of those nominated as final signatories, together with their qualifications, be notified in advance to the Advertising Standards Unit, Vigilance and Risk Management of Medicines of the MHRA and to the PMCPA. The names and qualifications of designated alternative signatories must also be given. Changes in the names of nominees must be promptly notified.

The Panel noted that a number of promotional items were certified between February 2017 and April 2017 by a final signatory from only one company without prior notification to the MHRA and PMCPA as required by the Code. The Panel thus ruled a breach of Clause 14.4. Consequently, the materials that had been certified by only one company, whose signatory had not been notified in advance to the MHRA and

PMCPA as certifying on behalf of both Lundbeck and Otsuka, had not been certified in accordance with Clause 14.1 and its supplementary information. The Panel thus ruled a breach of Clause 14.1 in relation to those materials.

The Panel noted Lundbeck's submission that in April 2017 Lundbeck and Otsuka personnel met and agreed to change the approval process to comply with the 2016 Code. The change in approval process, agreed via email by senior executives of both companies, was that central and joint materials required certification from both companies' medical signatories and internal training/briefing materials and local meeting materials (small representative meetings) organised and executed by one company only required certification from one medical signatory from that respective company. The Panel noted it was clear from the email that both companies understood that both would still be accountable for the materials certified by only one company. The Panel noted that this arrangement was not reflected in any SOP.

The Panel considered its comments and rulings above which were relevant. The Panel noted that between April 2017 and mid-December 2017, numerous Abilify Maintena promotional materials/activities were certified by only one medical signatory from either Otsuka or Lundbeck without prior notification to the MHRA and PMCPA as required by the Code. The Panel noted that its ruling of a breach of Clause 14.4 above applied here and it made no additional ruling in this regard. The Panel noted that the materials that had been certified between April 2017 and mid-December 2017 by only one company, whose signatory had not been notified in advance to the MHRA and PMCPA as certifying on behalf of both Lundbeck and Otsuka, had not been certified in accordance with Clause 14.1 and its supplementary information. The Panel thus ruled a breach of Clause 14.1 in relation to these materials.

The Panel noted Lundbeck's submission that it was brought to its attention in December 2017 that the PMCPA required all promotional materials including materials for local representative meetings to be certified by medical signatories from both companies. The Panel noted Lundbeck's submission about advice given by the PMCPA on this matter in January 2018. The Panel noted that the PMCPA could not approve any activities or materials, it could only give informal guidance based on its interpretation of the Code. In the event of a complaint being received about a matter upon which advice had been given, it would be considered in the usual way. The Panel had no details with regard to the advice which Lundbeck stated had been given but in the Panel's view it was clear in the supplementary information to Clause 14.1 that under co-promotion arrangements the companies concerned could agree to have only one final signatory to certify on behalf of all the companies, however, this must be agreed beforehand and the MHRA and PMCPA must be informed in advance who the signatory would be.

The Panel noted that a member of the Lundbeck medical department confirmed in emails sent to

Lundbeck employees in mid-December 2017 and again in January 2018 that all Abilify Maintena materials for use from 14 December that required certification under the Code, required certification by medical signatories from both companies. The Panel noted that this was documented in a memorandum of understanding which started in January 2018 but was not finalised until June 2018.

The Panel noted that from January 2018 to August 2018, four Abilify Maintena materials were not certified by a medical signatory from both companies. The Panel noted Lundbeck's submission that one of these materials (UK/AM/0518/0225) was only certified by an Otsuka medical signatory due to a technical error in the Zinc approval system which resulted in the Lundbeck medical signature not being captured on the certificate. The second (UK/AM/0618/0261) was only certified by a Lundbeck medical signatory and the company gave no reason for this. The third (UK/AM/0118/0005) was only certified by a Lundbeck medical signatory and the company stated that this was due to the Otsuka

medical signatory leaving the company prior to certification. The fourth (UK-ABIM-0104) was only certified by a Lundbeck medical signatory and the company stated that this was an error. The Panel noted that its ruling of a breach of Clause 14.4 above applied here and it made no additional ruling in this regard. The Panel noted its comments above about the relevant supplementary information to Clause 14.1. The above four promotional materials that had been certified by only one company, whose signatory had not been notified in advance to the MHRA and PMCPA as certifying on behalf of both Lundbeck and Otsuka, had not been certified in accordance with Clause 14.1 and its supplementary information. The Panel thus ruled a breach of Clause 14.1 in relation to those materials.

Complaint received	20 August 2018
Case completed	19 December 2018

HEALTH PROFESSIONAL v FERRING

Conduct of a representative

A nurse specialist complained about the conduct of a named Ferring representative alleging that he/she was harassing his department's staff for appointments.

The complainant provided a copy of the complaint he/she had sent directly to Ferring.

The complainant explained that the main focus of the complaint was the representative's repeated calls and abuse of the patient telemedicine voicemail which clearly stated on the answerphone message that it was for patients only. All in all, the representative had upset 3 clinical members of the team.

The complainant further stated that Ferring had failed to come back to him/her by the date agreed.

The detailed response from Ferring is given below.

The Panel noted that the parties' accounts differed in this regard. The Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was often impossible in such circumstances to determine precisely what had happened. The introduction to the Constitution and Procedure stated that a complainant had the burden of proving their complaint on the balance of probabilities. The Panel noted, however, that a high degree of dissatisfaction was usually required before an individual was moved to submit a formal complaint.

The Panel noted Ferring's submission that the representative called the complainant to arrange another appointment as he/she had not seen him when visiting the named hospital in July. According to Ferring the representative asked to speak to the complainant and was put through by the switchboard. The representative left a voice message but could not recall if this was on the IBD helpline or a personal telephone message. Ferring submitted that only one call was made to the hospital that day as reflected in the representative's call log and no calls were made directly to the patient helpline.

The Panel noted the complainant's submission that he/she carefully and specifically explained to the representative that the named sector which included a number of named hospitals could not facilitate a meeting with him/her until the new year and asked him/her to recontact then. In the complainant's view the representative should therefore not have contacted a second named hospital. The Panel noted a discrepancy in that the complainant initially stated that he/she had spoken to the representative and explained that he/she did not use the medicines that the representative was selling. In later

correspondence the complainant submitted that he/she had asked the representative to make contact in the New Year as the department was currently busy.

The Panel noted that the fact that the complainant was busy and that the representative should wait until January 2019 to engage was reflected in the representative's call notes. The Panel further noted Ferring's submission that the representative viewed the second named hospital as an independent entity with its own IBD clinical team and wanted to invite the new IBD nurse to a meeting.

The Panel noted Ferring's submission that only one call was placed to the patient telemedicine helpline on 8 August as advised by a secretary at the second named hospital. This was shown by the representative's company telephone records. Any other calls were made via the telephone switchboard and the representative asked to speak to a named individual not the helpline so the extension he/she was directed to was not within his control.

The Panel noted that the Code stated that representatives must ensure that the frequency, timing and duration of calls on health professionals and other relevant decision makers in hospitals and NHS and other organisations, together with the manner in which they are made, did not cause inconvenience. The wishes of individuals on whom representatives wish to call and the arrangements in force at any establishment, must be observed. The Panel noted the parties' differing accounts and its comments above on this point. Overall, the Panel did not consider that on the balance of probabilities the complainant had proved that the representative had contravened the requirements of the Code in relation to seeking appointments. The Panel thus ruled no breaches of the Code.

The Panel considered that there was no evidence that the representative had been instructed to overcall on clinicians or contact health professionals in a way that would be likely to lead to a breach of the Code. The Panel therefore ruled no breach in that regard.

A nurse specialist complained about a named Ferring representative harassing his/her department's staff for appointments.

COMPLAINT

The complainant requested advice from the PMCPA about the best way to report a representative from practically harassing the department's staff for appointments. The complainant stated he/she spoke to the representative already by phone and explained that they did not use the medicines that

he/she was selling. Furthermore, the representative was now abusing the patient telemedicine line leaving messages on it for staff members and had also left messages with secretarial staff members.

The complainant provided a copy of the complaint he/she had sent directly to Ferring.

The complainant explained that the main focus of the complaint was the representative's repeated calls and abuse of the patient telemedicine voicemail which clearly stated on the answerphone message that it was for patients only. All in all, the representative had upset 3 clinical members of the team.

The complainant further stated that Ferring had failed to come back to him/her by the date agreed.

When writing to Ferring, the Authority asked it to consider the requirements of Clauses 15.2, 15.4, 15.9, and 9.1.

RESPONSE

Ferring stated that it was disappointed to receive this complaint regarding the conduct of one of its representatives. Ferring noted that it had received the same complaint directly from the complainant in August 2018 which it had acknowledged. Ferring submitted that it informed the complainant that following a thorough investigation Ferring concluded that there had not been a breach of the Code. Ferring also stated that it would fully co-operate with the PMCPA investigation. Ferring was disappointed that it was not given the opportunity to respond to the complainant before it was escalated to the Authority.

Ferring submitted that from the evidence collected, it contended that its representative, had not breached the Code, either through the frequency or mode of contacts or the nature of his/her conduct.

Ferring UK did not require its sales representatives to adhere to a formal call rate. The sales representative's activity was guided by their account objectives which were formulated in conjunction with their area sales manager (ASM). The representative had not yet defined individual account plans with his/her ASM and was therefore working towards a set of personal objectives. This included understanding key stakeholder networks, familiarizing himself with local strategy documents and making appointments with relevant key stakeholders in various accounts. There were no requirements for the sales representatives to contact a prespecified number of customers within a defined time period.

Ferring explained the sequence of events as detailed by the representative who had met the complainant before and reported a previous collaborative working environment where the complainant helped to set up multi-disciplinary meetings. The representative was therefore surprised to receive this complaint as he/she viewed their working relationship to be amicable and indeed the individuals were on first-name terms.

In July 2018 the representative sent an email to the complainant details were provided including that the representative wanted to discuss National IBD Nurse meeting that Ferring was holding in Birmingham in September and to discuss the current ulcerative colitis patient pathway within the hospital so that the representative could understand the current situation.

First Hospital

The representative received no response to this email. In July 2018 the representative visited the hospital and his/her first point of contact was with a secretary who directed the representative to the complainant and another nurse as the most appropriate members of staff instructing the representative on how to find their office and to 'pop down' as they were approachable. The complainant and the other nurse would decide if the representative should approach the consultants if any further discussions were warranted. The office was empty when the representative arrived. At the same time another member of staff arrived and the representative introduced himself/herself and the purpose of his visit. He/she then asked the staff member to declare his/her visit to the complainant and his/her colleague, and to pass on leavetickets around two of Ferring's products and an invitation to the IBD Nurse meeting. This was not met with an objection and the representative left the department and went to the pharmacy to ascertain the formulary status of Ferring's products. He/she met with a pharmacist and the call was captured on the customer relations management (CRM) system. In view of the fact that the representative did not have any contact with the health professional in question, he/she placed a call to the complainant to arrange another appointment. The representative was connected to the main switchboard, he/she asked to speak to the complainant and was put through by switchboard. The representative left a voice message but was unable to recall if this was the IBD helpline or a personal telephone message that he/she was put through to by switchboard. There was one call placed to the hospital on that day as reflected in the representative's call log and no calls made directly to the patient helpline.

On 1 August the complainant called the representative and explained that the department was presently under resourced and stretched and as such could not speak with him until the new year. This was acknowledged and documented by the representative in the CRM.

Second Hospital

The representative was directed by his/her line manager to visit the second hospital to invite the new IBD nurse to an annual IBD meeting organized by Ferring. The previous IBD nurse had attended earlier events.

The representative called the hospital and spoke with one of the secretaries and enquired about the contact details for the new IBD nurse in order to make an introduction and extend an invitation to

the annual IBD nurse meeting. The secretary gave the name of the new IBD nurse and the best way to contact, which he/she was advised was via the patient telemedicine helpline. The representative's call log reflected that only one call was placed to the patient telemedicine helpline since he/she joined Ferring Pharmaceuticals. This call was preceded by a telephone call to the hospital switchboard which supported the representative's narrative. Ferring submitted that this was not an uncommon phenomenon as many health professionals asked members of the sales team to contact them on these numbers as they were always manned and easy to access.

The website link to the area mentioned eleven hospitals and there was no indication to show which hospitals were linked and where health professionals might cover different communities/hospitals within the same trust. The representative therefore viewed this hospital as an independent entity with its own IBD clinical team and wanted to invite the new IBD Nurse to the conference.

Ferring submitted that each interaction with the individual units was appropriate and distinct.

Ferring summarized that the representative's proactive contacts with the complainant were an email, a telephone message via hospital switchboard, and he/she also left promotional materials for him with another colleague. The representative therefore only spoke with one member of the clinical team and three administrative personnel. The conversations were all conducted in a professional manner and the representative viewed the contact with the individuals as positive and well received. No individual had suggested otherwise to the representative or Ferring other than the complainant and in the absence of any further specific details relating to the representative's conduct Ferring therefore concluded that there was no evidence of a breach of the Code.

FURTHER COMMENTS FROM THE COMPLAINANT

Upon viewing Ferring's response, the complainant stated that a named Ferring employee first contacted him/her by email on 9 August. This was following the complainant's initial complaint to Ferring about the representative's conduct. This email stated that he would investigate the matter and get back to the complainant by 17 August. As the complainant heard nothing that week, he/she contacted the ABPI on Monday, 20 August and received a letter from Ferring on 21 August stating that it would co-operate with the ABPI investigation. It was the complainant's strong feeling that Ferring would not have cooperated fully to investigate and resolve this issue had he/she not made the complaint to the ABPI.

The complainant stated that the representative left two messages, the second after being specifically asked not to by the complainant on the patient telemedicine voicemail. The voicemail service offered clearly stated on its automated message that it was a patient service only. It could only hold a certain number of voicemail messages. If it was full of calls from external contacts, then patients

would not be able to leave messages and care would be delayed. The complainant alleged that the representative was lying that he/she only left one message. The complainant noted that Ferring's response stated that the representative could not remember; the complainant considered that that was blatantly false.

The complainant stated that he had not seen the email that was said to be sent to him/her by the representative.

The complainant stated that the department's secretarial team was fully aware that it did not have a process set up that representatives could freely 'pop down' to the department's office – which was shared with other health professionals. Nor did the department have any jurisdiction over whether it was appropriate for a representative to see a consultant. It was up to the secretary to contact the doctor, to make arrangements - not the complainant. The complainant also did not appreciate messages and promotional 'paraphernalia' being left on his/her desk due to the potential implications that this could have for the Nursing and Midwifery Council (NMC) code of conduct. The complainant found it highly unlikely that a member of staff or anyone in the office would have asked the representative to leave anything on his desk.

The complainant stated that when he spoke to the representative on the telephone he/she carefully and specifically explained to him/her that the area – which included the two named hospitals and others – could not facilitate a meeting until the new year and asked him/her to recontact then as they were currently busy. Despite this, the representative went to the second hospital. The complainant clarified that the colleague who he/she line managed was not a 'New IBD Nurse'. In fact he/she had been in post for 2 years. The complainant explained that the department had three nurses currently covering all three sites. The complainant thought that having had the discussion with the representative, he/she should have understood that by deciding to attend the second hospital, again unannounced, would be wrong.

The complainant remembered meeting with the representative around 3 years ago, when he/she worked for a different pharmaceutical company.

The complainant stated that the representative was once again being economical with the truth. The complainant did not have any recollection of setting up meetings for the representative before and he/she was not on any of the department's lists for the last few years. The complainant stated that they had never had a collaborative relationship, nor did the complainant feel that they were on 'First named terms'; the complainant had only met the representative once before, several years ago. The complainant summarised by stating that he/she believed the representative was acting unprofessionally, had lied in his/her statement in several places and his/her approach was 'wrong, pushy and ignorant despite clear dialogue to him/her'.

FURTHER COMMENTS FROM FERRING

Ferring submitted that both the company and the representative stood by the original response to the complaint and could see no new evidence in the complainant's further comments.

Ferring submitted that in view of the formal complaint lodged with the PMCPA, Ferring was compelled to follow the appropriate complaints procedure and thus wait for the formal response from the PMCPA before responding. Ferring explained that it conducted a thorough investigation which was initiated on receipt of the complaint and entailed gathering written and oral testimony from the representative who was interviewed in person. The formal complaint from the PMCPA was received on 22 August. Ferring submitted that it therefore took the complaint very seriously and investigated it as soon as possible.

Ferring submitted that as per its original response, the representative's company telephone records clearly showed only one call placed to the patient telemedicine helpline on a particular day in August as advised by the gastroenterology secretary at the second hospital. Any other calls were made via the telephone switchboard and the representative asked to speak to a named individual not the helpline so the extension he/she was directed to was not within his/her control.

The email sent by the representative to the complainant was provided with Ferring's original response and was retrieved from the representative's sent items.

Ferring stood by the representative's description of events and did not accept that it was in any way unlikely or unusual that the secretary told him/her to pop down to the complainant's offices and that another member of staff would have asked him/her to leave material on the complainant's desk.

Ferring submitted that the representative was directed by his/her manager to contact the second hospital as an invitation from the head office to the Ferring IBD nurse meeting had bounced back saying the individual had left the organization. The representative wanted to invite the replacement nurse to the meeting, offering high quality education. He/she did not arrive unannounced at the hospital seeking an appointment, instead he/she called the department.

Ferring submitted that the training of the representative was provided at the request of the PMCPA.

Ferring submitted that the representative wrote to the complainant to make him/her aware of his/her new role. The tone and content of the email implied that the representative knew the complainant professionally. Ferring expected that he/she followed up in person having received no reply.

PANEL RULING

The Panel noted the complainant's allegation that the Ferring representative was harassing his/her department's staff for appointments and leaving messages for staff on the patient telemedicine line and with secretarial staff members. The Panel noted that the parties' accounts differed in this regard. The Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was often impossible in such circumstances to determine precisely what had happened. The introduction to the Constitution and Procedure stated that a complainant had the burden of proving their complaint on the balance of probabilities. The Panel noted, however, that a high degree of dissatisfaction was usually required before an individual was moved to submit a formal complaint.

The Panel noted Ferring's submission that the representative called the complainant to arrange another appointment as he/she had not seen him/her when visiting the named hospital on 26 July. According to Ferring the representative asked to speak to the complainant and was put through by the switchboard. The representative left a voice message but could not recall if this was on the IBD helpline or a personal telephone message. Ferring submitted that only one call was made to the hospital that day as reflected in the representative's call log and no calls were made directly to the patient helpline. The Panel noted the complainant's submission that when speaking to the representative he/she carefully and specifically explained that the named sector which included a number of named hospitals could not facilitate a meeting until the new year as they were busy and asked him/her to recontact then. In the complainant's view the representative should therefore not have contacted the second named hospital. The Panel noted a discrepancy in that the complainant initially stated that he/she had spoken to the representative and explained that he did not use the medicines that the representative was selling. In later correspondence the complainant submitted that he/she had asked the representative to make contact in the New Year as the department was currently busy.

The Panel noted that the fact that the complainant was busy and that the representative should wait until January 2019 to engage with him/her was reflected in the representative's call notes. The Panel further noted Ferring's submission that the representative viewed the second named hospital as an independent entity with its own IBD clinical team and wanted to invite the new IBD nurse to a meeting.

The Panel noted Ferring's submission that only one call was placed to the patient telemedicine helpline in August as advised by a secretary at the second named hospital. This was shown by the representative's company telephone records. Any other calls were made via the telephone switchboard and the representative asked to speak to a named individual not the helpline so the extension he/she was directed to was not within his control.

The Panel noted that Clause 15.4 stated that representatives must ensure that the frequency, timing and duration of calls on health professionals and other relevant decision makers in hospitals and NHS and other organisations, together with the manner in which they were made, do not cause inconvenience. The wishes of individuals on whom representatives wished to call and the arrangements in force at any establishment, must be observed. The Panel noted the parties' differing accounts and its comments above on this point. Overall, the Panel did not consider that on the balance of probabilities the complainant had proved that the representative had contravened the requirements of this clause. The Panel thus ruled no breach of Clause 15.4.

Given its ruling regarding Clause 15.4, the Panel did not consider that the representative had failed to maintain a high standard of ethical conduct. The Panel thus ruled no breach of Clause 15.2.

The Panel noted that Clause 15.9 of the Code required companies to prepare detailed briefing material for representatives on the technical aspects of each medicine which they would promote. Briefing material must comply with the relevant requirements of the Code and, in particular, was subject to the certification requirements of Clause 14. Briefing material must not advocate, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code.

The Panel noted Ferring's submission that it did not require its sales representatives to adhere to a formal call rate; their activity was guided by their account objectives which were formulated in conjunction with their area sales manager (ASM). The representative had not yet defined individual account plans with his/her ASM and was therefore working towards a set of personal objectives. These included understanding key stakeholder networks, familiarizing himself/herself with local strategy documents and making appointments with relevant key stakeholders. There were no requirements for the sales representatives to contact a prespecified number of customers within a defined time period. The Panel noted Ferring's submission about the representative's training. The Panel considered that there was no evidence that the representative had been instructed to overcall on clinicians or contact health professionals in a way that would be likely to lead to a breach of the Code. The Panel therefore ruled no breach of Clause 15.9.

The Panel noted its rulings above and did not consider that Ferring had failed to maintain high standards. No breach of Clause 9.1 was ruled.

Complaint received **21 August 2018**

Case completed **26 October 2018**

HEALTH PROFESSIONAL v SANOFI

Toujeo leaflet

A consultant physician complained about a six-page A5 gate-folded leavepiece produced by Sanofi. The leavepiece related to Toujeo (insulin glargine 300 units/mL) which was indicated for the treatment of diabetes mellitus in adults.

The complainant was concerned that the leavepiece misrepresented a clinical trial. He/she was not suggesting any factual errors; however, he/she considered the leavepiece, describing a study that compared Toujeo with insulin degludec, misleading. The complainant alleged that the leavepiece highlighted results from the titration period which appeared to favour Sanofi's product. These were presented graphically over two prominent pages. According to the complainant, the overall results of the study, which showed no difference between the two insulins, appeared only in text on a 'back page' of the leavepiece and stated, 'Comparable incidence and event rates of anytime and nocturnal hypoglycaemia in the maintenance and full 24-week study periods'. The complainant estimated that this took up around 5% of the space devoted to the results from the titration period, as well as having a much less prominent position. The complainant stated that the hypoglycaemia rate during 0-12 weeks was not described as a primary or secondary endpoint, only featured as one of three safety endpoints and was not mentioned on clinicaltrials.gov. The complainant alleged that Sanofi produced misleading promotional material which placed undue emphasis on favourable results from a safety endpoint obtained from 12 weeks of a 24-week study, with only brief mention of the overall results of the study.

The detailed response from Sanofi is given below.

The Panel noted that the leavepiece solely discussed the BRIGHT study (Rosenstock *et al*, 2018). The BRIGHT study was a head-to-head 24-week study which demonstrated non-inferiority of Toujeo vs insulin degludec for the primary endpoint; HbA1c change from baseline to week 24. The Panel noted Sanofi's submission that pre-specified safety endpoints included the incidence and event rates of hypoglycaemia during the 24-week on-treatment period, which consisted of the active titration period (weeks 0-12), and the maintenance period (weeks 13-24).

The Panel noted that the safety endpoints, hypoglycaemia incidence and event rates (anytime and nocturnal) over 24 weeks, were comparable with both insulins. The Panel noted the clinical relevance of the hypoglycaemia data during the titration period. The Panel considered that it was not unreasonable to present secondary endpoint data, nor was it unreasonable to present such

data from the titration period, if it was presented in the context of the full study period and with proportionate emphasis. The Panel acknowledged the bullet points referencing comparable hypoglycaemia incidence and event rates during the maintenance and 24-week study periods at the bottom of the middle and third inside pages and as the second bullet point on the summary back page. In the Panel's view, a single bullet point at the bottom of the middle and third inside pages was disproportionate to the prominent graphical representation of the titration period data which occupied most of those pages; insufficient weight had been given to the hypoglycaemia results for the full 24-week treatment period, which were comparable between the treatment arms. The Panel considered the immediate impression to a busy health professional; in the Panel's view, the titration period hypoglycaemia results were designed to be the primary take home message of the leavepiece. The leavepiece predominately highlighted the hypoglycaemia results during the 12-week titration period, which favoured Toujeo, without sufficient balance. The Panel considered that the leavepiece placed disproportionate emphasis on the results that had favoured Sanofi's product and, in that regard, misrepresented the study and the immediate impression was a misleading comparison of the two insulins. Breaches of the Code were ruled.

A consultant physician complained about a six-page A5 gate-folded leavepiece (SAGB.TJO.18.06.0924(1)) produced by Sanofi. The leavepiece related to Toujeo (insulin glargine 300 units/mL) which was indicated for the treatment of diabetes mellitus in adults.

COMPLAINT

The complainant was concerned that the leavepiece misrepresented a clinical trial. He/she was not suggesting any factual errors; however, he/she considered the leavepiece, describing a study that compared Toujeo with insulin degludec, misleading. The study consisted of two phases: an initial 12-week titration period during which insulin doses were adjusted, followed by a second 12-week period during which doses could be adjusted, if necessary, but without this being a specific target. The complainant alleged that the leavepiece highlighted results from the titration period which appeared to favour Sanofi's product. These were presented graphically over two prominent pages. According to the complainant, the overall results of the study, which showed no difference between the two insulins, appeared only in text on a 'back page' of the leavepiece and stated, 'Comparable incidence and event rates of anytime and nocturnal hypoglycaemia in the maintenance and full 24-week study periods'. The complainant estimated that this took up around

5% of the space devoted to the results from the titration period, as well as having a much less prominent position.

The complainant highlighted the study endpoints from the BRIGHT study which he/she reproduced below and noted that the hypoglycaemia rate during 0-12 weeks was not described as a primary or secondary endpoint, and only featured as one of three safety endpoints.

- The primary endpoint was the change in HbA1c from baseline to week 24.
- Secondary efficacy endpoints included change in fasting plasma glucose (FPG), fasting self-measured plasma glucose (SMPG), and eight-point SMPG profiles from baseline to week 24; change in variability of 24-h SMPG, based on eight-point profiles; percentage of participants reaching target HbA1c <7.0% (<53 mmol/mol) at week 24; and percentage of participants reaching target HbA1c <7.0% (<53 mmol/mol) at week 24 without confirmed hypoglycaemia (<70 mg/dL and <54 mg/dL) during the 24-week treatment period.
- Safety endpoints included the incidence and event rates of hypoglycaemia during the 24-week on-treatment period, the active titration period (weeks 0–12), and the maintenance period (weeks 13–24).
- Documented symptomatic hypoglycaemia was defined as an event that was symptomatic with a confirmatory blood glucose reading (≤ 70 mg/dL or <54 mg/dL). Severe hypoglycemia was defined as an event requiring assistance from another person to administer carbohydrate, glucagon, or other resuscitative actions. Confirmed hypoglycaemia included documented symptomatic or asymptomatic hypoglycemia (≤ 70 mg/dL or <54 mg/dL) and severe events, if any. Hypoglycemia that occurred between 0000 h and 0559 h was defined as nocturnal. Other safety outcomes included body weight and adverse events (AEs). Change in basal insulin dose was also assessed, although this was not a pre-specified endpoint.

The complainant stated that he/she also looked at the study entry (NCT02738151) on clinicaltrials.gov where the only relevant pre-specified outcome mentioned was the secondary outcome measure 'Event rate of hypoglycaemia per ADA classification [Time Frame: Baseline to Week 24]'. There was no mention of hypoglycaemia rates during the 0-12 week period.

The complainant alleged that Sanofi produced misleading promotional material which placed undue emphasis on favourable results from a safety endpoint that was not a primary or secondary outcome and he/she was unclear whether it was a pre-specified endpoint. Furthermore, these data were obtained from 12 weeks of a 24-week study, with only brief mention of the overall results of the study.

When writing to Sanofi, the Authority asked it to consider the requirements of Clauses 7.2 and 7.3 of the Code.

RESPONSE

Sanofi submitted that the leavepiece in question was based on the BRIGHT study, the results of which were presented as three posters at the American Diabetes Association, June 2018. The BRIGHT study was the first head-to-head randomised controlled trial comparing the efficacy and safety of insulin glargine 300 units/mL and insulin degludec 100 units/mL in combination with oral anti-hyperglycaemic drugs with or without glucagon-like peptide-1 receptor agonists in 929 people with type 2 diabetes. The primary endpoint of the study was the change in HbA1c from baseline to week 24. Pre-specified safety endpoints included the incidence and event rates of hypoglycaemia during the 24-week on-treatment period, which consisted of the active titration period (weeks 0–12), and the maintenance period (weeks 13–24). Sanofi stressed it was important to note that this study used identical titration algorithms for the comparator insulin and a pre-stated objective of achieving appropriate titration within the defined 12-week titration period, meaning a comparison of this predefined period was valid and clinically relevant. A full publication of the study was also now available online.

Sanofi understood that the complainant alleged that the leavepiece was misleading as it placed undue emphasis on one of the safety endpoints. Sanofi disagreed with this assessment and submitted that it accurately reflected the BRIGHT study in a fair, unambiguous and scientifically balanced way and fulfilled all the requirements of the Code, both in letter and in spirit. Sanofi denied breaches of Clauses 7.2 and 7.3.

Sanofi explained that the folded leavepiece on its first page clearly stated the overall study objectives ie to compare efficacy and safety of the two insulins. The results of the primary endpoint of the study were also stated prominently on this page. Since the primary endpoint of the study was met, Sanofi did not consider it inappropriate or misleading to present secondary endpoint data, especially when they pertained to patient safety. The following page (the third page of the leavepiece when folded, and 'incorrectly' called the 'back page' by the complainant) contained four summary messages; the first reiterated the results of the primary endpoint and the second cited the results of two of the three safety endpoints that were comparable between the two products. The results of the remaining safety endpoint (which is the subject of the complaint) were cited in the third and fourth bullet points. Sanofi submitted that these results showed a difference between the two arms and were therefore covered in more detail inside the leavepiece and were clearly presented from the outset within the context of the primary endpoint and the overall safety results. The first page inside the leavepiece (when opened fully) included a visual presentation of important features of the study design, including inclusion criteria, target fasting plasma glucose (FPG) range and a statement on baseline demographics. The primary and safety endpoints were also clearly and prominently presented. Sanofi considered, in the context of a leavepiece, that this was

sufficient information displayed upfront on essential components of the study for the reader to understand its design and main endpoints. Sanofi appreciated that two inner pages of the folded leavepiece highlighted the hypoglycaemia results of the titration phase in a visual manner, however, it strongly believed that this was justifiable and allowable under the Code for several reasons:

- 1 The titration phase of the study (typically 0-12 weeks) was critical in any randomised clinical trial assessing the safety and efficacy of a basal insulin analogue. Patient's insulin was aggressively titrated in this period to achieve target FPG before the right dose could be determined and maintained for the remaining study period, ie maintenance phase (12-24 weeks). It could be argued that, particularly in this insulin naïve group of patients, any incidence of hypoglycaemia in this period could adversely affect the clinician's/patient's confidence with insulin therapy thereby preventing efficient titration of insulin to achieve desired FPG level as well as impacting patient adherence/compliance and motivation with therapy, eventually affecting overall management of diabetes. This critical phase and any potential incidence of hypoglycaemia carried even greater significance to clinicians in real world clinical practice of managing patients with type 2 diabetes. This was reflected in clinical guidelines eg the American Association of Clinical Endocrinologists (AACE) guidelines stated that 'minimising risk of hypoglycaemia is a priority'. The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) guidelines stated 'Personalisation is necessary, balancing the benefits of glycaemic control with its potential risks, taking into account the adverse effects of glucose lowering medications (particularly hypoglycaemia)'. Sanofi submitted it was therefore absolutely relevant (as required by Clause 7.3) to discuss the titration phase results in this leavepiece.
- 2 Titration phase hypoglycaemia incidence and event rate was clearly a 'pre-specified' endpoint therefore it had made no attempt to highlight a result that was not stated as a pre-specified endpoint in the study. This was also discussed in the full publication.
- 3 Titration phase incidence and event rate of hypoglycaemia were 'safety' endpoints. Sanofi stated that it was important to appreciate that safety endpoints of hypoglycaemia in diabetes trials were of major clinical significance to prescribers along with HbA1c change. An episode of hypoglycaemia independent of the severity, frequency and time of the day could adversely affect a patient's condition both in the short-term and may also cause long-term complications. Sanofi considered that highlighting hypoglycaemia endpoints for discussion was essential with reference to the BRIGHT study.
- 4 Whilst the titration phase hypoglycaemia results were graphically presented, Sanofi submitted that it was important to emphasise here that the

results of anytime and nocturnal hypoglycaemia in the maintenance and full study period were stated in clear bold statements on the same pages where titration phase results were presented. Sanofi stated that the overall study results and maintenance period results (where no difference between the two insulins were noted) had been stated as clear statements at three different places in the leavepiece. Sanofi submitted that it was also worth pointing out that these statements had been written in the same font size, font type and carried equal space as the statements on titration phase. Using the Forest plot was designed to show not just the result, but also the confidence intervals, which would give health professionals a greater depth of information of the results. The results for the titration phase safety endpoint had been shown in full, with some results crossing the unity line, further showing desire for full transparency. Sanofi stated that it should be appreciated that visual presentation was the most appropriate method to explain forest plots results with confidence intervals at various thresholds and there had been no attempt to visually over-emphasise the results. Moreover, Sanofi submitted that it was expected that any leavepiece was read altogether as one standalone item therefore, any discussion on the balance of one particular endpoint should be seen in the context of the full leavepiece not individual pages or sides.

- 5 The study reported the primary endpoint as showing non-inferiority in change in HbA1c for insulin glargine 300 units/mL vs insulin degludec 100 units/mL. Sanofi submitted that whilst titration phase, anytime hypoglycaemia incidence and event rate showed favourable results for Toujeo, all other secondary efficacy and safety endpoints reported similar results for the two comparator insulins therefore Sanofi did not consider that any attempt was made to selectively highlight or report results that benefitted Toujeo. Sanofi submitted that it had generated a fair and accurate leavepiece based on the study evidence where the only difference between the two insulins was showing a favourable result for Toujeo.

Based on these arguments, Sanofi stated it was confident that the leavepiece was not only factually accurate (as also acknowledged by the complainant) but it also clearly and fairly reflected the relevant and most important outcomes of the study. In Sanofi's opinion it was sufficiently complete to allow the reader to place appropriate weight to the results presented. Sanofi did not consider that the item was misleading or misrepresenting and therefore denied any breach of Clauses 7.2 and 7.3.

PANEL RULING

The Panel noted that the leavepiece solely discussed the BRIGHT study (Rosenstock *et al*, 2018). The front page of the leavepiece featured the BRIGHT study logo next to the title 'First head-to-head randomised controlled trial comparing the efficacy and safety of Toujeo vs. insulin degludec 100 units/

mL in insulin-naïve patients with Type 2 diabetes'. Below the heading it was stated that Toujeo showed comparable HbA1c reduction vs insulin degludec with lower incidence and event rates of anytime hypoglycaemia (≤ 3.9 mmol/L and < 3.0 mmol/L) and lower event rates of nocturnal hypoglycaemia (≤ 3.9 mmol/L) in the titration period, which was qualified with a footnote as being the period 0-12 weeks.

The Panel noted the parties' submissions about the two different orders in which the pages were likely to be read; the page identified as the back page by the complainant was considered by Sanofi to be the third page. There was no evidence before the Panel about the order in which recipients would read the leavepiece. Nonetheless, the Panel considered that although readers would likely see the outside back page when first opening the gate-folded leavepiece, a reasonable number would read the detail of the inside triple page spread first. That the outside back page in question summarised what might be described as the previous four pages, supported the Panel's view.

When opened, the first inside page gave a description of the primary endpoint (change in HbA1c from baseline to week 24) and the non-inferiority margin. Below this, two secondary endpoints were described: incidence and event rates of anytime confirmed hypoglycaemia and incidence and event rates of nocturnal confirmed hypoglycaemia, followed by a description of the study design, a multicentre, open-label, 24-week study. The Panel noted that these endpoints were listed in the study as pre-specified safety endpoints. The Panel noted that the secondary outcome measures on clinicaltrials.gov that the complainant referred to differed from those currently on the website.

The middle page of the inside triple page spread showed a graphical representation of the results for anytime confirmed hypoglycaemia during the titration period. Two forest plots of the titration period results (incidence and event rates per patient per year) for anytime confirmed hypoglycaemia (≤ 3.9 mmol/L and < 3.0 mmol/L) along with related claims occupied most of the page, followed by two bullet points at the bottom of the page: the first bullet point highlighted the anytime hypoglycaemia (≤ 3.9 mmol/L) titration period results in favour of Toujeo, and the final bullet point stated 'Comparable anytime hypoglycaemia incidence and event rates during the maintenance period and 24-week study period'. A similar layout was used on the third inside page with regard to the results for nocturnal confirmed hypoglycaemia, with the graphical representation of the titration period results with related claims occupying most of the page, followed by two bullet points at the bottom of the page: the first bullet point highlighted the nocturnal hypoglycaemia (≤ 3.9 mmol/L) titration period results in favour of Toujeo, and the final bullet point stated 'Comparable nocturnal hypoglycaemia incidence and event rates during the maintenance period and 24-week study period'.

The page on the outside cover contained four summary statements: the first pertained to comparable and effective HbA1c reduction with Toujeo and insulin degludec 100 units/mL in insulin-naïve patients with type 2 diabetes at 24 weeks (primary endpoint); the second stated 'Comparable incidence and event rates of anytime and nocturnal hypoglycaemia in the maintenance and full 24-week study periods'; the third stated 'Lower anytime (24hr) confirmed hypoglycaemia during the titration period' and gave the relative percentage reduction for incidence and events (≤ 3.9 mmol/L) in favour of Toujeo; the fourth statement stated 'Lower nocturnal (00.00-06.00hr) confirmed hypoglycaemic events during the titration period' and gave the relative percentage reduction for events (≤ 3.9 mmol/L) in favour of Toujeo. Incidence and events rates for nocturnal confirmed hypoglycaemia during the titration period where the 95% confidence interval crossed 1 were not highlighted as text statements in the leavepiece. According to the study, the rate of confirmed nocturnal hypoglycaemia (< 3.0 mmol/L) was comparable with both treatments during the titration period. Further, the incidence of nocturnal confirmed hypoglycaemia (≤ 3.9 mmol/L and < 3.0 mmol/L) was comparable with both treatments during the titration period; this was not highlighted on the front page, summary page or in the claims below the forest-plots.

The final page was the prescribing information for Toujeo.

The Panel noted that the BRIGHT study was a head-to-head 24-week study which demonstrated non-inferiority of Toujeo vs insulin degludec for the primary endpoint, which was HbA1c change from baseline to week 24. The Panel further noted that the safety endpoints, hypoglycaemia incidence and event rates (anytime and nocturnal) over 24 weeks, were comparable with both insulins.

The Panel noted Sanofi's submission that pre-specified safety endpoints included the incidence and event rates of hypoglycaemia during the 24-week on-treatment period, which consisted of the active titration period (weeks 0-12), and the maintenance period (weeks 13-24) and that the study used identical titration algorithms for both treatment arms. The Panel further noted Sanofi's justification that dedicating two pages of the leavepiece to the visual representation and description of the hypoglycaemia results from the titration period was relevant as that time-period (0-12 weeks) was critical when assessing the safety and efficacy of a basal insulin analogue. The Panel noted Sanofi's submission that since the primary endpoint of the study was met, it could not be considered inappropriate or misleading to present secondary endpoint data, especially when they pertained to patient safety.

The Panel noted the clinical relevance of the hypoglycaemia data during the titration period. The Panel considered that it was not unreasonable to present secondary endpoint data, nor was it unreasonable to present such data from the titration period, if it was presented in the context of the full

study period and with proportionate emphasis. The Panel acknowledged the bullet points referencing comparable hypoglycaemia incidence and event rates during the maintenance and 24-week study periods at the bottom of the middle and third inside pages and as the second bullet point on the summary back page. In the Panel's view, a single bullet point at the bottom of the middle and third inside pages was disproportionate to the prominent graphical representation of the titration period data which occupied most of those pages; insufficient weight had been given to the hypoglycaemia results for the full 24-week treatment period, which were comparable between the treatment arms. The Panel considered the immediate impression to a busy health professional; in the Panel's view, the titration period hypoglycaemia results were designed to be the primary take home message of the leavepiece and the final bullet points at the very bottom of the pages in question were wholly insufficient to qualify the immediate impression given. The Panel further noted that the secondary efficacy endpoint result, change in FPG from baseline to week 24, which showed a greater reduction with insulin degludec vs Toujeo, was not mentioned in the leavepiece at all and this appeared to the Panel not to be consistent

with Sanofi's submission that all other secondary efficacy and safety endpoints reported similar results for the two insulins. The Panel disagreed with Sanofi's submission that it did not make any attempt to selectively highlight or report results that benefitted Toujeo. The leavepiece predominately highlighted the hypoglycaemia results during the 12-week titration period, which favoured Toujeo, without sufficient balance. The Panel disagreed with Sanofi's submission that it accurately reflected the BRIGHT study in a fair, unambiguous and scientifically balanced way and that it had fulfilled all the requirements of the Code. The Panel considered that the leavepiece placed disproportionate emphasis on the results that had favoured Sanofi's product and, in that regard, misrepresented the study and the immediate impression given by the second and third pages of the inside triple page spread was a misleading comparison of the two insulins. A breach of Clause 7.2 and 7.3 was ruled.

Complaint received **22 August 2018**

Case completed **17 October 2018**

VOLUNTARY ADMISSION BY DR FALK PHARMA

Promotion to the public via YouTube

Dr Falk Pharma UK voluntarily admitted breaches of the Code in that a video made by the company, which discussed the use of mesalazine tablets and granules to treat inflammatory bowel disease, appeared on YouTube. Dr Falk Pharma marketed Salofalk (mesalazine) in a number of different forms including tablets and granules.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Dr Falk Pharma.

Dr Falk Pharma explained that the video, made in 2015 in conjunction with a third party, for use for a limited period within the NHS Alliance, was available on YouTube without the knowledge or permission of Dr Falk Pharma.

The video discussed the cost of inflammatory bowel disease to the NHS and used a patient case study. A clinician commented that mesalazine granules could be more effective than tablets in reaching the inflamed areas of the bowel and mentioned a study supported by Dr Falk Pharma that looked at the effectiveness of granules and the savings that might accrue for the NHS. A senior executive at the company was interviewed and further discussed the study and the benefits of mesalazine granules.

Following an investigation into the matter, Dr Falk Pharma recognized that the video posted on the NHS Alliance website did not meet the requirements of the Code. It was not known how many people viewed the video on this website and how many of them were not health professionals. The company therefore accepted breaches of the Code as a prescription only medicine might have been promoted to the public and members of the public might have been encouraged to ask their health professional to prescribe that medicine. These breaches were due to a failure to meet internal requirements relating to document review. The video had not been intended as promotional but in hindsight should have been certified; high standards had not been maintained and further breaches of the Code were acknowledged.

The video had been viewed 131 times on YouTube and was removed on 6 August 2018. The company investigated further and found that an unknown person placed the video on YouTube in December 2015 and the reason for the upload was unknown. Dr Falk Pharma stated that it did not monitor social media outside of its control and so it was entirely unaware that the video in question was on YouTube; it was no longer available on the NHS Alliance website.

The detailed response from Dr Falk Pharma is given below.

The Panel considered that given the content of the film and its focus on the advantages of Salofalk, it was difficult to understand how the company decided that the film was not promotional. It appeared that Dr Falk Pharma now accepted that the film was promotional. The video had not been certified and thus the Panel ruled a breach of the Code.

The Panel noted that Dr Falk Pharma did not place the material on YouTube. The video was to be distributed by the NHS Alliance and to be hosted on its website for 12 months to encourage social sharing and promotion of the programme. It was to be sent to various organisations and promoted via a programme press release to relevant journalists. It was also part of the programme at the NHS Alliance Conference on 9 December 2015.

The company had no documentation which covered the archiving/withdrawal of the film at the end of the one year contract and there was no evidence that Dr Falk had been clear about the access to the film or had limited viewing to those to whom prescription only medicines could be advertised.

If the promotional film had been seen by the public it would have constituted advertising a prescription only medicine to the public. On the narrow ground that the company had not made the film available to the public on YouTube the Panel ruled no breach of the Code.

However, the Panel considered that Dr Falk Pharma's voluntary admission included that the availability of the film on the NHS Alliance website meant that the company had promoted its prescription only medicine to the public. There was no justification from Dr Falk Pharma that the audience for the NHS Alliance, including its website, was an appropriate audience for the advertising of prescription only medicines. The Panel considered that on the available information, Dr Falk Pharma had promoted a prescription only medicine to the public and ruled a breach of the Code. Statements had been made which would encourage members of the public to ask their health professionals to prescribe a prescription only medicine and a further breach was ruled.

The Panel considered that high standards had not been maintained. The failure to recognise the film as promotional material showed poor understanding of the Code as did the failure to certify the film and the lack of due diligence on the particulars in the agreement with the third party. A breach of the

Code was ruled. On balance, the Panel considered that the circumstances did not warrant a ruling of a breach of Clause 2 and ruled accordingly.

Dr Falk Pharma UK Ltd voluntarily admitted breaches of the Code in that a video made by the company, which discussed the use of mesalazine tablets and granules to treat inflammatory bowel disease, appeared on YouTube. Dr Falk Pharma marketed Salofalk (mesalazine) in a number of different forms including tablets and granules.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Dr Falk Pharma.

VOLUNTARY ADMISSION

Dr Falk Pharma explained that on 2 August 2018, a third party unconnected with the company informed it that an informational video, made in 2015 for use for a limited period within the NHS Alliance, was available on YouTube. The company took immediate steps to have the video removed from YouTube and this was achieved on 6 August. The video had been uploaded to YouTube without the knowledge or permission of Dr Falk Pharma but the company nonetheless recognized the need to take responsibility and to voluntarily admit breaches of the Code.

Dr Falk Pharma submitted that investigation into the placing of the video on YouTube brought to light further breaches of the Code in relation to the placement of the video on the NHS Alliance site.

Dr Falk Pharma explained that it made the video in conjunction with a third party for the NHS Alliance website as information on inflammatory bowel disease and its treatment. The video was to be available on the NHS Alliance site for 12 months. A transcript was provided.

The video discussed the cost of inflammatory bowel disease to the NHS and illustrated the personal impact of the disease using a patient case study. A clinician described the use of mesalazine tablets to treat inflammatory bowel disease and commented that mesalazine granules could be more effective in reaching the inflamed areas of the bowel compared with tablets. The doctor mentioned a study supported by Dr Falk Pharma that looked at the effectiveness of granules and the savings that might accrue for the NHS. The study was adopted by the National Institute for Health and Care Excellence (NICE) as a quality and productivity case study. A senior executive of Dr Falk Pharma was then interviewed and further discussed the study and the benefits of mesalazine granules. The video closed with the patient commenting on the personal benefit to him.

Following the investigation into the matter, Dr Falk Pharma now recognized that the final version of the video posted on the NHS Alliance website did not meet the requirements of the Code. It was not known how many people viewed the video on the NHS Alliance website and how many of them were

not health professionals. The company therefore accepted a breach of Clause 22.1 as a prescription only medicine might have been promoted to the public and a breach of Clause 22.2 as members of the public might have been encouraged to ask their health professional to provide the concerned medicine.

The investigation found that these breaches were due to a failure to meet internal requirements relating to document review. The video had not been intended as promotional but in hindsight should have been certified and therefore a breach of Clause 14.1 had occurred.

The company also accepted a breach of Clause 9.1 as high standards had not been maintained.

Dr Falk Pharma noted that the video had been viewed on YouTube 131 times before it was removed on 6 August 2018. The company could only find that an unknown person placed the video on YouTube in December 2015 and therefore the reason for the upload was unknown. As expected, the video was no longer available on the NHS Alliance site as the contract was for one year.

Dr Falk Pharma stated that it did not monitor social media outside of its control. The company only monitored its own social media accounts in case of any reports of adverse drug reactions due to its products, which was a requirement of the pharmacovigilance guidelines. The company only ran a Twitter account which was monitored twice a week and was entirely unaware that the video in question was on YouTube.

Dr Falk Pharma reiterated that it fully accepted responsibility under the Code, and the breaches outlined above, despite having no knowledge of, nor providing permission for, the video to be on YouTube.

Dr Falk Pharma was asked to consider the requirements of Clause 2 in addition to Clauses 9.1, 14.1, 22.1 and 22.2.

RESPONSE

Dr Falk Pharma reiterated that it made the video in conjunction with a third party for the NHS Alliance website as information on inflammatory bowel disease and its treatment. The video was to be available on the NHS Alliance site for 12 months from December 2015. Dr Falk Pharma provided the web address for the page where the video was posted; access to that page was not limited. It was impossible to determine how many people viewed the video during the year.

Dr Falk Pharma stated that it was contacted by letter of 31 July, received 2 August 2018, detailing the complaint. The letter made several points including that the video was found on YouTube and therefore breached Clauses 22.1 and 22.2 of the Code and as there was no certification reference there was a possible breach of Clause 14.1. Dr Falk Pharma provided its agreement with the third party.

Following correspondence with the case preparation manager who clarified that Clause 14.3 and Clauses 26.1 and 26.2 (instead of Clauses 22.1 and 22.2 referred to by Dr Falk Pharma) were relevant, Dr Falk Pharma confirmed that as the video was made in 2015, Clauses 14.1 and 14.3 of the 2015 Code were breached. The video was made available by NHS Alliance during 2016 and hence Clauses 26.1 and 26.2 of the 2016 Code applied. The video was on YouTube during 2016 until August 2018 and thus Clauses 26.1 and 26.2 of the 2016 Code applied. Dr Falk Pharma submitted that it had provided all of the information and documentation already and it had no further comments.

PANEL RULING

In considering this matter and given that Clauses 14.1 and 14.3 of the 2015 Code were the same in the 2016 Code, the Panel decided to consider the matter under the 2016 Code. The Panel also noted that the voluntary admission incorrectly referred to Clauses 22.1 and 22.2 of the Code rather than Clauses 26.1 and 26.2.

The Panel noted that Clause 1.2 defined promotion as any activity undertaken by a pharmaceutical company or with its authority which promoted the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicines.

Given the content of the film and its focus on the benefits of using Dr Falk Pharma's product it was difficult to understand how the company decided that the film was not promotional. The focus was on the advantages of Salofalk (mesalazine granules). The Panel noted that it appeared that Dr Falk Pharma now accepted that the film was promotional by its acknowledgement of a breach of Clause 14.1. The promotional material had not been certified and thus the Panel ruled a breach of Clause 14.1. The Panel noted that Clause 14.3 included a requirement that material for the public and patients was certified. The Panel noted its ruling regarding Clause 14.1 and considered that this covered the position and therefore in its view, there was no need to consider Clause 14.3.

The Panel noted that the company did not place the material on YouTube. It appeared from the signed agreement with the third party that Dr Falk Pharma had full editorial control over the film and owned the copyright in the segment. The programme was to be distributed by the NHS Alliance and the third party. It was to be hosted on the NHS Alliance website for 12 months to encourage social sharing and promotion of the programme. It was to be sent to various

organisations and promoted via a programme press release to relevant industry journalists of the care sector press. It was also part of the programme at the NHS Alliance Conference on 9 December 2015.

The company had no documentation which covered the archiving/withdrawal of the film at the end of the one year contract.

There was no evidence that Dr Falk Pharma had been clear about the access to the film or had limited viewing to those to whom prescription only medicines could be advertised.

If the promotional film had been seen by the public it would have constituted advertising a prescription only medicine to the public. On the narrow ground that the company had not made the film available to the public on YouTube the Panel ruled no breach of Clauses 26.1 and 26.2 of the Code.

However, the Panel considered that Dr Falk Pharma's voluntary admission included that the availability of the film on the NHS Alliance website meant that the company had promoted its prescription only medicine to the public. The Panel considered that the agreement with the third party implied that the distribution of the film was wide. There was no justification from Dr Falk Pharma that the audience for the NHS Alliance, including its website, was an appropriate audience for advertising of prescription only medicines. The Panel considered that on the available information, Dr Falk Pharma had promoted a prescription only medicine to the public and ruled a breach of Clause 26.1. Statements had been made which would encourage members of the public to ask their health professionals to prescribe a prescription only medicine and a breach of Clause 26.2 was also ruled.

The Panel considered that high standards had not been maintained by Dr Falk Pharma. The failure to recognise the film as promotional material showed poor understanding of the Code. As did the failure to certify the film and the lack of due diligence on the particulars in the agreement with the third party. Dr Falk Pharma had not maintained high standards and a breach of Clause 9.1 was ruled. On balance, the Panel considered that the circumstances did not warrant a ruling of a breach of Clause 2 and ruled accordingly.

Voluntary admission received **6 September 2018**

Case completed **12 November 2018**

HEAD OF MEDICINES OPTIMISATION v GLAXOSMITHKLINE

List Price Reduction Claims

A head of medicines optimisation at a clinical commissioning group (CCG), complained about a letter dated 30 August 2018 sent by GlaxoSmithKline and headed 'Seretide List Price Reduction'. Seretide was a fixed dose combination of salmeterol and fluticasone (SFC) used in the treatment of asthma and of chronic obstructive pulmonary disease (COPD).

The letter explained that the list price of the three most commonly prescribed packs of Seretide would be reduced on 1 September 2018 providing the NHS an estimated annual saving of £52 million. The new Seretide prices were now lower than the equivalent dose/formulation of a branded generic. Under the heading 'What does this mean if you have a Seretide rebate contract in place?', readers were informed that for non-branded SFC prescriptions, they would pay the new lower NHS tariff price and thus see additional savings. The complainant noted, however, that the price had not been reduced in the September Drug Tariff as suggested and so there were no savings to be made from non-branded SFC prescriptions. Further, in the preface of the September Drug Tariff, where it referred to October changes, there was no reference that the changes as suggested would occur. In that regard the complainant referred to a footnote on page 2 of the letter which stated that estimated savings were based on, *inter alia*, 'both Seretide and non-branded scripts for SFC [salmeterol fluticasone], as Seretide is used as the reference price in the drug tariff. Savings based on NHS Drug Tariff for Seretide Evohaler 25/125, 25/250 and Seretide Accuhaler 50/500 from October 2018'.

The complainant had tried to contact GlaxoSmithKline but it was unable to provide him/her with a response.

The detailed response from GlaxoSmithKline is given below.

The Panel noted that the claim of an estimated annual saving to the NHS of £52 million from 1 September 2018 was qualified by five bulleted footnotes which appeared in small font on the second page of the letter. The third bullet point read 'It includes both Seretide and non-branded scripts for SFC, as Seretide is used as the reference price in the drug tariff. Savings based on NHS Drug Tariff for Seretide Evohaler 25/125, 25/250 and Seretide Accuhaler 50/500 from October 2018'.

The Panel noted GlaxoSmithKline's submission that the price reduction would provide significant financial benefit for the NHS directly, as from 1 September, the price of Seretide was reduced, and

indirectly as the Seretide list price was used as the reference price for all generic SFC equivalents. The indirect savings would be realised when the Drug Tariff was updated with the new lower Seretide prices which GlaxoSmithKline assumed would be in October.

The Panel noted that the second paragraph of the letter referred to the reduction of the list price on 1 September 2018 and gave estimated NHS savings. In the Panel's view the bullet point on the first page of the letter which stated 'For non-branded salmeterol fluticasone (SFC) scripts you will pay the new lower NHS tariff price and therefore you will see additional savings' implied that the savings for non-branded salmeterol fluticasone prescriptions could also be realised from 1 September 2018, which was not so. The Panel noted that the supplementary information to Clause 7 stated, *inter alia*, 'In general claims should not be qualified by the use of footnotes and the like'. In the Panel's view the qualification to the claim of an estimated annual saving of £52 million to the NHS which appeared in small font on the second page of the letter as a footnote did not negate the otherwise misleading impression of the claim at issue. The misleading implication was not capable of substantiation. Breaches of the Code were ruled.

The Panel noted that the complainant was variously in contact with GlaxoSmithKline from 3 September to 20 September without getting a satisfactory response. The Panel noted GlaxoSmithKline's submission that since the complaint came to its attention (21 September), the senior executive ultimately responsible for Seretide within the UK had had a telephone conversation with the complainant and followed that up with an email.

The Panel was concerned that it was only after receipt of this complaint that GlaxoSmithKline contacted the complainant to answer his/her query. In the Panel's view, GlaxoSmithKline should have been able to supply the answer sooner particularly given readers of the letter were encouraged to contact the company if they required further information. The Panel did not agree with GlaxoSmithKline's submission that the information requested did not relate to data supporting a claim but rather the provision of specific budgetary information. In the Panel's view the complainant was simply querying how the claim that savings based on non-branded salmeterol fluticasone prescriptions could be realised from 1 September when the lower Seretide prices were not yet reflected in the Drug Tariff. The Panel did not consider that GlaxoSmithKline provided the complainant with the relevant and accurate

information promptly or substantiated the claim as soon as possible and within ten working days upon the complainant's request and breaches of the Code were ruled. In the Panel's view, GlaxoSmithKline had failed to maintain high standards and a further breach of the Code was ruled.

A head of medicines optimisation at an NHS clinical commissioning group (CCG), complained about a letter dated 30 August 2018 (ref UK/SFC/0007/18b) sent by GlaxoSmithKline and headed 'Seretide List Price Reduction'. Seretide was a fixed dose combination of salmeterol and fluticasone (SFC) used in the treatment of asthma and of chronic obstructive pulmonary disease (COPD).

The letter explained that the list price of the three most commonly prescribed packs of Seretide would be reduced on 1 September 2018 providing the NHS an estimated annual saving of £52 million. The new Seretide prices were now lower than the equivalent dose/formulation of a branded generic. The statement at issue appeared as the second bullet point under the heading 'What does this mean if you have a Seretide rebate contract in place?' where readers were informed that for non-branded salmeterol fluticasone prescriptions, they would pay the new lower NHS tariff price and thus see additional savings.

COMPLAINT

The complainant noted the statement at issue and that the price had not been reduced in the September Drug Tariff as suggested and so there were no savings to be made from non-branded SFC prescriptions. The complainant also noted that in the preface of the September Drug Tariff, where it referred to October changes, there was no reference that the changes as suggested would occur. In that regard the complainant referred to a footnote on page 2 of the letter which stated that estimated savings were based on, *inter alia*, 'both Seretide and non-branded scripts for SFC [salmeterol fluticasone], as Seretide is used as the reference price in the drug tariff. Savings based on NHS Drug Tariff for Seretide Evohaler 25/125, 25/250 and Seretide Accuhaler 50/500 from October 2018'.

The complainant further noted that he/she had tried to contact GlaxoSmithKline but it was unable to provide him/her with a response.

When writing to GlaxoSmithKline, the Authority asked it to consider the requirements of Clauses 7.1, 7.2, 7.4, 7.5 and 9.1 of the Code.

RESPONSE

GlaxoSmithKline stated that on 8 August, it received official permission from the Department of Health and Social Services (DHSS) to reduce the list price of three different formulations/doses of Seretide. Official approval for the reduced Seretide list prices was received on 31 August. Accordingly, GlaxoSmithKline reduced the list prices for Seretide 50/125, and 50/250 Evohaler and Seretide 50/250 Accuhaler with effect from 1 September 2018 and so

savings for these three Seretide preparations were available with effect from that date.

On 31 August, the letter at issue was sent to inform those with NHS budgetary responsibility about the price change, so that they could plan their budgets accordingly. Apart from any positive promotional messages which could be made from this list price reduction, GlaxoSmithKline was also aware of the supplementary information to Clause 3.1 of the Code, which read:

'NHS organisations and others involved in the purchase of medicines need to estimate their likely budgets in advance and there is a need for them to receive advance information about the introduction of new medicines, or changes to existing medicines, which may significantly affect their level of expenditure.'

GlaxoSmithKline noted that the Seretide price reduction was substantial and amounted to around 33% for some of the dose/formulations. The price reduction would provide significant financial benefit for the NHS both directly (as the price of Seretide itself was reduced), but also indirectly (as the Seretide list price was used as the reference price for all generically prescribed SFC preparations).

GlaxoSmithKline noted that the complainant had highlighted the second bullet in the section of the letter headed 'What does that mean if you have a Seretide rebate contract in place?' which stated: 'For non-branded salmeterol fluticasone (SFC) scripts you will pay the new lower NHS price and therefore you will see additional savings ...' and that the complainant had noted that the price had not been reduced in the September Drug Tariff so there were no savings to be made for non-branded SFC prescriptions.

GlaxoSmithKline noted that it did not claim that the savings would be available from 1 September. The letter included an estimate of the savings that would be achieved by the NHS when the reduced Drug Tariff Price for Seretide was introduced, which the company assumed would be in October. This assumption was clearly set out in the third bullet point, under the section headed 'Estimated Savings are based on' which read:

'Savings based on the NHS Drug Tariff price for Seretide Evohaler and Accuhaler are **from October 2018**' (emphasis added).

GlaxoSmithKline stated that although it had approval for the list price reduction, it had no control as to when this would be adopted by the Drug Tariff as the Tariff was managed by the NHS Prescription Service and there were no DHSS Guidelines which indicated the timelines that might be anticipated in updating the Drug Tariff. The estimated savings referred to in the letter were based on the assumption that the Drug Tariff would be updated in October throughout the whole of the UK.

GlaxoSmithKline also noted that the complainant assumed that the list price reduction for Seretide

would also not be seen in the October Drug Tariff Price list. However, as referred to above, this assumption was incorrect.

GlaxoSmithKline reiterated that it had clearly set out in its letter the basis on which the estimated savings had been calculated and it considered that the information provided was accurate, balanced, fair, and capable of substantiation. The company thus denied any breach of Clauses 7.2 and 7.4.

GlaxoSmithKline stated that since sending its letter on 31 August, there had been several communications with the complainant; the information sent to him/her was quite general rather than a specific tailored response to his/her question for the CCG. However, since this complaint had come to the company's attention, a senior executive had had a telephone conversation with the complainant and followed that up with an email to answer his/her specific question.

GlaxoSmithKline noted that Clause 7.1 related to the provision of information 'about the medicines which the company markets'. In that regard, the information provided in the GlaxoSmithKline letter was not information about Seretide itself, but about a price change.

The complainant had requested specific budgetary information for an individual CCG, and an estimated forecast based on the model provided. GlaxoSmithKline noted that Clause 7.5 typically related to the provision of clinical trial data supporting a claim. The information requested did not relate to data supporting a claim.

GlaxoSmithKline denied a breach of Clauses 7.1 and 7.5.

GlaxoSmithKline submitted that it had provided correct and factual information for budgetary purposes and followed up accordingly to specific questions raised by the complainant. Therefore, high standards had been maintained and the company denied a breach of Clause 9.1.

When it reviewed the file in relation to this case, the Panel noted that the email correspondence between the complainant and GlaxoSmithKline, as provided by the complainant to the Authority, was, in error, not provided to GlaxoSmithKline in its entirety. GlaxoSmithKline was provided with this information and asked for any comments it might have.

In response GlaxoSmithKline submitted that when it received the complaint on 23 September, it fully investigated exchanges which had occurred between its employees and the complainant and therefore it was already aware of the correspondence. GlaxoSmithKline stated that the correspondence showed the ongoing dialogue before the complaint was submitted in September and which continued until 3 December 2018 and demonstrated the complexity of the complainant's questions.

GlaxoSmithKline stated that in its letter to the Authority, the complainant in his/her capacity as the

head of medicines optimisation in a named CCG, referred to the additional savings that 'the impact of the Seretide price reduction on non-branded salmeterol/fluticasone propionate preparations' not being available for September would have on his/her CCG, whereas the letter at issue referred to a 12 month period for the whole of the UK commencing on 1 October 2018. Although the calculation relating to the above was relatively easy to undertake at a national level, it was more complex at a CCG level as it required an in-depth analysis of the data available for that CCG, including the number of patients (asthma and COPD), Seretide prescriptions, other branded SFC prescriptions (of which there were 5) and non-branded SFC prescriptions. Such data needed to be fed into a budget impact model and then independently verified; all of which took time. However, in future, GlaxoSmithKline would provide payors and such-like, better clarity regarding anticipated timelines for providing answers to these more complex budgetary questions.

GlaxoSmithKline submitted that contrary to the complainant's expectations, the October 2018 Drug Tariff was updated with the reduced Seretide prices and validated the assumption made on the letter at issue. In addition, GlaxoSmithKline highlighted that following the complaint in September 2018, there had been ongoing email and verbal dialogue with the complainant regarding various other commercial considerations related to Seretide and which GlaxoSmithKline considered came to a successful conclusion on 3 December 2018 (details of the correspondence was provided). GlaxoSmithKline therefore denied any breach of Clauses 7.1, 7.2, 7.4, 7.5, and 9.1.

PANEL RULING

The Panel noted that the letter at issue, dated 30 August 2018, began by informing readers of important pricing changes for Seretide. It stated that on 1 September 2018, GlaxoSmithKline would reduce the list price of the three most commonly prescribed packs of Seretide providing the NHS an estimated annual saving of £52 million. This savings claim was referenced to data on file and had an asterisk which pointed to a footnote which appeared in small font on the second page of the letter titled 'Estimated savings are based on' and listed five bullet points. The first bullet point stated 'Using the difference between the current list price (August 2018) and the new price for Seretide Evohaler 25/125, 25/250 and Seretide Accuhaler 50/500'. The second bullet point stated 'Calculations use the data from the last twelve months of Seretide and non-branded Salmeterol Fluticasone (SFC) scripts and assumes that there will be no change in prescribing volumes over the next twelve months'. The third bullet point highlighted by the complainant stated 'It includes both Seretide and non-branded scripts for SFC, as Seretide is used as the reference price in the drug tariff. Savings based on NHS Drug Tariff for Seretide Evohaler 25/125, 25/250 and Seretide Accuhaler 50/500 from October 2018'.

The Panel noted GlaxoSmithKline's submission that the price reduction would provide significant

financial benefit for the NHS both directly (as the price of Seretide itself was reduced), but also indirectly (as the Seretide list price was used as the reference price for all generically prescribed salmeterol/fluticasone propionate preparations).

The Panel noted GlaxoSmithKline's submission that the list prices for Seretide 50/125, and 50/250 Evohaler and Seretide 50/250 Accuhaler were reduced with effect from 1 September 2018 and so savings for those three preparations were available with effect from that date. The Panel understood that this was the direct saving referred to by GlaxoSmithKline, if prescriptions for Seretide were received.

The Panel noted GlaxoSmithKline's submission that it was not claimed in the letter in question that the savings related to non-branded prescriptions would be available from 1 September. The Panel understood these to be the indirect savings referred to by GlaxoSmithKline when non-branded prescriptions for SFC were dispensed. The Panel noted GlaxoSmithKline's submission that the letter included an estimate of the savings that would be achieved by the NHS when the reduced Drug Tariff Price for Seretide was introduced, which the company assumed would be in October and which GlaxoSmithKline submitted was clearly set out in the footnote referred to above. GlaxoSmithKline further stated that although it had official approval for the list price reduction, it had no control as to when this would be adopted by the Drug Tariff. The estimated savings referred to in the letter were based on the assumption that the Drug Tariff would be updated in October throughout the whole of the UK. The Panel noted that the October 2018 Drug Tariff provided by GlaxoSmithKline did appear to reflect the new lower Seretide prices.

It appeared to the Panel that the direct savings referred to based on Seretide prescriptions could be realised from 1 September 2018 but the savings based on the non-branded SFC prescriptions could not be realised until the new lower Seretide reference prices were reflected in the Drug Tariff which occurred in October.

The Panel noted that the second paragraph of the letter in question referred to the reduction of the list price on 1 September and gave estimated NHS savings. In the Panel's view the bullet point highlighted by the complainant on the first page of the letter which stated 'For non-branded salmeterol fluticasone (SFC) scripts you will pay the new lower NHS tariff price and therefore you will see additional savings' implied that the savings for non-branded salmeterol fluticasone prescriptions could also be realised from 1 September 2018, which was not so. The Panel noted that the supplementary information to Clause 7 stated, *inter alia*, 'In general claims should not be qualified by the use of footnotes and the like'. In the Panel's view, the qualification to the claim of an estimated annual saving of £52 million to the NHS which appeared in small font on the second page of the letter as a footnote did not negate the otherwise misleading impression of the claim at issue. The misleading implication was not capable of

substantiation. Breaches of Clauses 7.2 and 7.4 were ruled.

The Panel noted the complainant's statement that he/she had tried to contact GlaxoSmithKline with regard to the fact the Seretide price was not reduced in the September Drug Tariff, and it did not appear that it would be reduced in the October Drug Tariff so there were no savings to be made from non-branded SFC prescriptions; GlaxoSmithKline was unable to provide him/her with a response.

The Panel noted that the letter at issue told readers that if they would like to discuss the matter further then they should contact their GlaxoSmithKline local key account manager and named a GlaxoSmithKline employee and provided his/her email address. The Panel noted that the complainant first contacted GlaxoSmithKline by replying to an email, the content of which was similar to the letter at issue, on 3 September. The complainant contacted the GlaxoSmithKline employee named in the letter at issue on 5 September after not receiving a response to his/her email of 3 September. The GlaxoSmithKline employee responded the same day stating that he/she had forwarded the query to the head office team which was dealing specifically with rebate logistics and would respond as soon as possible. The GlaxoSmithKline employee followed up on 12 September and informed the complainant that the head office team was pulling together the figures to demonstrate the savings his/her CCG would see as a result of the price change but had to wait for it to be approved before sharing it with the complainant the following week. The complainant replied the following day reiterating his/her concerns and on 20 September the GlaxoSmithKline employee replied that the best thing would be for one of the Seretide team to telephone him/her to answer the questions in depth and asked if the complainant would be happy for him/her to arrange it. The Panel noted GlaxoSmithKline's submission that since the complaint came to its attention, a senior executive had spoken to the complainant directly by telephone and followed up with an email to answer his/her specific question.

The Panel noted GlaxoSmithKline's submission that it was already aware of the correspondence between the complainant and GlaxoSmithKline, as provided by the complainant to the Authority, which in error, was not previously provided to GlaxoSmithKline in its entirety. The Panel noted that GlaxoSmithKline provided additional correspondence which it submitted showed the ongoing dialogue between the complainant and GlaxoSmithKline which continued until 3 December 2018 and demonstrated the complexity of the questions being asked.

The Panel disagreed with GlaxoSmithKline's submission that the complaint referred to the additional savings that the impact of Seretide price reduction on non-branded SFC preparations not being available for September would have on the complainant's CCG. In the Panel's view, the complaint was more general: whether the suggested additional savings for non-branded SFC prescriptions could be realised when the September Drug Tariff did

not yet reflect the lower Seretide prices. It appeared that on 30 November, after the complaint was received and following GlaxoSmithKline's response, the complainant contacted GlaxoSmithKline with more specific questions. These subsequent questions did not form part of the complaint.

The Panel noted that Clause 7.1 stated that upon reasonable request, a company must promptly provide members of the health professions and other relevant decision makers with accurate and relevant information about the medicines which the company markets.

Clause 7.5 stated, *inter alia*, that substantiation for any information, claim or comparison must be provided as soon as possible, and certainly within ten working days, at the request of members of the health professions or other relevant decision makers. The Panel noted the supplementary information to Clause 7 stated that the application of the clause was not limited to information or claims of a medical or scientific nature. It included, *inter alia*, information or claims relating to pricing and market share.

The Panel noted that whilst GlaxoSmithKline appeared to be in contact with the complainant with regards to his/her query it was of concern that it was only after receipt of this complaint that

GlaxoSmithKline contacted him/her to answer it. In the Panel's view GlaxoSmithKline should have been able to answer the complainant's question sooner particularly given readers of the letter were encouraged to contact the company if they required further information. The Panel did not agree with GlaxoSmithKline's submission that the information requested did not relate to data supporting a claim but rather the provision of specific budgetary information. In the Panel's view the complainant was simply querying how the claim that savings based on non-branded SFC prescriptions could be realised from 1 September when the lower Seretide prices were not yet reflected in the Drug Tariff. The Panel did not consider that GlaxoSmithKline provided the complainant with the relevant and accurate information promptly or substantiated the claim as soon as possible and within ten working days upon the complainant's request and a breach of Clauses 7.1 and 7.5 were ruled. In the Panel's view GlaxoSmithKline had failed to maintain high standards and a breach of Clause 9.1 was ruled.

Complaint received **21 September 2018**

Case completed **17 April 2019**

ANONYMOUS, NON-CONTACTABLE v IPSEN

Promotion of Cabometyx

An anonymous, non-contactable complainant alleged that a meeting organised by Ipsen was a glorified sales pitch for Cabometyx (cabozantinib). Cabometyx was indicated for the treatment of advanced renal cell carcinoma (RCC).

The complainant stated that overall the meeting advocated the use of Cabometyx as the new gold standard. Side effects seemed only to occur with competitor products. Despite the mention of comparators, Votrient (pazopanib, marketed by Novartis) was not considered as a viable therapeutic option despite its effective use in first line therapy. Ipsen focused on Sutent (sunitinib, marketed by Pfizer) to publicise its new phase II study data irrespective of the current therapeutic landscape.

The complainant alleged that the meeting was biased and the scientific integrity of its content, questionable.

The detailed response from Ipsen is given below.

The Panel noted that materials associated with the meeting clearly stated that the meeting was promotional and was organised and funded by Ipsen; they included prescribing information for Cabometyx.

The Panel considered that the promotional nature of the meeting would be clear to those invited, Cabometyx was mentioned in the title of the meeting Stepping up: Bringing Cabometyx (cabozantinib) to the forefront of advanced renal cell carcinoma (RCC) treatment. The Panel did not consider that given the numerous mentions of the promotional nature of the meeting that those invited would have been expecting anything other than a promotional meeting. The Code required such meetings to include educational content. It was not disguised and the Panel therefore ruled no breach of the Code.

The Panel noted that according to the SPC the recommended dose of Cabometyx was 60mg once daily. Management of suspected adverse drug reactions might require temporary treatment interruption and/or dose reduction. When dose reduction was necessary it was recommended to reduce to 40mg daily and then to 20mg daily. Details for when dose interruptions were recommended were given.

The Panel noted Ipsen's submission regarding the responses to an unprompted question from the Chair to the panel at the end of the real-world experience section in relation to whether they were starting all patients on 60mg cabozantinib.

The Panel noted that one speaker stated that he/she would probably start at 60mg in normal weight patients but admitted that he/she needed to reduce to 40mg in a good number of patients which was then 'very nicely tolerated'. Escalating the dose if a patient tolerated 40mg never happened, so it was better to reduce the dose.

The second speaker stated, however, that he/she often started patients on 40mg, particularly the older and smaller patients and would then work up and down from that. The speaker further stated that individualised decisions should be made but many patients were not on 60mg long term.

The Panel noted that the briefing material for company attendees was clear that questions concerning off-label use of the medicine would not be forwarded to the Chair. It stressed that promotional representatives could only discuss on licence and anything out of licence had to be referred to the medical department through the usual process. The Panel noted that the speakers and the Chair had been similarly briefed with regard to questions concerning off label use of the medicine.

The Panel noted that the Cabometyx SPC stated that no specific dose adjustment in older people (≥ 65 years) was recommended nor was there any mention of a dose adjustment recommendation based on weight. The Panel considered that Ipsen's description of the second speaker's comment with regard to older and smaller patients often starting on 40mg at Ipsen's meeting amounted to advocating the use of a lower starting dose as alleged. This was inconsistent with the SPC and a breach of the Code was ruled. The Panel noted that Ipsen had briefed the speakers on the need to comply with the Code and that although the speaker was referring to his/her clinical approach, it was an established principle that pharmaceutical companies were responsible for what contracted speakers said on their behalf. Taking all the circumstances into account the Panel did not consider that the reference to starting older and smaller patients on 40mg meant that high standards had not been maintained and no breach of the Code was ruled. Further this did not bring discredit upon or reduce confidence in the pharmaceutical industry and the Panel ruled no breach of Clause 2.

The Panel noted that as submitted by Ipsen the presentation titled 'The RCC treatment landscape: where are we now?' included reference to pazopanib on a number of slides, and was variously referred to as first and second line therapy. The Panel did not consider that Votrient (pazopanib) was deliberately omitted or that it was not considered as

a viable therapeutic option as alleged and the Panel therefore ruled no breach of the Code.

The Panel noted that the complainant had not provided any specific detail in relation to his/her concern that side effects seemed to only occur with competitor products. The Panel noted that the presentation titled 'Cabometyx in advanced RCC' referred to the adverse events experienced during Cabometyx registration studies. During the real world experience part of the meeting, adverse events with cabozantinib were described. In the Panel's view the complainant had not provided evidence to show that Ipsen had misleadingly referred to only competitor medicines having side effects and not Cabometyx as alleged. No breach of the Code was ruled.

The Panel could find no reference to Cabometyx as the 'new gold standard' of care as alleged; it was described in the meeting closing remarks as a new first line option which helped set a new standard of care. The Panel further noted the complainant's comment that the success of Ipsen advocating Cabometyx as the new gold standard was evident when a member of the audience asked if it would be used as a competitor in future clinical trials. According to Ipsen, the question asked was what impact the CABOSUN data would have on trials that were currently set up to have sunitinib as a current standard of care. The Panel considered that there was no evidence that Ipsen had advocated Cabometyx as the new gold standard as alleged and no breach of the Code was ruled.

The complainant was further concerned that Ipsen focused on sunitinib to publicise its new Phase II study irrespective of the current therapeutic landscape. The Panel noted Ipsen's submission that in oncology generally, and in particular aRCC, the environment was rapidly evolving. This was a challenge for companies and clinicians because the pace of change often meant by the time a product became licensed, the comparator arm in the trial might no longer be a relevant standard of care. The Panel noted that CABOSUN was a Phase II study designed to evaluate the efficacy and safety of cabozantinib vs sunitinib. In the Panel's view it was not misleading for Ipsen to refer to sunitinib when discussing the CABOSUN study as it was the treatment in the comparator arm; Ipsen had within the meeting provided information on the current therapeutic landscape including currently licensed treatments and their position in the treatment guidelines referred to above. The Panel therefore ruled no breach of the Code.

The Panel noted that the meeting agenda referred to real-world experience with Cabometyx and not real-world evidence as referred to by the complainant. In the Panel's view it was not necessarily unacceptable to refer to a selection of case studies to demonstrate real world experience provided the way in which it was done was not misleading and complied with the Code. The Panel did not consider that the complainant provided evidence to show that the three case studies were presented as real-world evidence as alleged. The case studies were clearly

described as real-world experience and no breach of the Code was ruled.

The Panel noted its comments and rulings above and did not consider that Ipsen had failed to maintain high standards nor had it brought discredit upon or reduced confidence in the industry, no breach of the Code was ruled including no breach of Clause 2.

An anonymous, non-contactable complainant complained about the promotion of cabozantinib by Ipsen Limited at a meeting in September 2018. Ipsen marketed cabozantinib as film-coated tablets (Cabometyx) for the treatment of advanced renal cell carcinoma.

COMPLAINT

The complainant stated that he/she had attended a meeting organised by Ipsen, in London with an option for virtual attendance from a centre or from home. The complainant stated that he/she was horrified and shocked to find that the meeting was just a glorified sales pitch for cabozantinib. Plenty of subliminal messages were eventually distilled into advocating the use of cabozantinib as the new gold standard. This proved to be effective as demonstrated by a question from a member of the audience querying whether cabozantinib would be used as a comparator in future clinical trials.

The complainant stated that while other companies endeavoured to follow the right route by providing evidence of safety and efficacy via the legitimate regulatory channels, Ipsen circumvented this and advocated the use of lower starting doses via the chairman, especially to those who had not used it before.

The section on real-world evidence comprised a handful of case studies. Notwithstanding that the definition of real-world evidence was unclear, it could not be based on the observation of a few patients to generalise and present as evidence. The in-built messages were a mixture of general comments woven in with facts intended to emphasise cabozantinib as the gold standard. Side-effects seemed to only occur with competitor products. Despite the individual mention of comparators, one was deliberately omitted. Votrient (pazopanib, marketed by Novartis) was not considered as a viable therapeutic option despite its effective use in first line therapy. Ipsen's focus was on Sutent (sunitinib, marketed by Pfizer) to publicise its new phase II study data irrespective of the current therapeutic landscape.

The complainant alleged that the meeting content was highly biased, and the scientific integrity of its content questionable. Ipsen's behaviour was unacceptable; it needed to step up.

When writing to Ipsen, the Authority asked it to consider the requirements of Clauses 2, 3.2, 7.2, 7.4, 7.9, 9.1 and 12.1 of the Code.

RESPONSE

Ipsen explained that cabozantinib was a small molecule that inhibited multiple receptor tyrosine kinases. It was granted a marketing authorization in September 2016 for the treatment of advanced renal cell carcinoma (aRCC) in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy. In May 2018, the European Commission confirmed that cabozantinib had been granted a marketing authorization variation for the treatment of aRCC in treatment-naïve adults with intermediate or poor risk per the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) criteria.

Ipsen assumed that the meeting to which the complainant referred, was one which it organised, funded and hosted on the evening of Wednesday, 26 September 2018. The title of the event was 'Stepping Up: Bringing Cabometyx ▼(cabozantinib) to the forefront of advanced renal cell carcinoma (aRCC) treatment'. The title was aimed at representing the fact that the newer indication for the medicine, which received a marketing authorization this year, was for first line/front line patients. It was a promotional meeting focussed on educating appropriate UK health professionals involved in the clinical management of RCC on the use of Cabometyx for the treatment of aRCC. Ipsen submitted that the event had been meticulously and carefully planned and executed to meet the requirements of the Code and Ipsen's high standards for the quality of content, and the company's robust internal processes. The feedback received from the evening was very positive (copies of evaluation forms were provided).

Ipsen regretted that one of the attendees was horrified and shocked to find that the meeting was just a glorified sales pitch for Cabometyx. Working with a panel of leading international and UK experts in RCC management, the meeting was designed to provide fair, accurate, objective and balanced information regarding Cabometyx as a treatment option in aRCC to appropriate UK health professionals, in a manner compliant with the Code, in order to provide good quality medical education and thus help to improve patient care.

Ipsen noted that Clause 12.1 of the Code stated that promotional material and activities must not be disguised. Ipsen had acted in accordance with Clause 12.1, Clause 9.10 ('Material relating to medicines and their uses, whether promotional or not, and information relating to human health or diseases which is sponsored by a pharmaceutical company must clearly indicate that it has been sponsored by that company') and Clause 22.4 ('When meetings are sponsored by pharmaceutical companies, that fact must be disclosed in all of the papers relating to the meetings and in any published proceedings. The declaration of sponsorship must be sufficiently prominent to ensure that readers are aware of it at the outset'). The meeting was clearly advertised as a promotional event organised and funded by Ipsen. All invitations and other related documents and materials for the meeting (including its title) included a clear statement to that effect. Further, the content of the meeting, and the way in which it was presented and to whom, gave a very

clear indication of its promotional nature which was aligned with Clause 1.2 ('The term "promotion" means any activity undertaken by a pharmaceutical company or with its authority which promotes the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicines'). Ipsen provided copies of materials associated with the meeting, eg invitations and 'Save the Date' items.

Ipsen disputed the complainant's submission that plenty of subliminal messages were eventually distilled into advocating the use of Cabometyx as the new gold standard for the following reasons:

- 1 The meeting was clearly advertised as a promotional meeting on the use of Cabometyx in aRCC, as outlined above, so attendees should have expected discussion on this treatment. Education was the primary purpose of this meeting and this was reflected in the objectives outlined in the meeting approval form, speaker briefings and in the relevant materials such as the programme and invitations.
- 2 The faculty comprised nationally and internationally recognised experts in the area with extensive experience across the treatment landscape for aRCC. Speaker biographies were provided in the meeting booklet (CMX-UK-001496).
- 3 The faculty was extensively briefed by Ipsen by way of a speaker contract, a written briefing, and a telephone/face-to-face briefing. The briefing document, contracts and a document containing extra briefing guidance were provided.
- 4 The presentations included full reference to all licensed products in the current treatment pathway, two sets of internationally recognised guidelines from reputable professional societies in oncology and a faculty-proposed treatment pathway consistent with both of the aforementioned;
- 5 All attendees had the opportunity to question the faculty. The questions were screened by the medical advisor (a qualified medical final signatory) before being passed on to the chair to ensure that they were not inconsistent with the particulars in the summary of product characteristics (SPC), nor likely to elicit answers inconsistent with the SPC.
- 6 Cabometyx was never labelled as a 'gold standard' during the meeting nor was there anything to suggest that the tyrosine kinase inhibitor (TKI) should be used as the treatment of choice. This was clearly supported by the accurate, fair, balanced, objective, unambiguous and up-to-date content of the presentations delivered during the meeting, consistent with Clause 7.2, and by the briefing delivered to the speakers before the meeting. Furthermore, the debate amongst the panel, and the summary in the penultimate slide from the meeting, focussed on whether Cabometyx should be considered as:

a new standard of care in 1L aRCC patients of intermediate or poor risk. This was consistent with the SPC, current scientific opinion and international clinical guidelines.

a standard of care in 2L patients previously treated with a vascular endothelial growth factor (VEGF)-targeted treatment. This was consistent with the SPC, current scientific opinion and international clinical guidelines.

- 7 Ipsen provided a full list of questions submitted by the attendees and in particular noted one question passed on to the chair which was 'Could the faculty comment on how it feels about changing practice based on an underpowered phase 2 study? Are our regulatory bodies losing academic rigour?'. Ipsen submitted that the question demonstrated that it had facilitated a balanced debate about cabozantinib.

In summary, Ipsen did not agree with the complainant's statement about advocating the use of Cabometyx as a gold standard for the reasons described above. Every effort was made to ensure that the information communicated to the audience was accurate, balanced and not misleading, particularly around the use of Cabometyx and its position within the treatment landscape. Ipsen referred to the speaker briefing document.

Ipsen noted that the complainant had referred to a question raised from a member of the audience querying whether Cabometyx would be used as a comparator in future clinical trials. Ipsen submitted that the question, 'What do you think the impact of the CABOSUN data will have on trials that are currently set up to have sunitinib as a current standard of care?', from a clinical research nurse who attended the meeting in London, was spontaneous and unprompted. This was a valid and appropriate question when new treatments became available. In oncology generally, and in aRCC in particular, the environment was rapidly evolving. This was a challenge for companies developing medicines and for clinicians involved in trials and the treatment of patients in routine clinical practice, because the pace of change often meant by the time a product became licensed, the comparator arm in the trial might no longer be a relevant standard of care eg the METEOR trial for Cabometyx. Although compared against everolimus (Afinitor, marketed by Novartis) as a standard of care when the trial began, it did not provide randomised controlled data compared to newer agents. Everolimus was now used in a limited number of patients in the second line setting in aRCC so it was therefore difficult for clinicians to make assessments of relative efficacy.

Ipsen stated that it did not advocate the use of lower starting doses as alleged.

The registration studies of Cabometyx (METEOR and CABOSUN) were presented in detail during the 'Cabometyx in advanced RCC' session and, the study designs, including the clinical trial starting dose of 60mg (consistent with the recommended dose in the SPC) were clearly displayed in the slides

(CMX-UK-001658 Slides 18 and 38) and articulated verbally by the speaker.

Five slides, which appeared at the start of each presentation, stated where the Cabometyx prescribing information could be found; the prescribing information included the recommended starting dose of 60mg. The prescribing information also appeared at the end of every presentation. The case study presented by a speaker referred to a patient started on 60mg, which was documented on slide 7.

As stated above, Ipsen clearly briefed the speakers with a certified briefing, which included the statement: 'All presentations must be consistent with the licensed indications of cabozantinib' (ref CMX-UK-001500). In addition, prescribing information was sent to the speakers with the brief. Ipsen reinforced the briefing, and specifically mentioned the importance of referring to the licensed recommended dose on the briefing calls with the faculty.

The prescribing information was included in all applicable materials, both electronic and printed, distributed or displayed to health professionals as a part of this meeting, consistent with Clause 4.

During the panel discussion at the end of the real-world experience section, the chair asked the panel an unprompted and spontaneous question:

'I just maybe want to ask something on dose, which is something we have not really, ... talked a bit about it then we haven't talked about it very much, with cabozantinib for people who are just starting to use the drug in the first place, are you starting everybody on 60mg? What's your feeling? What feeling, we both use the drug I think quite a lot now, or is there a bit of variation on that, again in real world type of practice, again it is all about patients tolerating it, isn't it?'

In response to that question the panel members gave the following response:

'So I would say in a normal weight patient I would probably start on 60mg but I have to admit that in a good number of patients we need to reduce to 40mg which is then very nicely tolerated. This was exactly what was also shown in the phase 3 trial METEOR trial, so probably if 60mg is quite challenging for many patients but 40mg is well tolerated. But we would nevertheless try to start on 60mg because then escalating the dose if a patient tolerates 40mg this never happens in fact, so better reducing the dose then also you can offer something because when a patient complains about side effects, you need to offer something, dose reduction is something you can offer, going from 40 escalating to 60 I think is difficult the other way around doesn't really work in clinical practice.'

and

'We often particularly with the older and smaller

patients start at 40mg and then work up and down from that. Many of these patients, I only have second line experience very few of them are on the full dose of Sunitinib by the time we meet them and I think you need to be, you know you have to use individualised decisions but I would say many patients are not on 60 long term.'

Ipsen submitted that it had taken every opportunity to brief the speakers to ensure that they spoke in accordance with the terms of the marketing authorization and were not inconsistent with the particulars listed in the Cabometyx SPC. A video recording of the interaction noted above demonstrated that it was very brief, it was a statement purely of an individual clinician's personal practice and experience and was, on the whole, not inconsistent with the SPC and the panel quickly moved the discussion on.

Given the information above, the use of a lower starting dose was not advocated by or on behalf of Ipsen during the meeting and every effort was made to ensure that the content of the presentations and the speakers' briefs were not inconsistent with the Cabometyx SPC and in accordance with Clause 3.2 of the Code.

Ipsen submitted that the 'real-world evidence section' that the complainant appeared to refer to was the presentation on 'Real-world experience with Cabometyx: The impact across the spectrum of aRCC'. The terms 'real-world evidence' and 'real-world experience' were not the same and thus were not to be used interchangeably. The segment of the meeting programme entitled 'real-world experience' was for the speakers to share their clinical experience gained in real-world practice. They were presented as case studies and were not presented in the context of real-world evidence. The presented cases were based on real patients, describing real events and the individual case studies were not presented in a way to suggest generalisability. The case studies were shared with the attendees who were all specialists in oncology and RCC and therefore it was appropriate and was fully understood in the context it was presented.

During this presentation, three patient cases were presented by two speakers. The purpose was to demonstrate the clinicians' real-life experience of managing aRCC patients in the second line setting in their clinical practice and not to generalise the case study findings.

With regard to the complainant's comment that 'side-effects seemed to only occur with competitor products', Ipsen noted that the case studies presented on Cabometyx included a number of adverse drug reactions related to its use, and therefore upheld the principle of Clause 7.9.

Case study 1 included an adverse drug reaction of hypomagnesaemia experienced as a result of treatment with Cabometyx. In the same case study, the patient had a 9-month response to treatment with Cabometyx, and on progression started treatment with nivolumab (Opdivo, marketed by

Bristol-Myers Squibb), to which the patient had no documented adverse reactions and a good response and he/she currently remained on that treatment.

The case study presented by a speaker included adverse reactions for a patient who received Cabometyx as a second line treatment including diarrhoea grade 3 when receiving a 60mg dose and following dose reduction to 40mg experienced grade 2 hypertension, diarrhoea and hand-foot syndrome and grade 1 hypothyroidism, fatigue, dysphonia and hair and skin-depigmentation (slides 7 and 8, CMX-UK-001676).

In summary, the case studies presented during the meeting were not atypical of individual patients in clinical practice. Every effort was made to ensure the results were not misconstrued as 'real-world evidence' and that they did not mislead on the efficacy and tolerability of Cabometyx.

With regard to the allegation that pazopanib had been deliberately omitted, Ipsen noted that the presentation entitled: 'The RCC treatment landscape: where are we now?' included a balanced representation of the currently licensed treatments for aRCC. Slide 7 featured a timeline which outlined the year of marketing authorization granted for all licensed products in aRCC since 2006, not just Cabometyx. Pazopanib was documented on that slide. Slides 8 and 9 showed the current treatment guidelines for metastatic clear cell RCC from the European Association of Urology (EAU) and the European Society of Medical Oncology (ESMO), which had been adapted for currently licensed treatments. Pazopanib was referred to on slide 8 as a first-line treatment in International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) favourable-risk disease patients and on slide 9 as first- and second-line standard treatment choices for clear cell RCC and as a therapeutic option for non-clear cell RCC.

On slide 16, a treatment pathway proposed by an internationally-recognised expert in aRCC, consistent with current scientific opinion (as evidenced by the aforementioned guidelines) included pazopanib as a first-line treatment option for metastatic clear-cell RCC.

In summary, Ipsen stated that the complainant's statement about pazopanib was incorrect. Pazopanib had been mentioned on numerous slides within the appropriate presentation and was considered a treatment option for aRCC.

Ipsen stated that the presentation entitled 'Cabometyx in advanced RCC' (ref CMX-UK-001657) included a balanced representation of the two registration trials for Cabometyx – CABOSUN and METEOR. Ipsen noted the complainant's comment regarding Ipsen's 'focus on sunitinib'. Cabometyx was licensed for untreated patients with aRCC of intermediate or poor risk as defined by IMDC criteria as a result of CABOSUN trial where cabozantinib was compared to sunitinib. It was therefore only appropriate to focus on sunitinib as a comparator because it was consistent with the data in the

summary of product characteristics (SPC), and cross-trial comparison would be inappropriate. Ipsen's view was that any attempt to compare cabozantinib to pazopanib would not be consistent with Clause 7 of the Code.

In summary, Ipsen stated that the meeting fully represented the available treatment options and the current treatment pathway consistent with published data from the phase 2 CABOSUN trial, and current scientific opinion.

General comments relating to Clause 7

Ipsen noted that the meeting was a single event comprised of the following presentations:

Chair's welcome and introduction to the UK environment for advanced RCC management, Cabometyx in advanced RCC; The RCC treatment landscape: where are we now?; Cabometyx in advanced RCC; Real world experience with Cabometyx: the impact across the spectrum of advanced RCC and summary and hub meeting close.

The overall balance of the presentations reflected the efficacy and safety balance for Cabometyx as a treatment for advanced renal cell carcinoma, and all presentations were substantiated. As part of the presentations, the full study design, primary endpoint, relevant secondary endpoints, and summary of safety information were presented by one member of the faculty. This could be found on slides 16-20, 26, 35, 38-45 of the Cabometyx in aRCC presentation. The safety and efficacy of the TKI was also highlighted by the speakers for the individual patient cases during the session: 'Real-world experience with Cabometyx: The impact across the spectrum of advanced RCC', which demonstrated actual patient adverse drug reactions seen by clinicians in the clinical setting. Slides 3 and 7 of the chair's introduction included an overview of the objectives of the meeting and one slide outlined the licensed indications for all currently approved treatments for aRCC.

In summary, Ipsen stated that it had demonstrated that none of the presentations were inconsistent with the marketing authorization for Cabometyx and they all met the requirements of the Code. The information presented on the efficacy and safety of the product was accurate and balanced.

Ipsen stated that patients with aRCC, and in particular with intermediate or poor risk RCC per IMDC criteria, by definition had a very poor prognosis and it was an area of unmet clinical need. Ipsen was proud of the work it did to help improve the outcomes of patients with aRCC, and took seriously its responsibility to ensure promotional activities were carried out in a manner that was not inconsistent with the marketing authorization of Cabometyx, which protected and promoted patient safety, provided valuable medical education to relevant health professionals so as to improve patient care, and upheld the reputation of the UK pharmaceutical industry.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the Prescription Medicines Code of Practice Authority stated that anonymous complaints would be accepted but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties.

The Panel noted that the save the date printed and electronic notifications, template for emailing the save the date information, invitations, and meeting agenda clearly stated that the meeting was promotional and was organised and funded by Ipsen. The documents included prescribing information for Cabometyx. The Ipsen key account managers were to discuss the meeting in more detail when showing the invitation to the health professional. The registration confirmation and reminder sent by Cabometyx marketing, stated that the meeting was promotional and included prescribing information. The registration portal pages also mentioned that the meeting was promotional on the registration page and included access to the prescribing information and the SPC. The rolling banner, meeting booklet, webcast pages and signing in sheets stated that the meeting was promotional. The speakers' slides stated that the meeting was a promotional meeting.

The Panel considered that it would be clear to those invited to the meeting, whether that be to the London venue or other venues or online, that the meeting was promotional. Health professionals would be very aware that the meeting was organised by Ipsen about one of its products; Cabometyx was mentioned in the title of the meeting (Stepping up: Bringing Cabometyx (cabozantinib) to the forefront of advanced renal cell carcinoma (RCC) treatment) which was included on the materials listed above. The Panel did not consider that given the numerous mentions of the promotional nature of the meeting that those invited would have been expecting anything other than a promotional meeting. The Code required such meetings to include educational content. It was not disguised and the Panel therefore ruled no breach of Clause 12.1.

The Panel noted that the Ipsen briefing documents for speakers and chairs were clear regarding the need to comply with the ABPI Code and that questions about unlicensed medicines or indications could not be answered during the event. Ipsen's medical information department would respond to such questions.

The Panel noted that according to the SPC the recommended dose of Cabometyx was 60mg once daily. Treatment should continue until the patient was no longer clinically benefitting from therapy or until unacceptable toxicity occurred. Management of suspected adverse drug reactions might require temporary treatment interruption and/or dose reduction. When dose reduction was necessary it was recommended to reduce to 40mg daily and then to 20mg daily. Details for when dose

interruptions were recommended were given. Dose reductions were recommended for events that if persistent could become serious or intolerable. Section 4.4 Special warnings and precautions for use of the SPC referred to most events occurring early in the course of treatment and the need for the physician to evaluate the patient closely during the first eight weeks of treatment to determine if dose modifications were warranted. The SPC referred to renal cell carcinoma following prior VEGF targeted therapy and that dose reductions and dose interruptions due to adverse events occurred in 59.8% and 70% respectively of cabozantinib treated patients in the pivotal clinical trial (METEOR). Two dose reductions were required in 19.3% of patients. The median time to the first dose reduction was 55 days and to the first dose interruption was 38 days. In treatment-naïve renal cell carcinoma, dose reductions and dose interruptions occurred in 46% and 73%, respectively, of cabozantinib treated patients in the clinical trial (CABOSUN).

The Panel noted Ipsen's submission regarding the responses to an unprompted question from the Chair to the panel at the end of the real-world experience section in relation to whether they were starting all patients on 60mg cabozantinib.

The Panel noted that one speaker stated that he/she would probably start at 60mg in normal weight patients but admitted that he/she needed to reduce to 40mg in a good number of patients which was then 'very nicely tolerated' and this was what was also shown in the METEOR trial. He/she would nevertheless try to start patients on 60mg because escalating the dose if a patient tolerated 40mg never happened, so it was better to reduce the dose. Dose reduction could then be offered if a patient complained about side effects.

Another speaker stated, however, that he/she often started patients on 40mg, particularly the older and smaller patients and would then work up and down from that. The speaker further stated that individualised decisions should be made but many patients were not on 60mg long term.

The Panel noted that the briefing material for company attendees was clear that questions concerning off label use of the medicine would not be forwarded to the Chair. It stressed that promotional representatives could only discuss on licence and anything out of licence had to be referred to the medical department through the usual process. The Panel noted that the speakers and the Chair had been similarly briefed with regard to questions concerning off label use of the medicine.

The Panel noted that the Cabometyx SPC stated that no specific dose adjustment in older people (≥ 65 years) was recommended nor was there any mention of a dose adjustment recommendation based on weight. The Panel considered that Ipsen's description of the second speaker's comment with regard to older and smaller patients often starting on 40mg at Ipsen's meeting amounted to advocating the use of a lower starting dose as alleged. This was inconsistent with the SPC and a breach of Clause 3.2

of the Code was ruled. The data in the SPC showed that many patients had dose reductions. The Panel noted the company's instructions regarding the need to comply with the Code and that the speaker was referring to his clinical approach. The Panel noted, however, that it was an established principle that in such circumstances, pharmaceutical companies were responsible for what contracted speakers said on their behalf. Taking all the circumstances into account the Panel did not consider that the reference to starting older and smaller patients on 40mg meant that high standards had not been maintained and no breach of Clause 9.1 was ruled. Further this did not bring discredit upon or reduce confidence in the pharmaceutical industry and the Panel ruled no breach of Clause 2 of the Code.

The Panel noted that as submitted by Ipsen the presentation titled 'The RCC treatment landscape: where are we now?' included reference to pazopanib on a number of slides. Slide 7 featured a timeline which outlined the year of marketing authorization granted for RCC products in Europe since 2006. Slides 8 and 9 showed the current treatment guidelines for metastatic clear cell RCC from the European Association of Urology (EAU) and the European Society of Medical Oncology (ESMO), which had been adapted for currently licensed treatments. Pazopanib was referred to on slide 8 as a first-line treatment in IMDC favourable-risk disease and IMDC intermediate and poor-risk disease patients and on slide 9 as first-and second-line standard treatment choices for clear cell RCC and as a therapeutic option for non-clear cell RCC. According to Ipsen, slide 16 showed a treatment pathway proposed by an internationally-recognised expert in RCC, consistent with current scientific opinion (as evidenced by the aforementioned guidelines) included pazopanib as a first-line treatment option for metastatic clear-cell RCC. Pazopanib was further mentioned in the presentation titled 'Cabometyx in advanced RCC'. The Panel did not consider that Votrient (pazopanib, marketed by Novartis) was deliberately omitted or that it was not considered as a viable therapeutic option as alleged and the Panel therefore ruled no breach of Clause 7.2.

The Panel noted that the complainant had not provided any specific detail in relation to his/her concern that side-effects seemed to only occur with competitor products. The Panel noted that the presentation titled 'Cabometyx in advanced RCC' which discussed the two main Cabometyx registration studies referred to the adverse events experienced during those studies. Further, the conclusion slide of that presentation stated, *inter alia*, that the side effect profile of Cabometyx was well known and not really different from tyrosine kinase inhibitors (TKIs) that had been used over the last 12 years and advised that proactive adverse event management was crucial.

The Panel further noted that whilst the presentation of the first case study during the real-world experience section stated that cabozantinib was generally well tolerated, it stated that the patient experienced hypomagnesaemia as a result of treatment with Cabometyx. In the same case study,

the patient had a 9-month response to treatment with cabozantinib and on progression started treatment with nivolumab (Opdivo, marketed by Bristol-Myers Squibb), which the patient appeared to have tolerated well with a good response. The second case study involved a patient who was changed from sunitinib to cabozantinib due to significant skin toxicity experienced whilst on sunitinib and appeared to have minimal side effects whilst on cabozantinib. The third case study involved a patient that had to have a dose reduction from 60mg to 40mg cabozantinib after three weeks due to a prolonged episode of Grade 3 diarrhoea. A number of adverse events were listed that were experienced after the dose reduction including Grade 2 hypertension, diarrhoea and hand-foot syndrome and Grade 1 hypothyroidism, fatigue, dysphonia, and hair and skin depigmentation. In the Panel's view the complainant had not provided evidence to show that Ipsen had misleadingly referred to only competitor medicines having side effects and not Cabometyx as alleged and no breach of Clauses 7.2 and 7.9 were ruled.

The Panel could not find reference in the presentations to Cabometyx as the 'new gold standard' of care as alleged; it was described in the meeting closing remarks as a new first line option which helped set a new standard of care for treatment of aRCC patients which in the Panel's view reflected the marketing authorization variation that was granted for the treatment of aRCC in treatment-naïve adults with intermediate or poor risk. The Panel further noted the complainant's comment that the success of Ipsen advocating Cabometyx as the new gold standard was evident when a member of the audience asked if it would be used as a competitor in future clinical trials. The Panel noted that the presentations included reference to licensed products in the current treatment pathway and two sets of internationally recognised guidelines from professional societies in oncology. The Panel noted Ipsen's submission that a faculty-proposed treatment pathway consistent with both of the aforementioned guidelines was also included. Further, according to Ipsen, the question asked by the audience member was what impact the CABOSUN data would have on trials that were currently set up to have sunitinib as a current standard of care. The Panel considered that there was no evidence that Ipsen had advocated Cabometyx as the new gold standard as alleged and

no breach of Clauses 7.2 and 7.4 were ruled. The complainant was further concerned that Ipsen focused on sunitinib to publicise its new Phase II study irrespective of the current therapeutic landscape. The Panel noted Ipsen's submission that in oncology generally, and in particular aRCC, the environment was rapidly evolving. This was a challenge for companies developing medicines and for clinicians involved in trials and the treatment of patients in routine clinical practice, because the pace of change often meant by the time a product became licensed, the comparator arm in the trial might no longer be a relevant standard of care. The Panel noted that CABOSUN was a Phase II study designed to evaluate the efficacy and safety of cabozantinib vs sunitinib in patients with previously untreated locally advanced or metastatic RCC. In the Panel's view it was not misleading for Ipsen to refer to sunitinib when discussing the CABOSUN study as it was the treatment in the comparator arm; Ipsen had within the meeting provided information on the current therapeutic landscape including currently licensed treatments and their position in the treatment guidelines referred to above. The Panel therefore ruled no breach of Clause 7.2.

The Panel noted that the meeting agenda referred to real world experience with Cabometyx and not real-world evidence as referred to by the complainant. In the Panel's view it was not necessarily unacceptable to refer to a selection of case studies to demonstrate real world experience provided the way in which it was done was not misleading and complied with the Code. The Panel did not consider that the complainant provided evidence to show that the three case studies were presented as real-world evidence as alleged. In the Panel's view the case studies were clearly described as real-world experience, and thus the Panel ruled no breach of Clauses 7.2 and 7.4.

The Panel noted its comments and rulings above and did not consider that Ipsen had failed to maintain high standards nor had it brought discredit upon or reduced confidence in the industry and no breach of Clauses 9.1 and 2 were ruled.

Complaint received **3 October 2018**

Case completed **6 December 2018**

ANONYMOUS, NON-CONTACTABLE HEALTH PROFESSIONAL v MERCK SERONO

Terms of trade

An anonymous, non-contactable complainant, who described him/herself as a consultant gynaecologist, complained about terms of trade offered by Merck Serono in association with the purchase of Gonal-F (follitropin alfa) and Ovitrelle (choriogonadotrophin alfa). The complainant alleged that the company would be willing to off-set the price of Gonal-F and Ovitrelle by reducing the cost of equipment and providing other business support services to the complainant's clinic. If the complainant did not buy Gonal-F he/she would have to pay the full price for any of Merck Serono's equipment he/she wanted to purchase, and for Ovitrelle. The complainant stated that he/she was surprised by this proposition, especially as in the past the price of his/her medicines had not been linked to the purchase price of equipment or sponsorship and support.

The detailed response from Merck Serono is given below.

The Panel noted that according to Merck Serono there would be no offers linking its medicines and its equipment. The Panel further noted Merck Serono's submission that it would not link the price of prescription medicines or the purchase of fertility products to sponsorship and support.

The complainant had not provided evidence to demonstrate on the balance of probabilities that Merck Serono had linked the price of its medicines to the cost of equipment or to any sponsorship and/or support. The Panel therefore ruled no breaches of the Code including Clause 2.

An anonymous, non-contactable complainant, who described him/herself as a consultant gynaecologist, complained about terms of trade offered by Merck Serono in association with the purchase of Gonal-F (follitropin alfa) and Ovitrelle (choriogonadotrophin alfa). Gonal-F and Ovitrelle were both indicated, *inter alia*, for use in in vitro fertilisation (IVF) techniques.

COMPLAINT

The complainant alleged that managers from Merck Serono had informed him/her that they would be willing to off-set the price of Gonal-F and Ovitrelle by reducing the cost of their laboratory equipment and providing other business support services to the complainant's clinic. If the complainant did not buy Gonal-F he/she would have to pay the full price for any of Merck Serono's laboratory equipment he/she wanted to purchase, and for Ovitrelle.

The complainant stated that he/she was surprised by this proposition, especially as in the past the price of his/her medicines had not been linked to the purchase price of laboratory equipment or sponsorship and support.

The complainant understood from colleagues in other clinics that they had had the same type of 'offers' extended to them.

When writing to Merck Serono, the Authority requested that it consider the requirements of Clauses 2, 9.1, 18.1, 19.1 and 19.2.

RESPONSE

Merck Serono submitted that it was difficult to conduct a comprehensive investigation as the complainant did not identify a specific manager or clinic, nor a timeframe during which the alleged interaction took place.

Merck Serono stated that various staff were interviewed and/or contacted about the complaint and to understand if any submission for exceptional requirements for pricing proposals was approved and for details about any interaction that could have led to the complaint. No further information or evidence of an interaction that could have led to the complaint came to light.

Merck Serono stated that it currently sold and distributed fertility technology products (such as laboratory equipment) and prescription medicines. This part of the business was organised into one fertility business franchise with managers who worked with fertility technology products and prescription medicines and interacted with NHS and private fertility clinics. However, commercial offerings and contracts for the procurement, supply or pricing of fertility technology products or prescription medicines were separate.

Merck Serono explained that currently all prescription products were made available to the NHS via tenders. Fertility technology products might occasionally be made available to the NHS via separate tenders, but in general Merck Serono would be asked by the NHS trust to provide a written quote for the relevant fertility technology products.

Merck Serono stated that when it worked with private clinics it had two guidance documents on pricing - one related to pricing for its prescription medicines and the other related to pricing for fertility technology products. Merck Serono stated that it did not currently have any other pricing modules for private clinics.

The pricing guidance was the only financial offers Merck Serono had. The company did not currently have, nor had it had to date, any financial offers available to its customers whereby the price of Gonal-F and Ovitrelle (or any other prescription medicines) were offset by a reduction in the price of any of the fertility technology products or by the provision of business support services, including sponsorship and support.

Merck Serono submitted that its fertility team was last trained on the pricing guidance in October 2018 at the quarterly fertility team meeting. Merck Serono submitted that the pricing guidance was comprehensive and no other instructions or direction on pricing was provided.

With regard to Clauses 18.1, 19.1 and 19.2, Merck Serono stated that it had a strict policy in relation to sponsorship, grants and medical education services. This was governed by a policy called 'Appropriate Interactions between Medical and Commercial Functions' which did not allow commercial functions to be involved in any decisions relating to grants and sponsorships. All requests received by Merck Serono's commercial teams must be sent to the medical team which independently reviewed each request and also operated with a budget independent of the budget operated by commercial teams. In addition, the internal approval system did not allow staff working in commercial functions to enter or approve any such requests.

Merck Serono thus refuted any claims that it would ever link the price of its prescription medicines or the purchase of its fertility technology products to sponsorship and support.

Merck Serono stated that it took compliance with the Code very seriously. The company was committed to full compliance with the Code and to maintaining the highest ethical standards in all of its commercial activities. The company submitted that this complaint was not founded, and it denied breaches of Clauses 2 and 9.1.

In summary, Merck Serono submitted that it had investigated the matter to the best of its ability based on the limited information provided and it sincerely regretted that the complainant did not provide further details. Its investigation did not lead the

company to believe that any manager or employee of the fertility team did not comply with the pricing guidance, or with the company's policy in relation to sponsorship, grants and medical education services, or with the Code. The company considered that its explanation and supporting documentation provided clear evidence as to why it had not breached the Code, and more particularly had not breached Clauses 2, 9.1, 18.1, 19.1 or 19.2.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the Prescription Medicines Code of Practice Authority stated that anonymous complaints would be accepted but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant had provided little detail to support his/her allegations and could not be contacted for more information.

The Panel noted Merck Serono's submission that its prescription products were made available to the NHS via tenders. Occasionally separate tenders might be used for fertility technology products. Further the commercial offerings and contracts for procurement, supply or pricing of fertility technology products and prescription medicines were kept separate.

The Panel noted that according to Merck Serono there would be no offers linking its medicines and its laboratory equipment. The Panel further noted Merck Serono's submission that it would not link the price of prescription medicines or the purchase of fertility products to sponsorship and support.

The complainant had not provided evidence to demonstrate on the balance of probabilities that Merck Serono had linked the price of its medicines to the cost of the laboratory equipment or to any sponsorship and/or support. The Panel therefore ruled no breach of Clauses 2, 9.1, 18.1, 19.1 and 19.2.

Complaint received **9 October 2018**

Case completed **21 November 2018**

PHARMACY TEAM LEADER v ELI LILLY

Compassionate supply of Olumiant

A hospital pharmacist complained that a compassionate supply of Olumiant (baricitinib) by Eli Lilly and Company Limited did not comply with the hospital's governance procedures for the procurement of medicines.

The complainant referred to the compassionate supply of Olumiant 4mg tablets by Lilly, as requested by a named consultant rheumatologist. According to the complainant Lilly discussed the matter with the named consultant; the supply of Olumiant was for a complex patient who had previously been refused commissioning for its use. At no point during the discussions did the Lilly team attempt to confirm if the hospital pharmacy knew about this compassionate request, and therefore Lilly did not adhere to the hospital's strict governance procedures when procuring medicines. Olumiant was restricted to patients upon approval by local commissioning groups for appropriateness and safety and supplied only via hospital pharmacies due to its specialist nature. The patient in question had not completed his/her essential pre-screening checks before Lilly agreed supply without pharmacy input. It was also suggested that the medicine could simply be delivered directly to the patient's local community pharmacy, therefore bypassing the specialist hospital pharmacy team completely. The complainant understood that Lilly had previously made similar supplies direct to community pharmacies in Wales and Scotland after approvals from the respective NHS Boards. This was not undertaken with NHS England in this case. The complainant submitted that this unacceptable practice raised significant safety concerns and undoubtedly put the patient at risk when commencing a specialist medicine without appropriate pharmacy oversight. The complainant stated that he/she had already discussed the issue with a senior manager at Lilly who would raise the issue with his/her team.

The detailed response from Lilly is given below.

The Panel noted that it had with the agreement of Lilly sent Lilly's response to the complainant for his/her comments. The complainant did not respond to the original or follow-up request for comments.

The Panel noted that the complainant provided an extract from the trust's medicines management policy which stated, *inter alia*, that all medicines must be ordered and received via the pharmacy purchasing service. The Panel noted Lilly's submission that it was aware of the hospital's medicine management policy and all aspects of the supply of Olumiant were in line with that policy. The Panel noted that the parties' accounts differed in this regard.

The Panel noted that the request to Lilly for six months supply of Olumiant on a compassionate use basis from a consultant rheumatologist was approved. The Panel noted the consultant rheumatologist's statement that when he/she was informed of the approval by Lilly he/she was told that the medication could be dispensed either from the hospital pharmacy or a local community pharmacy. The Panel queried whether this was in line with the trust's medicines management policy. The Panel noted that the following day the consultant rheumatologist, after discussions with the complainant, informed Lilly that the hospital pharmacy wanted to dispense the supply for governance reasons.

The Panel noted that although it appeared that Lilly had initially approved the consultant's request for the compassionate supply of Olumiant without the hospital pharmacy's involvement, it appeared that discussions between the consultant and the hospital pharmacy took place the following day. The complainant had not established that the supply of Olumiant was not in adherence with the hospital's governance procedures as alleged.

The Panel noted, however, that ultimately the supply of Olumiant in this case had been to the hospital pharmacy following a purchase order raised by it which in the Panel's view meant that the order and supply had occurred with the hospital pharmacy's agreement and in line with the extract of the trust's management policy provided by the complainant. The Panel therefore based on the evidence before it ruled no breach of the Code.

The Panel noted the complainant's further concern that the patient in question had not completed his/her essential pre-screening checks before Lilly agreed supply without pharmacy input. The Panel was unclear which checks the complainant was referring to; no further information was provided by the complainant. The Panel noted that during the conversation in which Lilly informed the consultant rheumatologist that his/her request was approved, the consultant rheumatologist confirmed that the patient was undergoing pre-treatment biologic screenings (as per Olumiant's SPC) which would delay the start of treatment by a week or so. In the Panel's view Lilly was aware that the appropriate screenings were being done and as noted above the pharmacy was involved before Olumiant was supplied by Lilly. Further when Lilly contacted the consultant to state that the hospital pharmacy had taken delivery of the medicine, the consultant rheumatologist stated that he/she was still awaiting the results from pre-treatment biologics screening. In the Panel's view, Lilly was aware that the patient would not receive the medication until the appropriate pre-screening as required by the SPC

had occurred. The Panel did not consider that the complainant had provided evidence to the contrary. The Panel therefore ruled no breaches of the Code including of Clause 2.

A pharmacy team leader complained that a compassionate supply of Olumiant (baricitinib) by Eli Lilly and Company Limited did not comply with the hospital's governance procedures for the procurement of medicines. Olumiant was used in adults with moderate to severe active rheumatoid arthritis.

COMPLAINT

The complainant referred to the compassionate supply of Olumiant 4mg tablets by Lilly, as requested by a local, named consultant rheumatologist. According to the complainant Lilly discussed the matter with the named consultant; the supply of Olumiant was for a complex patient who had previously been refused commissioning for its use. At no point during the discussions, did the Lilly team attempt to confirm if the hospital pharmacy knew about this compassionate request, and therefore Lilly did not adhere to the hospital's strict governance procedures when procuring medicines. Not only was Olumiant a prescription only medicine, it had 'black triangle' status, was high cost and was restricted to patients upon approval by local commissioning groups for appropriateness and safety. It was supplied only via hospital pharmacies due to its specialist nature. The patient in question had not completed his/her essential pre-screening checks before Lilly agreed supply without pharmacy input. It was also suggested that the medicine could simply be delivered directly to the patient's local community pharmacy, therefore bypassing the specialist hospital pharmacy team completely. The complainant understood that Lilly had previously made similar supplies direct to community pharmacies in Wales and Scotland after approvals from the respective NHS Boards. This was not undertaken with NHS England in this case. The complainant submitted that this unacceptable practice raised significant safety concerns and undoubtedly put the patient at risk when commencing a specialist medicine without appropriate pharmacy oversight. The complainant stated that he/she had already discussed the issue with a senior manager at Lilly who would raise the issue with his/her team.

When writing to Lilly, the Authority asked it to consider the requirements of Clauses 2, 9.1 and 15.4 of the Code.

RESPONSE

Lilly submitted that the request for six months' free supply of Olumiant was initiated by the consultant rheumatologist named by the complainant. The consultant had confirmed this in a letter addressed to Lilly. The consultant had also explained the circumstances and the reasons for his/her request along with the relevant timelines. Furthermore, Lilly had conducted its own investigation, details of which are explained below.

Circumstances and key timelines:

30 July 2018 –The local Lilly representative, during his/her call with the consultant rheumatologist, was told by him/her that an individual funding request (IFR) for Olumiant for a patient with long standing rheumatoid arthritis had been rejected by the IFR panel. The consultant's subsequent unsolicited request to Lilly for support in that matter was forwarded by the representative to Lilly's local healthcare development manager (HDM).

16 August –The HDM emailed the consultant to clarify the details of the request.

21 August –The consultant replied and explained the details of the request and asked whether Lilly would be able to provide 6 months' compassionate supply of Olumiant to help inform his/her IFR appeal.

22 August –The HDM forwarded the request to the Lilly pricing reimbursement and access manager.

31 August –The compassionate supply request was approved by Lilly.

10 September –The HDM telephoned the consultant to let him/her know that Lilly had approved the request and that distribution preferences needed to be finalised. The consultant was satisfied with the outcome and told the HDM that the patient was undergoing pre-treatment biologics screening (as per Olumiant's summary of product characteristics (SPC)).

11 September –The consultant contacted the HDM to inform him/her that the hospital pharmacy wanted to dispense the supply for governance reasons. The consultant gave the HDM the complainant's contact details and asked that arrangements were made directly with him/her. The consultant stated that he/she had told the pharmacy that there was no commitment to continue treatment beyond 6 months from Lilly or the trust and that the patient accepted that, pending reapplication to the IFR panel.

12 September – Lilly telephoned the complainant to discuss the free of charge supply of Olumiant. The complainant provided the contact details of the pharmacy supplier and asked Lilly to ask the pharmacy supplier to raise a purchase order.

13 September – Lilly telephoned the pharmacy supplier to inform him/her of the above conversation with the complainant and requested a formal purchase order which was issued.

14 September – Two packs of Olumiant 4mg x 84 tablets were delivered to the hospital pharmacy. The HDM contacted the consultant to inform him/her that the trust had taken the delivery of the supply. The consultant reiterated that he was still awaiting the results from pre-treatment biologics screening.

21 September –The consultant telephoned the HDM to explain that the pharmacy was no longer willing to dispense the compassionate supply of Olumiant despite receiving the delivery and would prefer

to wait for an IFR appeal decision. The consultant reiterated to the pharmacy that neither Lilly, nor the trust, nor the clinical commissioning group (CCG), were under any obligation to provide more than the 6 months supply of Olumiant and that the patient was aware of this situation.

25 September – A Lilly senior medical employee, telephoned the complainant to discuss his/her concerns.

18 October – Lilly received a letter from PMCPA stating that a complaint had been received from the complainant.

In summary Lilly stated that it put patient safety at the heart of all decision making and took compliance very seriously and understood and fully respected the Code. Lilly strove to ensure that all of its activities adhered with the relevant compliance requirements, rules and regulations. As evident from the above, Lilly's response was to an unsolicited request from a consultant rheumatologist. Additionally, as stated by the consultant, the patient was undergoing appropriate pre-treatment biologics screening. Lilly staff were aware of the hospital's medicine management policy and all aspects of this supply were in line with the policy. The approval of supply followed Lilly's local process. The consultant contacted the HDM on 11 September to inform him/her that the hospital pharmacy wanted to dispense the Olumiant supply for governance reasons and provided the complainant's contact details. The consultant further confirmed that he/she had informed the pharmacy that there was no commitment to continue treatment beyond 6 months from Lilly or the trust and that the patient had accepted that, pending reapplication to the IFR panel. On 12 September, Lilly contacted the hospital pharmacy and spoke with the complainant to discuss the consultant's request. Lilly was then given the contact details of the pharmacy supplier by the complainant. On 13 September, a purchase order was issued by the hospital pharmacy (pharmacy purchasing service in line with the hospital's medicines management policy) and sent to Lilly, following which the product supply was dispatched to the hospital pharmacy.

Lilly submitted that it did not, intentionally or unintentionally, try to bypass the specialist hospital pharmacy team at the hospital pharmacy. Lilly contacted the pharmacy to discuss the request and only dispatched the product supply upon receipt of a purchase order from the hospital pharmacy. Since receiving this complaint Lilly had been informed by the consultant that the hospital pharmacy had decided to dispense the supply of Olumiant to the patient in question.

Lilly stated that, in its view, it had acted in the best interest of the patient and the NHS and had strictly adhered to internal procedures and the Code at all times. Lilly denied breaches of Clauses 15.4, 9.1 and 2.

PANEL RULING

The Panel noted that it had with the agreement of Lilly sent Lilly's response to the complainant for his/her comments. The complainant did not respond to the original or follow-up request for comments.

The Panel noted that Clause 15.4 stated, *inter alia*, that the arrangements in force at any particular establishment must be observed.

The Panel noted that the complainant had provided an extract from the trust's medicines management policy which stated, *inter alia*, that all medicines that were supplied for use in the trust must be ordered and received via the pharmacy purchasing service. The Panel noted Lilly's submission that it was aware of the hospital's medicine management policy and all aspects of the supply of Olumiant were in line with that policy. The Panel noted that the parties' accounts differed in this regard. The complainant alleged that the supply of Olumiant by Lilly did not comply with the hospital's governance procedures for the procurement of medicines. According to the complainant Lilly did not attempt to confirm if the hospital pharmacy knew about the request and it was suggested that the medicine could be delivered directly to the patient's local community pharmacy, bypassing the specialist hospital pharmacy team completely.

The introduction to the Constitution and Procedure stated that a complainant had the burden of proving their complaint on the balance of probabilities.

The Panel noted that the request to Lilly for six months supply of Olumiant on a compassionate use basis from a consultant rheumatologist was approved. The Panel noted the consultant rheumatologist's statement that when he/she was informed of the approval by Lilly he/she was told that the medication could be dispensed either from the hospital pharmacy or a local community pharmacy. The Panel queried whether this was in line with the trust's medicines management policy as noted above. The Panel noted that the following day the consultant rheumatologist, after discussions with the complainant, informed Lilly that the hospital pharmacy wanted to dispense the supply for governance reasons.

The Panel noted Lilly's submission that it contacted the complainant as requested by the consultant rheumatologist to discuss the arrangements. Lilly subsequently contacted the pharmacy supplier, as advised by the complainant, who then raised a purchase order for the supply of Olumiant. The Panel noted Lilly's submission that the pharmacy took delivery of two packs of Olumiant tablets and a week later the consultant rheumatologist contacted Lilly to explain that the pharmacy was no longer willing to dispense the compassionate supply of Olumiant despite receiving the delivery and would prefer to wait for an IFR appeal. The Panel further noted Lilly's submission that the consultant stated that since receiving the complaint the pharmacy had decided to dispense the supplied product to the patient involved.

The Panel noted that although it appeared that Lilly had initially approved the consultant's request for the compassionate supply of Olumiant without the hospital pharmacy's involvement, it appeared that discussions between the consultant and the hospital pharmacy took place the following day. The complainant had not established that the supply of Olumiant was not in adherence with the hospital's governance procedures as alleged.

The Panel noted, however, that ultimately the supply of Olumiant had been to the hospital pharmacy following a purchase order raised by it which in the Panel's view meant that the order and supply had occurred with the hospital pharmacy's agreement and in line with the extract of the trust's management policy provided by the complainant. The Panel therefore based on the evidence before it ruled no breach of Clause 15.4. The Panel ruled, on balance, no breach of Clause 9.1 and subsequently no breach of Clause 2.

The Panel noted the complainant's further concern that the patient in question had not completed his/her essential pre-screening checks before Lilly agreed supply without pharmacy input. The Panel was unclear which checks the complainant was referring to; no further information was provided by

the complainant. The Panel noted that during the conversation in which Lilly informed the consultant rheumatologist that his/her request was approved, the consultant rheumatologist confirmed that the patient was undergoing pre-treatment biologic screenings (as per Olumiant's SPC) which would delay the start of treatment by a week or so. In the Panel's view Lilly was aware that the appropriate screenings were being done and as noted above the pharmacy was involved before Olumiant was supplied by Lilly. Further when Lilly contacted the consultant to state that the hospital pharmacy had taken delivery of the medicine, the consultant rheumatologist stated that he/she was still awaiting the results from pre-treatment biologics screening. In the Panel's view, Lilly was aware that the patient would not receive the medication until the appropriate pre-screening as required by the SPC had occurred. The Panel did not consider that the complainant had provided evidence to the contrary. The Panel therefore ruled no breach of Clause 9.1 and consequently no breach of Clause 2.

Complaint received **8 October 2018**

Case completed **25 February 2019**

VOLUNTARY ADMISSION BY JANSSEN

Use of out-of-date prescribing information

Janssen-Cilag Limited voluntarily admitted that an advertisement for Zytiga (abiraterone) (ref PHGB/ZYT/0716/0009(1)) had been published on two occasions with out-of-date prescribing information. Zytiga was indicated for the treatment of certain adult men with metastatic prostate cancer.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Janssen.

Janssen stated that it had recently identified that a Zytiga advertisement which bore a superseded version of the prescribing information (November 2016) had been mistakenly placed in the September 2018 issue of The Journal of Clinical Oncology, Volume 30, Issue 9.

The prescribing information had been updated twice since November 2016, once in September 2017 and again in November 2017. The prescribing information for Zytiga dated November 2017 was the current version that should have been included in the advertisement.

The same advertisement was re-run in the October 2018 issue of the same journal without prior knowledge or authorisation of Janssen or its media buying agent. The publisher had taken it upon itself to repeat the advertisement.

The response from Janssen is given below.

The Panel noted that Janssen had informed its media buyer on 4 September 2017 that the Zytiga prescribing information had been updated and all advertisements bearing the November 2016 prescribing information should be withdrawn and destroyed. In the same email Janssen included the updated prescribing information dated September 2017. The advertisement in question (ref PHGB/ZYT/0716/0009(1)) fell within the scope of this instruction. Janssen received confirmation of deletion of materials from the media buyer on 11 September 2017 and confirmation that it had requested that its publishing partners do the same. The journal publisher confirmed to the media buyer on 13 September that it had deleted the copy from its systems.

The Panel noted that on 22 November Janssen issued another withdrawal and destruction notification to the media buyer relating to all materials containing the September 2017 prescribing information and included a copy of the updated Zytiga prescribing information dated November 2017, which continued to be current. The Panel noted Janssen's submission that there were no print advertisements in circulation at that

time, so no formal destruction notice was required. The media buyer acknowledged the instruction by confirming Janssen's approach to managing the links to the prescribing information from digital assets.

The Panel noted that on 31 July 2018, the journal publisher requested confirmation from the media buyer as to the correct advertisement for print and attached the withdrawn advertisement (ref PHGB/ZYT/0716/0009(1)) to the email. Despite the media buyer checking with Janssen which advertisement was to be used and receiving confirmation of the correct one, the media buyer responded to the publisher and approved the incorrect advertisement. The withdrawn advertisement (ref PHGB/ZYT/0716/0009(1)) bearing the out-of-date prescribing information was therefore published in the September 2018 issue of The Journal of Clinical Oncology.

The Panel noted that Janssen was also told on 26 September 2018 that the publisher decided independently of Janssen and the media buyer to run the same non-compliant advertisement in the October 2018 issue of the same journal. The publisher acknowledged its failure to locate and destroy copies of the withdrawn advertisement and confirmed that it had decided, independently, to run the advertisement in October.

The Panel noted that whilst Janssen had been let down by its media buyer and the publisher, it was an established principle under the Code that pharmaceutical companies were responsible for third parties even if that third party acted outside the instructions from the pharmaceutical company.

The advertisement published in the September 2018 issue of The Journal of Clinical Oncology contained out of date prescribing information which was not in line with the SPC. The Panel ruled a breach of the Code as acknowledged by Janssen.

The Panel noted that the publisher had decided independently to re-run the advertisement in the October 2018 issue of The Journal of Clinical Oncology. The Panel noted that whilst Janssen had been let down by its publisher, it was an established principle under the Code that pharmaceutical companies were responsible for third parties even if that third party acted outside the instructions from the pharmaceutical company. The Panel therefore ruled a breach of the Code as the advertisement containing out of date prescribing information was also published in the October issue.

Janssen-Cilag Limited voluntarily admitted that an advertisement for Zytiga (abiraterone) (ref PHGB/ZYT/0716/0009(1)) had been published on two

occasions with out-of-date prescribing information. Zytiga was indicated for the treatment of certain adult men with metastatic prostate cancer.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Janssen.

VOLUNTARY ADMISSION

Janssen stated that it had recently identified that a Zytiga advertisement which bore a superseded version of the prescribing information (November 2016) had been mistakenly placed in the September 2018 issue of The Journal of Clinical Oncology, Volume 30, Issue 9.

The prescribing information had been updated twice since November 2016, once in September 2017 and again in November 2017. The prescribing information for Zytiga dated November 2017 was the current version that should have been included in the advertisement.

The same advertisement was re-run in the October 2018 issue of the same journal without prior knowledge or authorisation of Janssen or its media buying agent. The publisher had taken it upon itself to repeat the advertisement.

Janssen submitted that it had investigated the circumstances that led to the incident and it provided a summary of the sequence of events. An email trail between Janssen, its media buyer and the publisher of the journal, was provided.

Janssen stated that it informed its media buyer on 4 September 2017 that the Zytiga prescribing information had been updated and all advertisements bearing the November 2016 prescribing information should be withdrawn and destroyed. In the same email Janssen included the updated prescribing information dated September 2017. The advertisement in question (ref PHGB/ZYT/0716/0009(1)) fell within the scope of this instruction. Janssen received confirmation of destruction from the media buyer on 11 September 2017.

The journal publisher confirmed to the media buyer on 13 September that it had deleted the copy from its systems.

On 22 November 2017 Janssen issued another withdrawal and destruction notification to the media buyer relating to all materials containing the September 2017 prescribing information and included a copy of the updated Zytiga prescribing information dated November 2017, which continued to be current. Janssen submitted that there were no print advertisements in circulation at that time, so no formal destruction notice was required. The media buyer acknowledged the instruction by confirming Janssen's approach to managing the links to the prescribing information from digital assets.

At that time Janssen believed that all artwork and copies of previous print advertisements which bore

either the November 2016 or the September 2017 prescribing information had been destroyed in line with previous instructions.

On 31 July 2018, the journal publisher requested confirmation from the media buyer as to the correct advertisement for print and attached the withdrawn advertisement (ref PHGB/ZYT/0716/0009(1)) to the email.

Despite the media buyer checking with Janssen which advertisement was to be used and receiving confirmation of the correct one, the media buyer responded to the publisher and approved the incorrect advertisement, the withdrawn advertisement (ref PHGB/ZYT/0716/0009(1)). Janssen stated that it was not party to the communication chain between the media buyer and the publisher.

Because of the media buyer's error, the publisher printed the incorrect Zytiga advertisement bearing the out-of-date prescribing information in the September 2018 issue of The Journal of Clinical Oncology. Janssen became aware of this mistake when file copies of the journal were received from the media buyer in late September. This triggered the internal investigation and a decision to self-report.

Janssen was also told on 26 September 2018 that the publisher decided independently of Janssen and the media buyer to run the same non-compliant advertisement in the October 2018 issue of the same journal. At that time, it was too late to halt production as the issue had already been despatched to recipients.

Janssen asked the publisher to clarify why it had printed an incorrect advertisement in the September issue and to confirm that neither Janssen nor the media buyer instructed any advertisement to be placed in the October edition. In an email of 3 October, the publisher acknowledged its failure to locate and destroy all copies of the withdrawn advertisement and confirmed that it had decided, independently, to run the advertisement in October.

Janssen stated that the main changes compared with the incorrectly published November 2016 prescribing information included:

- September 2017 prescribing information
 - Removal of the availability of a 250mg tablet and any information relating to its presentation, pack size and NHS cost.
 - Addition of allergic alveolitis to the list of 'other side-effects'.
- November 2017 prescribing information
 - Addition of an indication for adult men with newly diagnosed high risk metastatic hormone sensitive prostate cancer in combination with androgen deprivation therapy (ADT).
 - Additional clarification of the steroid dose to be used with the new indication.
 - Reclassification of abnormalities of liver function test from common to very common.
 - Addition of 'other arrhythmias' to the list of 'other side-effects'.

Janssen did not consider that the failure to provide the most current prescribing information had any significant implications for patient safety. The prescribing information stated that the summary of product characteristics (SPC) needed to be referred to before prescribing. Allergic alveolitis was rare and 'other arrhythmias' was listed in the SPC as uncommon. With regard to the common potential for abnormal liver function tests, prescribers were already very informed of this given the longstanding requirement to monitor liver function upon initiation of treatment and regularly thereafter.

In conclusion, Janssen stated that it had acted in good faith to comply with the requirements of the Code but was let down by its agents. Nevertheless, Janssen accepted its accountability for complying with the letter and spirit of the Code even where that extended to the actions of its agents. As such, it acknowledged a failure to provide up-to-date prescribing information and thus a breach of Clause 4.1 relating to the publication of the advertisement in the September 2018 issue of the Journal of Clinical Oncology.

Janssen did not consider that it should be held accountable for the second advertisement placed in the October 2018 issue of the Journal of Clinical Oncology given this was done without any knowledge or instruction from Janssen or its media buyer.

Janssen stated that it would review its relationship and ways of working with all its media buying agents to reduce the likelihood of a recurrence of a similar breach of the Code.

In considering this matter, the Authority asked Janssen to consider the requirements of Clause 4.1 as cited by the company.

RESPONSE

Janssen stated that it had no further comments.

PANEL RULING

The Panel noted that Janssen had informed its media buyer on 4 September 2017 that the Zytiga prescribing information had been updated and all advertisements bearing the November 2016 prescribing information should be withdrawn and destroyed. In the same email Janssen included the updated prescribing information dated September 2017. The advertisement in question (ref PHGB/ZYT/0716/0009(1)) fell within the scope of this instruction. Janssen received confirmation of deletion of materials from the media buyer on 11 September 2017 and confirmation that it had requested that its publishing partners do the same. The journal publisher confirmed to the media buyer on 13 September that it had deleted the copy from its systems.

The Panel noted that the updated September 2017 prescribing information included the removal of the availability of a 250mg tablet and any information relating to its presentation, pack size and NHS cost

and the addition of allergic alveolitis to the list of 'other side-effects'.

The Panel noted that on 22 November Janssen issued another withdrawal and destruction notification to the media buyer relating to all materials containing the September 2017 prescribing information and included a copy of the updated Zytiga prescribing information dated November 2017, which continued to be current. The Panel noted Janssen's submission that there were no print advertisements in circulation at that time, so no formal destruction notice was required. The media buyer acknowledged the instruction by confirming Janssen's approach to managing the links to the prescribing information from digital assets.

The updated November 2017 prescribing information included addition of an indication for adult men with newly diagnosed high risk metastatic hormone sensitive prostate cancer in combination with androgen deprivation therapy (ADT); additional clarification of the steroid dose to be used with the new indication; reclassification of abnormalities of liver function test from common to very common; and addition of 'other arrhythmias' to the list of 'other side-effects'.

The Panel noted that on 31 July 2018, the journal publisher requested confirmation from the media buyer as to the correct advertisement for print and attached the withdrawn advertisement (ref PHGB/ZYT/0716/0009(1)) to the email. Despite the media buyer checking with Janssen which advertisement was to be used and receiving confirmation of the correct one, the media buyer responded to the publisher and approved the incorrect advertisement. The withdrawn advertisement (ref PHGB/ZYT/0716/0009(1)) bearing the out-of-date prescribing information was therefore published in the September 2018 issue of The Journal of Clinical Oncology.

The Panel noted that Janssen was also told on 26 September 2018 that the publisher decided independently of Janssen and the media buyer to run the same non-compliant advertisement in the October 2018 issue of the same journal. The publisher acknowledged its failure to locate and destroy copies of the withdrawn advertisement and confirmed that it had decided, independently, to run the advertisement in October.

The Panel noted that whilst Janssen had been let down by its media buyer and the publisher, it was an established principle under the Code that pharmaceutical companies were responsible for third parties even if that third party acted outside the instructions from the pharmaceutical company.

The advertisement published in the September 2018 issue of The Journal of Clinical Oncology contained out of date prescribing information which was not in line with the SPC. The Panel ruled a breach of Clause 4.1 as acknowledged by Janssen.

The Panel noted that the publisher had decided independently to re-run the advertisement in

the October 2018 issue of The Journal of Clinical Oncology. The Panel noted that whilst Janssen had been let down by its publisher, it was an established principle under the Code that pharmaceutical companies were responsible for third parties even if that third party acted outside the instructions from the pharmaceutical company. The Panel therefore ruled a breach of Clause 4.1 as the advertisement containing out of date prescribing information was also published in the October issue.

During the consideration of this case, the Panel was concerned to note Janssen's submission that

it did not consider that its failure to provide the current prescribing information had any significant implications for patient safety. The Panel noted the changes included the addition and re-classification of side-effects which, in the Panel's view, failure to include could have potential patient safety implications. The Panel requested that Janssen be advised of its concerns.

Voluntary admission received **24 October 2018**

Case completed **28 January 2019**

COMPLAINANT v DAIICHI-SANKYO

Alleged promotion to the public

A complainant who described him/herself as a concerned UK health professional alleged that certain pages of the Daiichi-Sankyo website promoted products to the public.

The complainant provided a link and noted that the Daiichi-Sankyo website did not have separate areas for patients and health professionals. The complainant alleged that there was information on the pages leading from the link in question that promoted to the public since the information provided included the generic name, the brand name and the indication.

The detailed response from Daiichi-Sankyo is given below.

The Panel noted Daiichi-Sankyo's submission that it was not necessary for the website to have separate areas for health professionals and members of the public as the entire website was non-promotional and contained only reference information.

The Panel noted that the page which appeared when you clicked on the link provided by the complainant was headed 'Daiichi-Sankyo UK Ltd', followed by 'Products > UK Products'. The opening paragraph read 'Daiichi Sankyo's products treat and prevent serious illnesses as well as help people to live longer and have healthier lives. While maintaining its portfolio of marketed pharmaceuticals for acute coronary syndromes and atrial fibrillation, Daiichi-Sankyo is engaged in the development of treatments focussed on the discovery of novel oncology therapies'.

Medical professionals were advised that they could obtain more detailed information on Daiichi-Sankyo's products by contacting its medical services department on the email address or contact number provided.

The page then listed the brand names of Daiichi-Sankyo UK's eight 'key products' and included the non-proprietary name and indication in tabular format. The webpage stated that the products were listed in alphabetical order however this was not so; Efient (Prasugrel) and Lixiana (Edoxaban) were listed first and Evista (Raloxifene) and Motifene (Diclofenac sodium) last.

Below the table was information directed at patients including how to report adverse events and instructions to contact their health professional for queries about their medicine and/or health.

The Panel noted that there did not appear to be any further information available for the public regarding the majority of the prescription only medicines listed. Following the information about

reporting adverse events further information on Edoxaban (Lixiana) and Prasugrel (Efient) was provided which included a more detailed description of each medicine's indication and information on the condition(s) each was used to treat.

Beneath the heading Edoxaban it was explained that atrial fibrillation (AF) was the most common heart rhythm disturbance encountered by doctors and that the most worrying consequence of AF was stroke. The last paragraph stated that Edoxaban was a blood thinner that could be used in patients with atrial fibrillation to prevent strokes. In the Panel's view, this was a claim for Edoxaban.

Below the information regarding Edoxaban were two links directing the reader to further information: the first link went to a third party site and the second link appeared to no longer be active.

There were no links to the SPC or PIL for any of the eight medicines listed. The material did not appear to be a fair reflection of the medicines' risk/benefit profiles. In the Panel's view, the material was limited and did not qualify as reference information as referred to in the Code.

The Panel noted that the Code prohibited the promotion of prescription only medicines to the public. The Panel noted the opening paragraph on the webpage in question set out above, which stated that Daiichi-Sankyo's products treat and prevent serious illnesses as well as help people to live longer and have healthier lives which preceded the list of medicines and was therefore, in the Panel's view, a claim for those medicines. The Panel further noted that the webpage in question included the medicines' brand names, non-proprietary names and indications listed in one single table and included additional information on Edoxaban and Prasugrel. In addition, the Panel noted that members of the public looking for information on one particular medicine would automatically be faced with the brand name, non-proprietary name and indication of all of Daiichi-Sankyo's medicines. In the Panel's view, noting its comments above, the webpage in question advertised prescription only medicines to the public and a breach of the Code was ruled.

The Panel noted that the Code required that promotional material about prescription only medicines directed to a UK audience which was provided on the internet must comply with all relevant requirements of the Code. The supplementary information stated that unless access to promotional material about prescription only medicines was limited to health professionals and other relevant decision makers, a pharmaceutical company website or a company

sponsored website must provide information for the public as well as promotion to health professionals with the sections for each target audience clearly separated and the intended audience identified. This was to avoid the public needing to access material for health professionals unless they chose to. The MHRA Blue Guide stated that the public should not be encouraged to access material which was not intended for them. The Panel noted its comments and ruling above. The Panel noted that Daiichi-Sankyo considered that the webpage in question was reference information directed at members of the public. In the Panel's view, the webpage at issue promoted prescription only medicines and therefore access should have been restricted to health professionals and other relevant decision makers because information had not been provided for the public as required by the relevant supplementary information. The Panel noted that access to the webpage had not been so restricted and therefore a breach of the Code was ruled.

The Panel noted its comments and rulings above and considered that Daiichi-Sankyo had failed to maintain high standards and a breach of the Code was ruled.

The Panel did not consider that the particular circumstances in this case warranted a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such. No breach of Clause 2 was ruled.

A complainant who described him/herself as a concerned UK health professional alleged that certain pages of the Daiichi-Sankyo website promoted products to the public.

COMPLAINT

The complainant provided a link (<https://www.daiichi-sankyo.co.uk/products/european-products/>) and noted that the Daiichi-Sankyo website did not have separate areas for patients and health professionals. The complainant alleged that there was information on the pages leading from the link in question that promoted to the public since the information provided included the generic name, the brand name and the indication.

When writing to Daiichi-Sankyo, the Authority asked it to consider the requirements of Clauses 2, 9.1, 26.1 and 28.1.

RESPONSE

Daiichi-Sankyo noted that it had not been asked to consider the requirements of Clause 26.2 and its supplementary information. In the company's view this was a mistake on the part of the case preparation manager as Clause 26.2 was relevant to the complaint. Daiichi-Sankyo referred to the supplementary information to Clause 26.2 in relation to reference information.

Daiichi-Sankyo submitted that the information provided on the webpage at issue fitted the definition of reference information; the product trademark,

substance and indication information provided were non-promotional, factual, balanced and appropriate for the public. The information provided did not raise unfounded hopes of successful treatment, it did not mislead with respect to the safety of any of the products referred to and there were no statements that might encourage members of the public to ask their health professional to prescribe a specific prescription only medicine.

The company thus did not consider that the webpage in question was in breach of either Clause 26.1 or 26.2.

With regard to Clause 28.1, Daiichi-Sankyo stated that as that clause referred to promotional material on websites, and its separation from non-promotional material on the same website, it was not relevant. The complainant stated that the website did not have separate areas for patients and health professionals. Daiichi-Sankyo submitted that it was not necessary to have these separate areas as the entire website was non-promotional and thus, there had been no breach of Clause 28.1.

Given that the webpage in question was entirely in line with the requirements of Clauses 26.1 and 26.2, and that Clause 28.1 was not relevant, Daiichi-Sankyo did not consider that there had been a breach of either Clauses 9.1 or Clause 2.

Daiichi-Sankyo submitted that as the website was not promotional and contained only reference information there was no certificate approving the webpage in question.

PANEL RULING

The Panel noted Daiichi-Sankyo's submission that it was not necessary for the website to have separate areas for health professionals and members of the public as the entire website was non-promotional and contained only reference information.

The Panel noted Daiichi-Sankyo's comments about, and response to, the requirements of Clause 26.2 which was not raised by the case preparation manager. The Panel noted that the complaint concerned the promotion of prescription only medicines to the public which fell within the remit of Clause 26.1. In the Panel's view, the complainant's allegation did not raise a Clause 26.2 matter and hence that Clause had not been raised by the Case Preparation Manager and whilst the company had responded in relation to the requirements of Clause 26.2 the Panel could make no ruling under that Clause.

The Panel noted that the page which appeared when you clicked on the link provided by the complainant was headed 'Daiichi-Sankyo UK Ltd', followed by 'Products > UK Products'. The opening paragraph read 'Daiichi-Sankyo's products treat and prevent serious illnesses as well as help people to live longer and have healthier lives. While maintaining its portfolio of marketed pharmaceuticals for acute coronary syndromes and atrial fibrillation, Daiichi-Sankyo is engaged in the development of treatments

focussed on the discovery of novel oncology therapies’.

Medical professionals were advised that they could obtain more detailed information on Daiichi-Sankyo’s products by contacting its medical services department on the email address or contact number provided.

The page then listed the brand names of Daiichi-Sankyo UK’s eight ‘key products’ and included the non-proprietary name and indication in tabular format. The webpage stated that the products were listed in alphabetical order however this was not so; Efient (Prasugrel) and Lixiana (Edoxaban) were listed first and Evista (Raloxifene) and Motifene (Diclofenac sodium) last.

Below the table was information directed at patients including how to report adverse events and instructions to contact their health professional for queries about their medicine and/or health.

The Panel noted that there did not appear to be any further information available for the public regarding the majority of the prescription only medicines listed. Following the information about reporting adverse events further information on Edoxaban (Lixiana) and Prasugrel (Efient) was provided which included a more detailed description of each medicine’s indication and information on the condition(s) each was used to treat.

Beneath the heading Edoxaban it was explained that atrial fibrillation (AF) was the most common heart rhythm disturbance encountered by doctors and that the most worrying consequence of AF was stroke. The last paragraph stated that Edoxaban was a blood thinner that could be used in patients with atrial fibrillation to prevent strokes. In the Panel’s view, this was a claim for Edoxaban.

Below the information regarding Edoxaban were two links directing the reader to further information: the first link, <http://www.anticoagulation.org.uk>, went to a third party site and the second link, <http://www.anticoagulationeurope.org>, appeared to no longer be active.

There were no links to the SPC or PIL for any of the eight medicines listed. The material did not appear to be a fair reflection of the medicines’ risk/benefit profiles. In the Panel’s view, the material was limited and did not qualify as reference information as referred to in the supplementary information to Clause 26.2 of the Code.

The Panel noted that Clause 26.1 prohibited the promotion of prescription only medicines to the public. The Panel noted the opening paragraph on the webpage in question set out above, which stated that Daiichi-Sankyo’s products treat and prevent serious illnesses as well as help people to live

longer and have healthier lives which preceded the list of medicines and was therefore, in the Panel’s view, a claim for those medicines. The Panel further noted that the webpage in question included the medicines’ brand names, non-proprietary names and indications listed in one single table and included additional information on Edoxaban and Prasugrel. In addition, the Panel noted that members of the public looking for information on one particular medicine would automatically be faced with the brand name, non-proprietary name and indication of all of Daiichi-Sankyo’s medicines. In the Panel’s view, noting its comments above, the webpage in question advertised prescription only medicines to the public and a breach of Clause 26.1 was ruled.

The Panel noted that Clause 28.1 required that promotional material about prescription only medicines directed to a UK audience which was provided on the internet must comply with all relevant requirements of the Code. The supplementary information stated that unless access to promotional material about prescription only medicines was limited to health professionals and other relevant decision makers, a pharmaceutical company website or a company sponsored website must provide information for the public as well as promotion to health professionals with the sections for each target audience clearly separated and the intended audience identified. This was to avoid the public needing to access material for health professionals unless they chose to. The MHRA Blue Guide stated that the public should not be encouraged to access material which was not intended for them. The Panel noted its comments and ruling above. The Panel noted that Daiichi-Sankyo considered that the webpage in question was reference information directed at members of the public. In the Panel’s view, the webpage at issue promoted prescription only medicines and therefore access should have been restricted to health professionals and other relevant decision makers because information had not been provided for the public as required by the relevant supplementary information. The Panel noted that access to the webpage had not been so restricted and therefore a breach of Clause 28.1 was ruled.

The Panel noted its comments and rulings above and considered that Daiichi-Sankyo had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel did not consider that the particular circumstances in this case warranted a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such. No breach of Clause 2 was ruled.

Complaint received	29 October 2018
Case completed	22 February 2019

COMPLAINANT v MITSUBISHI TANABE PHARMA EUROPE

Promotion to the public

A complainant who described him/herself as a concerned UK health professional complained about four pharmaceutical companies' websites including that of Mitsubishi Tanabe Pharma Europe who market Exembol (argatroban – used for anticoagulation in certain adult patients) and Tanatril (imidapril – indicated for the treatment of essential hypertension in adults) in the UK.

The complainant noted that Mitsubishi Tanabe Pharma Europe was based in London. The complainant drew parallels with another company's website which he/she had complained promoted to the general public because there was information including the generic name, the brand name and the indication. The complainant stated that Mitsubishi Tanabe Pharma Europe's website similarly had no separate area for patients and merely stated that certain pages were for patients and that the product pages were similarly promoting to the general public, particularly if one selected the 'read more' button.

The detailed response from Mitsubishi Tanabe Pharma Europe is given below.

The Panel noted Mitsubishi Tanabe Pharma Europe's submission that its website was intended to provide corporate information in relation to the company and its products at a European level; and that the webpages in question were not promotional and provided accurate, factual information for health professionals and the public in relation to Exembol and Tanatril.

The Panel noted the webpage in question contained statements related to argatroban (non-proprietary name for Exembol) and Tanatril.

In relation to argatroban, the webpage stated:

'Developed in Japan, argatroban was the first licensed synthetic direct thrombin inhibitor. Approved in twelve European countries, argatroban is marketed for anticoagulation in adult patients with Heparin-Induced Thrombocytopenia Type II (HIT Type II) who require parenteral antithrombotic therapy. Argatroban is given as a continuous intravenous infusion.'

The same page had the following statement in relation to Tanatril:

'Tanatril is used to treat high blood pressure (hypertension). Tanatril is one of a group of medicines called ACE (angiotensin-converting

enzyme) inhibitors. Tanatril is available in 5mg, 10mg and 20mg tablet formulation.'

The Panel noted that there was a 'read more' button within the highlighted text box for each product and to the right of the page an adverse event reporting statement. At the bottom of each webpage within the products section, in small font, was the statement 'Please note: certain pages are intended for healthcare professionals only'. The Panel noted that the 'certain pages' were not identified and thus in the Panel's view the intended audience for each page was unclear. The section did not clearly separate pages aimed at health professionals from those containing information for the public. The Panel also noted Mitsubishi Tanabe's submission that the webpages were non-promotional and there was accordingly no requirement to restrict access.

The Panel noted that if the 'read more' button was selected for argatroban, the user was taken to a page which repeated the argatroban statement above and further stated: 'You can find specific information on our products in individual countries by choosing the relevant country from the menu below'. The four brand names for argatroban were listed with links to the relevant country/countries for each. If the user selected the UK link for Exembol, a pop-up box appeared stating that the following pages were intended for viewing by UK health professionals only. If the user selected 'continue' the user was taken to a page that contained: links to the Exembol summary of product characteristics and patient information leaflet; contact details for Mitsubishi Tanabe Pharma Europe; an adverse event reporting statement; and a link to an Exembol website. If the user had selected 'cancel' in response to the pop-up box, he/she would stay on the current page.

The Panel further noted that when the user selected the Tanatril 'read more' button from the main product webpage, he/she would be taken to a page titled 'How to order Tanatril' which gave information regarding ordering the product from a named wholesaler, including the wholesaler's contact details and the PIP codes for each tablet strength. The same page featured: links to the Tanatril summary of product characteristics and patient information leaflet; Mitsubishi Tanabe Pharma Europe's contact details; and an adverse event reporting statement. The bottom of the page stated: 'Please note: certain pages are intended for healthcare professionals only'. The Panel noted its comments on this statement above. The content of this page was such that it appeared to be aimed at health professionals.

The Panel queried whether the products homepage and the pages linked via the read more buttons could be considered reference information as set out in the supplementary information of the Code given the lack of information provided for members of the public. There appeared to be nowhere for members of the public to go to access further information on argatroban; the SPC and PIL could only be accessed after the reader confirmed that he/she was a health professional. The page for Tanatril, which included the SPC and PIL, related to how to order the product and appeared therefore to be aimed at health professionals.

The Panel considered that the statement '... argatroban was the first licensed synthetic direct thrombin inhibitor. Approved in twelve European countries ...' which appeared, *inter alia*, on the main product webpage constituted a product claim. The Panel noted that whilst the homepage of the products section in question did not include the brand name for argatroban it did include its non-proprietary name and indication. If a member of the public clicked on the read more button for argatroban they were provided with the brand name of the product in individual countries including Exembo in the UK. The initial webpage also included the brand name and indication for Tanatril.

The Panel also noted that members of the public looking for information on one particular medicine would automatically be faced with the non-proprietary or brand name and indication of Mitsubishi Tanabe Pharma Europe's other medicine.

Noting its comments above the Panel considered that the webpage advertised prescription only medicines to the public and a breach of the Code was ruled.

The Panel noted its comments and ruling above. In the Panel's view, the webpage at issue promoted prescription only medicines and therefore access should have been restricted to health professionals and other relevant decision makers because information had not been provided for the public as required by the relevant supplementary information. The Panel noted that access to the webpage had not been so restricted and therefore a breach of the Code was ruled.

The Panel noted its comments and rulings above and considered that Mitsubishi Tanabe Pharma Europe had failed to maintain high standards and a breach of the Code was ruled.

The Panel did not consider that the circumstances in this particular case warranted a ruling of a breach of Clause 2 and no breach was ruled accordingly.

A complainant who described him/herself as a concerned UK health professional complained about four pharmaceutical companies' websites including that of Mitsubishi Tanabe Pharma Europe who market Exembo (argatroban – used for anticoagulation in certain adult patients) and Tanatril (imidapril – indicated for the treatment of essential hypertension in adults) in the UK.

COMPLAINT

The complainant noted that Mitsubishi Tanabe Pharma Europe was based in London. The complainant drew parallels with another company's website which he/she had complained promoted to the general public because there was information including the generic name, the brand name and the indication. The complainant stated that Mitsubishi Tanabe Pharma Europe's website <http://www.mt-pharma-eu.com/products/> similarly had no separate area for patients and merely stated that certain pages were for patients and that the product pages were similarly promoting to the general public, particularly if one selected the 'read more' button.

When writing to Mitsubishi Tanabe Pharma Europe, the Authority asked it to consider the requirements of Clauses 26.1, 28.1, 9.1 and 2 of the Code.

RESPONSE

Mitsubishi Tanabe Pharma Europe stated that it was surprised and disappointed that such a complaint had been made; the company was committed to maintaining high standards in relation to all communications concerning its medicinal products and in complying with the Code in all relevant activities.

Mitsubishi Tanabe Pharma Europe stated that it sponsored the website which was intended to provide corporate information in relation to the company and its products at European level.

The European 'Products' webpage referred to two medicinal products: argatroban (marketed as Exembo in the UK) and Tanatril. Both products were the subject of UK marketing authorisations granted to Mitsubishi Tanabe Pharma Europe by the Medicines and Healthcare products Regulatory Agency (MHRA), as well as authorisations granted nationally in other EU Member States by other national competent authorities.

In relation to argatroban, the webpage stated:

'Developed in Japan, argatroban was the first licensed synthetic direct thrombin inhibitor. Approved in twelve European countries, argatroban is marketed for anticoagulation in adult patients with Heparin-Induced Thrombocytopenia Type II (HIT Type II) who require parenteral antithrombotic therapy. Argatroban is given as a continuous intravenous infusion.'

A 'Read More' button linked to a further webpage specifically dedicated to argatroban which stated:

'Test Developed in Japan, argatroban was the first licensed synthetic direct thrombin inhibitor. Approved in twelve European countries, argatroban is marketed for anticoagulation in adult patients with Heparin-Induced Thrombocytopenia Type II (HIT Type II) who require parenteral antithrombotic therapy. Argatroban is given as a continuous intravenous infusion.'

The user was informed that if he/she clicked on one of the EU countries listed he/she would find information on the products applicable to that country. If the UK symbol was selected, the user was asked to confirm that he/she was a UK health professional, following which he/she was directed to a webpage entitled 'Exembol® (UK)'. Exembol was the brand name for argatroban in the UK; different brand names were used in other Member States, which was why the initial European Products webpage referred to the product by its international non-proprietary name. The Exembol (UK) webpage provided links to both the UK summary of product characteristics (SPC) and the UK patient information leaflet (PIL) for Exembol, advising the user that they would be directed away from the Mitsubishi Tanabe Pharma Europe webpage if they chose to proceed. If the user clicked 'Continue', they were directed to the electronic Medicines Compendium (eMC) website, where the UK SPC and UK PIL for Exembol could be accessed.

Mitsubishi Tanabe Pharma Europe submitted that the statements made on the above webpages in relation to argatroban were factually correct and the complainant did not suggest otherwise.

In relation to Tanatril, the European Products webpage stated:

'Tanatril is used to treat high blood pressure (hypertension). Tanatril is one of a group of medicines called ACE (angiotensin-converting enzyme) inhibitors. Tanatril is available in 5mg, 10mg and 20mg tablet formulation.'

A 'Read More' button linked to a further webpage specifically dedicated to the product which provided details on how to order Tanatril which gave information regarding ordering the product from a named wholesaler, including the wholesaler's contact details and the PIP codes for each tablet strength. It stated that if you have any queries, please contact the wholesaler support team on the telephone number or email address provided.

It also provided the wholesaler's telephone number to call to set up a new account.

The webpage then provided links to the Tanatril UK SPC and PIL. When these links were clicked, the user was notified that they would be directed away from the Mitsubishi Tanabe Pharma Europe website if they chose to proceed. If the user clicked 'Continue', he/she was directed to the eMC website where the Tanatril UK SPC and PIL could be accessed.

Mitsubishi Tanabe Pharma Europe submitted that the statements made on the above webpages in relation to Tanatril were factually correct and the complainant did not suggest otherwise.

Mitsubishi Tanabe Pharma Europe noted Clause 26.1 and the relevant supplementary information.

Mitsubishi Tanabe Pharma Europe submitted that in relation to Clause 26, the PMCPA's 'Guidance about Digital Communications' stated:

'Whilst promotion is prohibited, factual and balanced information about prescription only medicines can be made available to the public either directly or indirectly. However, statements must not be made for the purpose of encouraging members of the public to ask a health professional to prescribe a specific prescription only medicine.'

The company submitted that Section 2(iv), Annex B of the 'EFPIA [European Federation of Pharmaceutical Industries and Associations] HCP [health professional] Code' and Section 7.5 of the MHRA's Blue Guide were also relevant.

Mitsubishi Tanabe Pharma Europe stated that Clause 26.1 prohibited advertising directed towards members of the public and that the complainant asserted that the European products webpage was promotional on the basis that it used both generic and brand names for medicinal products and identified the indications for use.

Mitsubishi Tanabe Pharma Europe submitted that it disagreed with the criticisms made by the complainant. The corporate webpages in question were not promotional. They provided accurate, factual information for health professionals and the general public in relation to Exembol and Tanatril consistent with the PMCPA guidance on digital communications and the EFPIA Code. The webpages included links to the approved UK SPC and PIL as required under the EFPIA Code.

Mitsubishi Tanabe Pharma Europe submitted that the use of both generic names was not promotional. The use of brand names was promotional only if such use was excessive. The European products webpage and subsequent pages used the brand name Exembol only once on two webpages and the brand name Tanatril seven times on two webpages. This did not involve excessive use of the brand for either product. A factual statement about the authorised indications for use was informative rather than promotional. The provision of such information reflected PMCPA guidance, the EFPIA Code and MHRA's advice that 'other non-promotional reference information about the product that fairly reflected the current body of evidence about the product and its benefit risk profile' was permitted. Furthermore, any prohibition of neutral, factual information stating the approved indication for use, would be inconsistent with the fact that companies are encouraged to include copies of or links to UK SPCs and PILs on websites aimed at members of the public. The European product webpage linked to a webpage containing instructions on how to order Tanatril directed towards health professionals and administrative staff. While the complainant did not criticise the provision of ordering information, this page was not in any event promotional and advised users 'Please note: certain pages are intended for healthcare professionals only'. None of the identified pages made product claims comparable to those which were the subject of criticism in Case AUTH/2436/9/11 and Case AUTH/3037/4/18 and none were made for the purpose of encouraging members of the public to ask a health professional to prescribe Exembol, Tanatril or any other specific prescription only medicine.

Mitsubishi Tanabe Pharma Europe noted the requirements of Clause 28.1 and the relevant supplementary information.

The company also referred to Section 2(iii) of Annex B to the EFPIA HCP Code and Section 6.3 of the MHRA's Blue Guide.

Mitsubishi Tanabe Pharma Europe submitted that Clause 28.1 was directed towards promotional material that may be accessed by members of the public. For the reasons set out in response to Clause 26.1, the information contained on the identified webpages were not promotional and Clause 28.1 was not therefore applicable. However, for completeness, Mitsubishi Tanabe Pharma Europe submitted that it identified on the website those pages which were intended for health professionals. As described above, the European 'Products' webpage listed both argatroban and Tanatril and stated beneath the brief factual information in relation to those products, 'Please note: certain pages are intended for healthcare professionals only.'

Argatroban

The 'Read More' button relevant to argatroban directed users to a webpage where users could select the correct jurisdiction in order to 'find specific information on [Mitsubishi Tanabe Pharma Europe] products'. Beneath this selection frame was a statement which read 'Please note, certain pages are intended for healthcare professionals only'. If a user clicked on the UK webpage, a pop-up appeared which stated:

'The following pages are intended for viewing by healthcare professionals residing in the UK only. By clicking "Continue" below you confirm that you are a resident of the UK and that you agree to the terms & conditions of use associated with this website. If you are not a resident of the UK or you do not agree to the terms & conditions of use associated with this website you should click "Cancel" now to return to the previous page. The full terms & conditions associated with this website can be accessed at "Terms of Use"'

If the user confirmed that they were a health professional, they were directed to a webpage entitled 'Exembol® (UK)'. At the bottom of this webpage, there was a message which stated 'Please note: certain pages are intended for healthcare professionals only'. If the user clicked on the links to these documents, they were directed to the eMC website, with the requisite notice that they would be directed away from Mitsubishi Tanabe Pharma Europe's webpage.

An alternative route to access the Exembol webpage was to open the main Mitsubishi Tanabe Pharma Europe webpage and then click 'Site Map', which opens a webpage that listed the company's product webpages. If the user clicked on 'Exembol® (UK)' a pop-up appeared which again stated:

'The following pages are intended for viewing by healthcare professionals residing in the UK only.

By clicking "Continue" below you confirm that you are a resident of the UK and that you agree to the terms & conditions of use associated with this website. If you are not a resident of the UK or you do not agree to the terms & conditions of use associated with this website you should click "Cancel" now to return to the previous page. The full terms & conditions associated with this website can be accessed at "Terms of Use"'

Tanatril

If the user clicked on the 'Read More' button relevant to Tanatril, the user was directed to the Tanatril webpage which repeated the previous statement, 'Please note: certain pages are intended for healthcare professionals only'. As well as providing information about how to order Tanatril, links were provided to the SPC and PIL for this product and these linked to the relevant page of the eMC which when clicked notified users that if they chose to proceed they would be directed away from Mitsubishi Tanabe Pharma Europe's webpages.

An alternative route to access the Tanatril webpage was to open the main Mitsubishi Tanabe Pharma Europe webpage and then click 'Site Map', which opened a webpage that listed the company's product webpages. If the user clicked on 'Tanatril' he/she was directed to the Tanatril webpage described above, which repeated the statement, 'Please note: certain pages are intended for healthcare professionals only'.

In summary, Mitsubishi Tanabe Pharma Europe stated that none of the webpages identified by the complainant were promotional and there was accordingly no objection, for the purposes of Clause 28.1, to the included material being accessed by members of the public as well as health professionals. Nevertheless, Mitsubishi Tanabe Pharma Europe provided information on the cited webpages which advised users that certain material (eg the ordering information for Tanatril) was not directed towards members of the public. For completeness, while in circumstances where the content of the webpages was not promotional, there was no requirement formally to restrict access to any of the identified pages to health professionals, the review of the website carried out for the purposes of this response, had shown that the approach followed was not fully consistent throughout. Mitsubishi Tanabe Pharma Europe therefore proposed to streamline the content of the website so that the messages were provided in a similar form throughout which would, it believed, improve the clarity of the messages.

Mitsubishi Tanabe Pharma Europe submitted that Clause 9.1 required member companies to maintain high standards at all times; it did not believe that any of the information contained in the cited webpages was of a promotional nature or that there was any inappropriate lack of delineation between pages intended for the general public and those intended for health professionals. It did not therefore believe there was any failure by Mitsubishi Tanabe Pharma Europe to meet high standards. Furthermore, the

website was managed by Mitsubishi Tanabe Pharma Europe's corporate function with cross-functional input. The website was last updated in June 2018 to reflect required changes related to disclosure and was recertified. This was in keeping with its Standard Operating Procedure on Managing & Maintaining Company Corporate Website, which required that the content of the website was maintained as current and relevant as it provided information about Mitsubishi Tanabe Pharma Europe and its products on the internet. Staff from all relevant functions were routinely trained on these SOPs using an electronic training system. The SOPs were in line with the company policies and regularly updated and reviewed on the electronic training system to ensure that the latest requirements were fulfilled. The Standard Operating Procedure on Managing & Maintaining Company Corporate Website was last updated on 26 April 2017. Mitsubishi Tanabe Pharma Europe submitted that any allegation that it had not maintained high standards was unfounded; there had been no breach of the relevant provisions of the Code, comprehensive SOPs were in place, and these SOPs were regularly updated and monitored in order to ensure that Mitsubishi Tanabe Pharma Europe did not fall below standard required by the applicable legislation and the Code.

Mitsubishi Tanabe Pharma Europe submitted that Clause 2 stated: 'Activities or materials associated with promotion must never be such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry' and the supplementary information provided in relation to this Clause stated: 'A ruling of a breach of this clause is a sign of particular censure and is reserved for such circumstances. Examples of activities that are likely to be in breach of Clause 2 include prejudicing patient safety and/or public health, excessive hospitality, inducements to prescribe, unacceptable payments, inadequate action leading to a breach of undertaking, promotion prior to the grant of a marketing authorization, conduct of company employees/agents that falls short of competent care and multiple/cumulative breaches of a similar and serious nature in the same therapeutic area within a short period of time'.

Mitsubishi Tanabe Pharma Europe stated that it had not breached any part of the Code and as such there was no basis for finding of breach of Clause 2. In particular, the identified webpages on the website were non-promotional and there was no inappropriate access by members of the public. The examples provided in the supplementary information to Clause 2 did not relate in any way to issues raised in the case and the website could not be considered to have brought discredit upon, or reduced the confidence in, the industry.

Overall conclusion

Mitsubishi Tanabe Pharma Europe stated it did not believe the criticisms raised by the complainant had merit.

The webpages identified in the complaint did not include any promotional information. The use of

brand names in relation to the two listed products was limited and the remaining information was accurate and factual. None of the information was provided for the purpose of encouraging members of the public to ask a health professional to prescribe a specific prescription only medicine. While the content of the webpages was non-promotional and there was accordingly no requirement to restrict access by members of the public, Mitsubishi Tanabe Pharma Europe nevertheless advised users where certain pages were intended for health professionals. Mitsubishi Tanabe Pharma Europe therefore respectfully suggested that there was no credible basis for findings of breach of Clauses 26.1 and 28.1 in this case.

Mitsubishi Tanabe Pharma Europe had robust SOPs in place for Managing & Maintaining Company Corporate Website and Preparation, Review and Approval of Promotional Materials respectively, which staff were expected to follow and upon which they were trained. In circumstances where there was no evidence of any breach of Clauses 26.1 or 28.1, Mitsubishi Tanabe Pharma Europe believed there could be no basis for a finding that it had failed to maintain high standards contrary to Clause 9 or had, in any way, brought discredit upon the pharmaceutical industry contrary to Clause 2.

As a result of this review, Mitsubishi Tanabe Pharma Europe had identified that, in some discrete areas, its webpages adopted different approaches to the provision of information and to meeting Code requirements. Whilst this situation did not constitute a breach of the Code, it proposed to update the website in order to implement a single approach throughout.

Following a request for further information from the Panel, Mitsubishi Tanabe Pharma Europe provided a certificate in relation to updates to the product pages in question, dated July 2016.

PANEL RULING

The Panel noted that Clause 26.1 prohibited the promotion of prescription only medicines to the public.

The Panel noted Mitsubishi Tanabe Pharma Europe's submission that its website was intended to provide corporate information in relation to the company and its products at a European level; and that the webpages in question were not promotional and provided accurate, factual information for health professionals and the public in relation to Exembool and Tanatril.

The Panel disagreed with Mitsubishi Tanabe Pharma Europe's submission that the use of generic names was not promotional and the use of brand names was promotional only if such use was excessive. The Panel noted that it was an accepted principle under the Code that a product could be promoted without its name ever being mentioned.

The Panel noted Mitsubishi Tanabe Pharma Europe's submission that a factual statement about the

authorised indications for use was informative rather than promotional and that the provision of such information reflected PMCPA guidance, the EFPIA Code and MHRA's advice that 'other non-promotional reference information about the product that fairly reflects the current body of evidence about the product and its benefit risk profile' was permitted. The Panel noted that its role was to consider the matter in relation to the Code.

The Panel noted that Clause 26.2 permitted information about prescription only medicines to be supplied directly or indirectly to the public but such information must be factual, presented in a balanced way, must not raise unfounded hopes of successful treatment and must not encourage members of the public to ask their health professional to prescribe a specific prescription only medicine. The Panel noted that the supplementary information to Clause 26.2 set out the detailed requirements for reference information which was intended to provide a comprehensive library resource for members of the public giving information relating to prescription only medicines which had marketing authorizations. Reference information must represent fairly the current body of evidence relating to a medicine and its benefit/risk profile.

The Panel noted the webpage in question contained statements related to argatroban (non-proprietary name for Exembol) and Tanatril.

In relation to argatroban, the webpage stated:

'Developed in Japan, argatroban was the first licensed synthetic direct thrombin inhibitor. Approved in twelve European countries, argatroban is marketed for anticoagulation in adult patients with Heparin-Induced Thrombocytopenia Type II (HIT Type II) who require parenteral antithrombotic therapy. Argatroban is given as a continuous intravenous infusion.'

The same page had the following statement in relation to Tanatril:

'Tanatril is used to treat high blood pressure (hypertension). Tanatril is one of a group of medicines called ACE (angiotensin-converting enzyme) inhibitors. Tanatril is available in 5mg, 10mg and 20mg tablet formulation.'

The Panel noted that there was a 'read more' button within the highlighted text box for each product and to the right of the page an adverse event reporting statement. At the bottom of each webpage within the products section, in small font, was the statement 'Please note: certain pages are intended for healthcare professionals only'. The Panel noted that the 'certain pages' were not identified and thus in the Panel's view the intended audience for each page was unclear. The section did not clearly separate pages aimed at health professionals from those containing information for the public. The Panel also noted Mitsubishi Tanabe's submission that the webpages were non-promotional and there was accordingly no requirement to restrict access.

The Panel noted that if the 'read more' button was selected for argatroban, the user was taken to a page which repeated the argatroban statement above and further stated: 'You can find specific information on our products in individual countries by choosing the relevant country from the menu below'. The four brand names for argatroban were listed with links to the relevant country/countries for each. If the user selected the UK link for Exembol, a pop-up box appeared stating that the following pages were intended for viewing by UK health professionals only. If the user selected 'continue' the user was taken to a page that contained: links to the Exembol summary of product characteristics and patient information leaflet; contact details for Mitsubishi Tanabe Pharma Europe; an adverse event reporting statement; and a link to an Exembol website. If the user had selected 'cancel' in response to the pop-up box, he/she would stay on the current page.

The Panel further noted that when the user selected the Tanatril 'read more' button from the main product webpage, he/she would be taken to a page titled 'How to order Tanatril' which gave information regarding ordering the product from a named wholesaler, including the wholesaler's contact details and the PIP codes for each tablet strength. The same page featured: links to the Tanatril summary of product characteristics and patient information leaflet; Mitsubishi Tanabe Pharma Europe's contact details; and an adverse event reporting statement. The bottom of the page stated: 'Please note: certain pages are intended for healthcare professionals only'. The Panel noted its comments on this statement above. The content of this page was such that it appeared to be aimed at health professionals.

The Panel queried whether the products homepage and the pages linked via the read more buttons could be considered reference information as set out in the supplementary information to Clause 26.2 given the lack of information provided for members of the public. There appeared to be nowhere for members of the public to go to access further information on argatroban; the SPC and PIL could only be accessed after the reader confirmed that he/she was a health professional. The page for Tanatril, which included the SPC and PIL, related to how to order the product and appeared therefore to be aimed at health professionals.

The Panel considered that the statement '... argatroban was the first licensed synthetic direct thrombin inhibitor. Approved in twelve European countries ...' which appeared, *inter alia*, on the main product webpage constituted a product claim. The Panel noted that whilst the homepage of the products section in question did not include the brand name for argatroban it did include its non-proprietary name and indication. If a member of the public clicked on the read more button for argatroban they were provided with the brand name of the product in individual countries including Exembol in the UK. The initial webpage also included the brand name and indication for Tanatril.

The Panel also noted that members of the public looking for information on one particular

medicine would automatically be faced with the non-proprietary or brand name and indication of Mitsubishi Tanabe Pharma Europe's other medicine.

Noting its comments above the Panel considered that the webpage advertised prescription only medicines to the public and a breach of Clause 26.1 was ruled.

The Panel noted that Clause 28.1 required that promotional material about prescription only medicines directed to a UK audience which was provided on the internet must comply with all relevant requirements of the Code. The supplementary information stated that unless access to promotional material about prescription only medicines was limited to health professionals and other relevant decision makers, a pharmaceutical company website or a company sponsored website must provide information for the public as well as promotion to health professionals with the sections for each target audience clearly separated and the intended audience identified. This was to avoid the public needing to access material for health professionals unless they chose to. The Panel noted its comments and ruling above. In the Panel's view

the webpage at issue promoted prescription only medicines and therefore access should have been restricted to health professionals and other relevant decision makers because information had not been provided for the public as required by the relevant supplementary information. The Panel noted that access to the webpage had not been so restricted and therefore a breach of Clause 28.1 was ruled.

The Panel noted its comments and rulings above and considered that Mitsubishi Tanabe Pharma Europe had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted that Clause 2 was used as a sign of particular censure and reserved for such use. The Panel did not consider that the circumstances in this particular case warranted a ruling of a breach of Clause 2 and no breach was ruled accordingly.

Complaint received **29 October 2018**

Case completed **20 February 2019**

ANONYMOUS v NAPP

Colour of inverted triangle symbol

An anonymous ‘concerned UK health professional’ complained that the inverted triangle symbol throughout Napp Pharmaceutical’s website was the incorrect colour and might confuse health professionals. The complainant provided a link to a page on the website in question on which the inverted triangles next to the brand name of two medicines were dark grey, not black.

The detailed response from Napp is given below.

The Panel considered the complaint in relation to health professionals and material directed at them.

The Panel noted that the Code required the inverted black triangle symbol to be included on material which related to a medicine which was subject to additional monitoring and which was intended for a patient taking that medicine. The Panel considered that the complainant had not established that the product webpage directed at health professionals was promotional and thus no breach of the Code was ruled in relation to the requirement for inverted black triangles on promotional material.

In the Panel’s view, the inverted black triangle was a well-known and established symbol. Its appropriate use was an important part of medicines regulation. Thus, in the Panel’s view, failure to publish the triangle in the correct colour was, at the very least, inappropriate and might potentially cause confusion. This was a serious matter. The Panel considered that high standards had not been maintained and ruled a breach of the Code.

An anonymous contactable complainant who described him/herself as a ‘concerned UK health professional’ complained about the colour of the inverted triangle symbol on Napp Pharmaceutical Limited’s website.

COMPLAINT

The complainant alleged that the inverted triangle symbol throughout Napp’s website was the incorrect colour and that this might confuse health professionals. The complainant provided a link to a page on the website in question on which the inverted triangles next to the brand name of two medicines were dark grey, not black.

When writing to Napp, the Authority asked it to consider the requirements of Clauses 4.10 and 9.1 of the Code.

RESPONSE

Napp submitted that it took the Code very seriously and aimed to maintain high standards at all times.

Napp noted the rulings in a similar case, (Case AUTH/3049/6/18).

Napp noted that Clause 4.10 stated that all promotional material must show an inverted black equilateral triangle to denote that additional monitoring was required. The black triangle symbol had been used for this purpose for many years and was well known to UK health professionals. The supplementary information to Clause 4.10 stated that the symbol should always be black and in digital communications the size must be easily readable. Napp acknowledged and agreed with the complainant that the font colour of the black triangle was bold dark grey (the text was also dark grey) on the non-promotional corporate website product pages. Napp had removed these pages from the website until the error was corrected.

Napp disagreed that this oversight was a breach of Clause 4.10 because a black triangle was only required to be included on promotional material. Napp submitted that the product pages of the Napp UK corporate website were non-promotional. The material in question was approved by an experienced medical final signatory.

Napp denied a breach of Clause 9.1 and stated that, as part of the spirit of the Code, certain oversights should not automatically constitute a fall in high standards. Napp noted that the complainant had referred to confusion amongst health professionals. As already stated the black triangle symbol had been used for many years in the UK so it was well known to health professionals. A subtle colour change from black to dark grey therefore was highly unlikely to result in confusion. Indeed, depending on computer monitor colour and contrast settings, dark grey might appear as black. This was the case for a number of Napp employees who thought the triangle was black on their computer screen. The final signatory had an additional privacy screen/filter over his/her computer screen which darkened the screen contrast. Whilst Napp acknowledged that the triangle was not black it was confident that if a health professional viewed the webpage, there would be no confusion as to what the triangle represented in terms of monitoring requirements. In the spirit and the principle of the Code, Napp contended that the bold dark grey colour of a black triangle would not jeopardise additional monitoring. Napp asked what overwhelming proof the complainant had provided that this would be the case. This would be more understandable if the symbol was a distinct colour change such as green or red, which it was not. The product pages in question on the Napp website included the names of the medicines with dark grey bold triangles where required, and links to the electronic medicines compendium (eMC) so as

to be able to view the relevant summary of product characteristics (SPC) and patient information leaflet (PIL). The first landing page of the SPC and PIL also contained prominent black triangles.

In summary, Napp accepted that it had inadvertently used a dark grey instead of a truly black inverted triangle on some medicines on its corporate non-promotional website. It had immediately taken down the webpages affected until corrected. However, for the reasons provided above, Napp did not agree that the mistake constituted breaches of either Clause 4.10 or 9.1.

PANEL RULING

The Panel noted that the complainant referred to the colour of the black triangles throughout Napp's website and provided a link to a specific webpage, the URL of which referred to health professionals. It appeared that the link provided by the complainant, despite the URL, linked to a webpage directed at patients which was closely similar to that on the Napp website directed at health professionals. The Panel noted Napp's submission that it had immediately removed the webpage at issue from the website when it was informed of the complaint. The complaint referred to material throughout the website potentially confusing health professionals. The Panel considered the complaint in relation to health professionals and material directed at them.

The Panel noted Napp's submission that the product pages of the Napp corporate website were non-promotional. The Panel noted that the biosimilars product page directed at health professionals included the medicines' names and links to the electronic medicines compendium where the reader

could view the SPC and PIL. The indication was not stated.

The Panel noted that Clause 4.10 stated that when required by the licensing authority, all promotional material must show an inverted black equilateral triangle to denote that additional monitoring was required in relation to adverse reactions. The Panel noted that contrary to Napp's view, it was not only promotional material that required the inclusion of a black triangle. The Panel noted that in addition, Clause 26.3 required the inverted black triangle symbol to be included on material which related to a medicine which was subject to additional monitoring and which was intended for a patient taking that medicine. The Panel noted that Clause 4.10 only required an inverted black triangle to be included on promotional material and considered that the complainant had not established that the product webpage directed at health professionals was promotional and thus no breach of Clause 4.10 of the Code was ruled.

In the Panel's view, the inverted black triangle was a well-known and established symbol. Its appropriate use was an important part of medicines regulation. Thus in the Panel's view, failure to publish the triangle in the correct colour was, at the very least, inappropriate and might potentially cause confusion. This was a serious matter. The Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

Complaint received **29 October 2018**

Case completed **3 January 2019**

COMPLAINANT v PFIZER

Legibility of prescribing information

A contactable complainant, who described him/herself as a concerned UK health professional, alleged that the prescribing information on Pfizer's PfizerPro website for Xeljanz (tofacitinib), Sutent (sunitinib) and Champix (varenicline) was very difficult to read and that there might be other examples.

The detailed response from Pfizer appears below.

The Panel noted that Clause 4.1 required that prescribing information be given in a clear and legible manner and the supplementary information listed recommendations to help achieve clarity. The Panel noted that the prescribing information at issue was published on a website and therefore the recommendations in the Code needed to be considered in the context of digital material.

The Panel noted Pfizer's submission that the prescribing information font size on the pages in question was such that all lower-case characters were approximately 2mm in size when viewed via Google Chrome on a standard desktop device under the default factory zoom setting of 100%. The Panel also noted Pfizer's submission that line-spacing and font-type were selected to facilitate easy reading and that the font-colour was dark grey on a white background and emboldened headings were used at the start of each section.

The Panel noted Pfizer's submission that the website at issue had been designed so that the character line length was determined by the size and orientation of the device screen or window being used as well as the viewer's personal zoom settings applied on his/her device. The Panel noted Pfizer's submission that for the prescribing information identified by the complainant, the average line character length, with factory zoom settings enabled, ranged from approximately 50 characters on a small smart phone to approximately 100 characters on a desktop device. The Panel noted Pfizer's submission that the text line length might occasionally exceed 100 characters on a desktop device, however, given the other legibility measures in place, Pfizer did not consider that this would impact the overall ease of reading the prescribing information on the website.

The Panel noted that the complainant had provided links to the webpages in question, however, he/she did not provide information regarding what device (smart phone, tablet, desktop) he/she had used to read the information and its settings. Nor had the complainant explained why he/she found the prescribing information difficult to read. The Panel noted that the screenshots provided by Pfizer appeared to be of the webpages as viewed from a desktop.

The Panel had some concerns with regard to the impact of the character line length when viewed from a desktop device, and the use of grey coloured font, on ease of readability.

The Panel considered that, on balance, based on the evidence before it, the prescribing information for Xeljanz, Sutent and Champix on the webpages at issue was on the limits of acceptability in terms of legibility and no breach of the Code was ruled.

The Panel noted that the complainant stated that there might be other examples of medicines where the prescribing information was difficult to read and that the entire site should be reviewed. The Panel noted Pfizer's submission that it had reviewed the prescribing information provided across the PfizerPro website and had not been able to identify any legibility issues. The Panel noted that the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant had provided no evidence to support his/her allegation regarding other medicines and no breach of the Code was ruled in this regard.

A contactable complainant, who described him/herself as a concerned UK health professional, complained about the legibility of prescribing information on Pfizer's PfizerPro website. The products in question were Xeljanz (tofacitinib), Sutent (sunitinib) and Champix (varenicline).

COMPLAINT

The complainant alleged that the prescribing information for medicines including Xeljanz, Sutent and Champix on Pfizer's website (<https://www.pfizerpro.co.uk/product>) was very difficult to read and that there might be other examples; the entire site should probably be reviewed.

When writing to Pfizer, the Authority asked it to consider the requirements of Clause 4.1.

RESPONSE

Pfizer submitted that it had reviewed the prescribing information provided across the PfizerPro website and had not been able to identify any legibility issues.

Pfizer noted that Clause 4.1 required all promotional material to include clear and legible prescribing information. The recommendations in the supplementary information to Clause 4.1 might help achieve clarity, particularly in the case of printed materials, however the company did not consider that, for prescribing information to be deemed

legible, each individual recommendation had to be implemented, particularly in relation to digital materials. Pfizer, however, reviewed the prescribing information identified by the complainant against these recommendations as a potential indicator of legibility. Screenshots of the webpages hosting the prescribing information for Xeljanz, Sutent and Champix were provided.

Font size

Pfizer submitted that the prescribing information font size on the pages in question was such that all lower-case characters were approximately 2mm in size when viewed via Google Chrome on a standard desktop device under the default factory zoom setting of 100%. This size would, however, change if the desktop window was minimised or the pages were viewed on a mobile device.

Line length

As PfizerPro had been designed as a 'responsive website', the character line length was determined by the size and orientation of the device screen or window being used as well as the viewer's personal zoom settings applied on his/her device. For the prescribing information identified by the complainant, the average line character length, with factory zoom settings enabled, ranged from approximately 50 characters on a small smart phone to approximately 100 characters on a desktop device. The text line length might occasionally exceed 100 characters on a desktop device, however, given the other legibility measures in place, this did not impact the overall ease of reading the prescribing information on the website.

Line spacing

The spacing between the lines of text was set at 1.4 which was designed to facilitate easy reading of the prescribing information.

Font type

The site was designed using an FS Albert font which was a standard, simple, widely used website font selected to facilitate easy reading on electronic devices.

Font colour and contrast

The prescribing information was provided in a dark grey font on a white background in order to provide optimal contrast between text and background.

Headings and section breaks

Emboldened headings were used for the start of each section and in many, but not all cases, each section started on a new line.

In conclusion, Pfizer considered that the prescribing information for the three medicines identified by the complainant was presented in a legible, easy to read format on the PfizerPro website, consistent with the requirements of Clause 4.1.

PANEL RULING

The Panel noted that this complaint should be considered under the requirements of the 2016 Code. The Panel noted that Clause 4.1 required that prescribing information be given in a clear and legible manner. The supplementary information to Clause 4.1, Legibility of Prescribing Information, in the 2016 Code, listed the following recommendations to help achieve clarity:

- type size should be such that a lower case letter 'x' was no less than 1mm in height
- lines should be no more than 100 characters in length, including spaces
- sufficient space should be allowed between lines to facilitate easy reading
- a clear style of type should be used
- there should be adequate contrast between the colour of the text and the background
- dark print on a light background was preferable
- emboldening headings and starting each section on a new line aids legibility.

The Panel noted that the prescribing information at issue was published on a website and therefore the recommendations in the supplementary information to Clause 4.1 regarding legibility of prescribing information needed to be considered in the context of digital material.

The Panel noted Pfizer's submission that the prescribing information font size on the pages in question was such that all lower-case characters were approximately 2mm in size when viewed via Google Chrome on a standard desktop device under the default factory zoom setting of 100%. The Panel also noted Pfizer's submission that line-spacing and font-type were selected to facilitate easy reading and that the font-colour was dark grey on a white background and emboldened headings were used at the start of each section.

The Panel noted Pfizer's submission that the website at issue had been designed so that the character line length was determined by the size and orientation of the device screen or window being used as well as the viewer's personal zoom settings applied on his/her device. The Panel noted Pfizer's submission that for the prescribing information identified by the complainant, the average line character length, with factory zoom settings enabled, ranged from approximately 50 characters on a small smart phone to approximately 100 characters on a desktop device. The Panel noted Pfizer's submission that the text line length might occasionally exceed 100 characters on a desktop device, however, given the other legibility measures in place, Pfizer did not consider that this would impact the overall ease of reading the prescribing information on the website.

The Panel noted that the complainant had provided links to the webpages in question, however, he/she did not provide information regarding what device (smart phone, tablet, desktop) he/she had used to read the information and its settings. Nor had the complainant explained why he/she found the prescribing information difficult to read. The

Panel noted that the screenshots provided by Pfizer appeared to be of the webpages as viewed from a desktop.

The Panel had some concerns with regard to the impact of the character line length when viewed from a desktop device, and the use of grey coloured font, on ease of readability.

The Panel considered that, on balance, based on the evidence before it, the prescribing information for Xeljanz, Sutent and Champix on the webpages at issue was on the limits of acceptability in terms of legibility and no breach of Clause 4.1 was ruled.

The Panel noted that the complainant stated that there might be other examples of medicines where the prescribing information was difficult to

read and that the entire site should be reviewed. The Panel noted Pfizer's submission that it had reviewed the prescribing information provided across the PfizerPro website and had not been able to identify any legibility issues. The Panel noted that the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant had provided no evidence to support his/her allegation regarding other medicines and no breach of Clause 4.1 was ruled in this regard.

Complaint received **29 October 2018**

Case completed **8 March 2019**

EX-EMPLOYEE v NOVARTIS

Medical Representatives Examination

An ex-employee of Novartis complained about a field-based manager not having completed the medical representatives' examination. The complainant alleged that the field-based manager stated that he/she had managed to avoid having to complete the ABPI examination for medical representatives for a given number of years and was still required to complete it.

The detailed response from Novartis is given below.

The Panel noted Novartis' submission that the employee in question had passed the medical representatives' examination prior to starting to work for Novartis. The Panel thus ruled no breaches of the Code in relation to the individual's employment at Novartis and because there was no evidence to show that the Novartis employee had made the statement in question.

An ex-employee of Novartis complained about a field-based manager not having completed the medical representatives' examination.

COMPLAINT

The complainant explained that in 2017 whilst working at Novartis he/she was made aware by a field-based manager at Novartis that he/she had managed to avoid having to complete the ABPI examination for medical representatives for a given number of years and was still required to complete it. The complainant alleged that it might be a breach of Clauses 2 and/or 15 and 16.

RESPONSE

Novartis confirmed that the named individual was an associate (the term Novartis used for an employee of the company) who had passed the ABPI examination for medical representatives prior to commencement of employment with Novartis. The associate categorically denied ever stating that he/she 'avoided the ABPI examination'.

Novartis submitted that whilst the complainant was quite broad in the clauses that he/she quoted (Clauses 2, 15 and 16), it was mindful of the very narrow nature of the complaint and the Authority's specific reference to Clause 16.3. Novartis submitted that it therefore focused on the pertinent aspects of those clauses and referred to the applicability of Clause 1.7. Novartis stated that Clause 16.3 was clear on the requirement for a representative to take an appropriate examination within the first year of employment and to have passed it within 2 years. Novartis submitted that the associate passed the ABPI examination for medical representatives whilst employed in another pharmaceutical company.

Regardless of the nature of the associate's role now or at any time during his/her employment at Novartis, the fact remained that he/she held the stated qualification for the entire length of his/her employment with Novartis and so there could have been no breach of Clause 16.3 during that time.

Novartis noted that Clause 15 was a broad clause that covered a number of different aspects relevant to the role of a representative. When considering this clause Novartis focused on the narrow nature of the complaint. Novartis submitted that Clause 15.2 was the only relevant clause in this case which stated that representatives must at all times maintain a high standard of ethical conduct in the discharge of their duties and must comply with all relevant requirements of the Code. Novartis stated that it had demonstrated that the named associate had passed the medical representatives' examination and on questioning, denied ever stating that he/she avoided taking the examination. Novartis therefore denied a breach of Clause 15.

Novartis noted that Clause 1.7 provided a definition of the term 'representative'. Novartis noted that regardless of whether the associate's current or prior roles fell within the scope of the definition in Clause 1.7, he/she held the qualification at issue in this complaint.

Novartis denied a breach of Clauses 15 and 16, and therefore considered that there could have been no breach of Clause 2. Novartis trusted that in confirming that the associate passed the ABPI medical representative examination prior to employment at Novartis and denied ever stating that he/she had avoided taking it, demonstrated that there had been no breach of the Code.

PANEL RULING

The Panel noted that Clause 16.3 required representatives to pass the relevant examination. It required that the medical representatives' examination be taken by representatives whose duties comprised or included one or both of 'calling upon doctors and/or dentists and/or other prescribers' and 'the promotion of medicines on the basis, *inter alia*, of their particular therapeutic properties'. The Panel noted that the named Novartis employee had passed the medical representatives' examination prior to starting to work for Novartis. The Panel noted Novartis' submission about the employee's current field-based role and regardless of the nature of the role now or at any time during his/her employment at Novartis, the fact remained that he/she held the stated qualification for the entire length of his/her employment with Novartis. The Panel had no information about the individual's

employment history prior to Novartis. The Panel thus ruled no breach of Clause 16.3 in relation to the individual's employment at Novartis.

The Panel noted that the parties' accounts differed with regard to what the Novartis employee stated about the examination. The complainant alleged that the Novartis employee had stated that he/she had managed to avoid taking the medical representatives' examination for a given number of years and was still yet to take it. The Novartis employee denied having said this. The Panel noted that the Novartis employee had completed the medical representative examination at the time he/

she was alleged to have made the comment. The Panel considered that there was no evidence to show that the Novartis employee had made the statement in question. The Panel ruled no breach of Clause 15.2.

The Panel noted its comments and rulings above and consequently ruled no breach of Clause 2.

Complaint received **6 November 2018**

Case completed **14 December 2018**

ANONYMOUS NON-CONTACTABLE v NOVO NORDISK

Advisory boards

An anonymous, non-contactable complainant who described him/herself as a concerned health professional submitted a complaint about Novo Nordisk advisory boards.

The complainant stated that in the current climate of companies using advisory boards as disguised promotion he/she wished to bring to the Authority's attention that Novo Nordisk had been working in breach of the ABPI Code by hosting multiple advisory boards with the same customers on a repeated basis over the last 5 years. The complainant alleged that the transfer of value of some of the health professionals attending such advisory boards was excessive and not a legitimate activity to gain insights but to reward.

The complainant referred to advisory boards hosted at a named embassy and in the presence and company of the ambassador. Often the advisory boards were vehicles for senior leaders to 'sell' strategic plans rather than elicit insights; these presentations lasted longer than was deemed an acceptable time limit. These strategic advisory boards were held every year and exactly the same key opinion leaders attended. The company also held product advisory boards and, in some years, had held them locally with the same thought leaders and between 2012 and 2018 over 250 advisory boards had been conducted. The complainant was bemused about what information Novo Nordisk was legitimately seeking for these numbers of advisory boards.

The detailed response from Novo Nordisk is given below.

The Panel was concerned at the number of advisory board meetings at around 200 in 6 years. Novo Nordisk needed to be very certain that each met the requirements of the Code, particularly the legitimate need for the services and the criteria for and number of consultants. The Panel was unsure whether there was always a justifiable need for similar advisory boards in different areas of the UK. However, the complainant had only provided limited information and no detailed allegations had been made in this regard.

The Panel was also concerned that there was a lack of pre-reading for some of the advisory boards, for example three of the four advisory boards held at the named embassy. The minutes/reports etc provided for some of the advisory boards showed some of the learnings gained. It was not always clear from the documentation that the focus was on obtaining feedback. For some meetings the proportion of time on the agenda allocated to presentations did not appear to allow adequate time for discussion. Feedback from the participants should be the main focus of these meetings and

only a small proportion of the time should be spent on company presentations. There were additional concerns about the advisory boards at the named embassy including the justification for the presence of the ambassador, the length of presentations compared to the time seeking advice (for example one meeting at the embassy the time allocated for presentations was just under two hours (not including the opening and concluding presentations) compared with just over two hours for feedback), the number of advisors and the ratio of Novo Nordisk staff to advisors at some meetings, and that dinner was provided despite the meetings starting at 11 or 12 including lunch and finishing between 5 and 6pm. The Panel queried whether it was usual for very senior Novo Nordisk staff to attend such an advisory board. Given all these concerns the Panel considered that Novo Nordisk had failed to maintain high standards in relation to the advisory boards in general and a breach was ruled.

The Panel noted that the complainant had provided no evidence with regard to the payments for attending advisory boards or that there was not a legitimate need for them. Although the Panel had concerns it did not consider that the complainant had shown on the balance of probabilities that the arrangements were unacceptable as alleged. The Panel ruled no breaches of the Code. This ruling applied to the range of meetings since 2012.

Although the Panel had concerns it did not consider the complainant had shown on the balance of probabilities that the advisory boards were disguised promotion and no breach of the Code was ruled. This ruling applied to the range of meetings since 2012.

The Panel noted its concerns about some of the hospitality provided. Again the complainant was not clear about his/her concerns and had provided no evidence. Given the generality of the allegations, the Panel's view was that the complainant had not satisfied the burden of proof. The Panel therefore ruled no breach of the Code. This ruling applied to the range of meetings since 2012.

The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure.

An anonymous, non-contactable complainant who described him/herself as a concerned health professional submitted a complaint about Novo Nordisk advisory boards.

COMPLAINT

The complainant stated that in the current climate of companies using advisory boards as disguised promotion he/she wished to bring to the Authority's

attention that Novo Nordisk had been working in breach of the ABPI Code by hosting multiple advisory boards with the same customers on a repeated basis over the last 5 years. The complainant alleged that when assessing the transfer of value of some of the health professionals attending such advisory boards, it was excessive and not a legitimate activity to gain insights but to reward.

The complainant referred to advisory boards hosted at a named embassy and in the presence and company of the ambassador. Often the advisory boards were vehicles for senior leaders to 'sell' strategic plans rather than elicit insights; these presentations lasted longer than was deemed an acceptable time limit. These strategic advisory boards were held every year and exactly the same key opinion leaders attended. The company also held product advisory boards and, in some years, had held them locally with the same thought leaders and between 2012 and 2018 over 250 advisory boards had been conducted. The complainant was bemused about what information Novo Nordisk was legitimately seeking for these numbers of advisory boards.

The complainant alleged breaches of the following and advised the PMCPA to investigate further.

- Clause 2 Bringing discredit to the industry
- Clause 9 High standards and suitability
- Clause 12 Disguised promotion
- Clause 18 Inducements and appropriate payments of officials
- Clause 22 Meetings, hospitality and sponsorship
- Clause 23 Use of consultants – legitimate service.

In writing to Novo Nordisk the Authority referred to Clauses 23.1, 18.1, 12.1, 9.1 and 2. The company was also advised that with regard to Clause 23.1 in the 2016 Code this clause had a different number in the 2011-2014 Codes. The date of the event was relevant.

RESPONSE

Novo Nordisk submitted that given the complainant stated that he/she had an in-depth knowledge of advisory boards which had been held by Novo Nordisk over a long period of time; in its view, and in light of attendees at its advisory board meetings (as detailed further below), such knowledge would be more akin to that of a senior level employee rather than an external health professional advisor. However, Novo Nordisk stated that it took the complaint very seriously and also its responsibilities with regard to holding advisory boards. Despite the broad ranging nature of the allegations, Novo Nordisk had done its best in the short time available to investigate and respond to the matters raised.

Advisory board procedures and policies

Novo Nordisk submitted it had robust processes and policies in place governing advisory boards and referred to its standard operating procedures (SOP) for services such as providing advice at an advisory board.

A specific Novo Nordisk Guidance Document created during 2016 which covered advisory board set up and planning ensured that advisory board meetings were conducted in compliance with PMCPA guidance with clear objectives, focussed questions and sufficient discussion time in order to allow for feedback from advisors. This guidance document also gave direction on inviting relevant advisors and clarified who could be invited based on feedback sought and how often. Furthermore, clear instructions were given regarding venues and locations of advisory boards as well as other factors such as how many advisors could be invited to a meeting and the relevant internal Novo Nordisk attendees who could be involved in such meetings.

Novo Nordisk consistently reviewed its need for advice and consultation reviewing the set-up, conduct and feedback from advisory boards multiple times a year. As part of this review it had evaluated who it had sought advice from as well as how it implemented that advice across the company through follow-up action plans.

Background to Novo Nordisk therapeutic areas

Novo Nordisk submitted that the main therapeutic areas for Novo Nordisk currently were diabetes and cardiometabolic disease, obesity, haemophilia, growth hormone therapy and women's health. Additionally, Novo Nordisk was also developing into newer therapeutic areas (brief details were provided) which impacted its activities and led to a significant need for further advice.

Diabetes had been and remained the mainstay of Novo Nordisk's therapeutic focus. Diabetes was very prevalent, affecting 6% of the UK population and costing the NHS approximately 10 billion pounds per year in direct costs with an equal amount in indirect costs. Furthermore, diabetes was linked with lifestyle choices and was, therefore, a disease which required constant and significant discussion and collaboration with health professionals to understand the social and medical implications of treatments. Within diabetes there were significant differences in treatment of patients with type 1 diabetes and type 2 diabetes. Within the NHS, diabetes care occurred across primary, intermediate and secondary care with multiple therapies and care pathways involving many specialities. Given the primary care focus on diabetes, there were substantial local and regional variations in care and types of therapies commissioned across different clinical commissioning groups (CCGs) and formularies around the country.

Overview of advisory boards November 2012 – November 2018

Novo Nordisk provided a summary document of the advisory boards held in the past 6 years, showing number held per year and related area of advice.

In the period November 2012 – November 2018 (inclusive) Novo Nordisk held 202 advisory board meetings to gain advice at national, regional or local levels across the various therapeutic areas. The

objectives had varied across the years from input to clinical trials, clinical care, NHS structure, patient pathways, to patient experience and funding.

UK healthcare evolution and Novo Nordisk's evolving focus had been the underlying driver for seeking external advice. During this timeframe Novo Nordisk launched 7 new medicines across its existing therapy areas (diabetes, obesity and haemophilia), expanded focus to cardiovascular disease as a result of an updated label for GLP1-RA therapies in patients with diabetes and cardiovascular disease, and changed its prices and pricing strategy post-launch for its basal insulin, Tresiba. Novo Nordisk had also updated its pipeline and therapeutic focus substantially and changed its strategy in its Women's Health franchise. (brief details were provided). Additionally, there had been a large volume of new data for which Novo Nordisk had sought advice on relevance and impact on UK practice and commissioning.

In addition, changes in NHS structure and devolved functioning such as the introduction of CCGs, sustainable and transformation partnership (STPs) and regional medicines optimisation committees (RMOCs) had had fundamental effects on medicine commissioning in primary and secondary care. With the primary care focus for diabetes, this led to significant heterogeneity of care across the UK and localization of medicine procurement across over 200 CCGs in 2013/2014. This, in turn, led to a change in therapeutic treatment across the country with significant localization of care leading to a differing availability of therapies across postcodes around the country which gave rise to a need for more localised advice. Further changes to NHS structure with the creation of STPs (with a clear mandate on diabetes) and RMOCs occurred in 2016. Given the nature of these changes and their effects on local commissioning, Novo Nordisk had sought advice from health professionals and other relevant decision makers working in the local areas on these changes during that time period.

Novo Nordisk provided a detailed overview of the advisory boards, including the dates they were held, location, number of advisors attending and objectives to give further granularity on the points raised above.

In line with PMCPA guidance, Novo Nordisk submitted it had continuously reviewed the nature and set up of its advisory boards and the feedback provided by each advisory board across the years. This had led to changes in the number, structure, function and attendees of its advisory boards over the years. For example, as the NHS commissioning structure had changed and commissioning had become more focussed across APCs (area prescribing committees) and larger formularies, Novo Nordisk had ceased to seek advice on local commissioning changes.

Venues

Novo Nordisk provided locations of various advisory boards and submitted that its SOP gave clear direction about suitable venues for meetings, and was in line with Clause 22.1.

In the last 6 years, Novo Nordisk had held 4 advisory board meetings at the meeting space at the embassy. These meetings occurred between December 2012 and November 2015. Novo Nordisk submitted that the costs for the meetings, including sustenance, were within the range of other local hotel venues and within ABPI limits. The embassy and meeting room were certainly not lavish. Any sustenance provided had been functional and not excessive. Novo Nordisk understood that over the years, the embassy meeting space had been used for multiple business and health related events; nevertheless, given the potential perception, Novo Nordisk elected in 2015 to stop using the embassy for advisory board purposes.

All other advisory board meetings had been held at hotels, conference centres, colleges and the Novo Nordisk offices.

Advisors attending multiple advisory board meetings

Novo Nordisk stated that the selection of advisors had been based on expertise, knowledge and ability to contribute on issues relevant to the objectives of the meeting. This had inevitably led to some overlaps between years.

In the timeframe, a number of advisors had attended more than one advisory board. This was because they were leading experts in their field, and were the right person to provide advice to fulfil the clear objective of the advisory board. Advisors who had attended multiple advisory boards were selected for their knowledge, research interests, participation in multiple clinical trials and expertise at national and regional levels. Some of these advisors also had key roles in multiple NHS and access committees at a national, regional or local level.

Documentation regarding meetings and advisor honoraria

Novo Nordisk carefully considered the PMCPA request for relevant materials such as meetings invitations, agenda and minutes and had strived to provide as full a picture as possible consistent with its other obligations of data privacy and resources and time available. Due to the volume of paperwork and respecting the timeframe, Novo Nordisk took an approach of providing all supporting documents for the past 2 years (2017-2018). This included invitations, agendas, minutes and follow-up documents. It provided a template invitation as an example of what was sent to advisors for these meetings; in those instances where a different template was used, that had been provided. Remaining documents (2012-2016) could also be available upon further request. All other requested details were provided for the full period.

Novo Nordisk stated it adhered to the data minimisation principle in accordance with General Data Protection Regulation (GDPR) requirements, and had, therefore, provided de-identified data in relation to remuneration, where it had redacted the names of the health professionals. Each advisor was assigned a numerical identifier and their payments

set out; thus, it was possible to see how many advisors attended multiple advisory boards over the 7 year period and fees for service paid.

Fair market value documents 2015 and 2018 outlining Novo Nordisk rates were provided. The payments had been disclosed.

Novo Nordisk submitted that the allegations were unfounded and it had not breached Clauses 23.1, 18.1, 12.1, 9.1 and 2 of the 2016 Code.

In response to a request for further information Novo Nordisk confirmed that the 'Ad board honoraria' tab provided data on the numbers of times each healthcare professional attended Novo Nordisk advisory boards during the period 2012 – 2018 (November to November). Unfortunately there was an error in the original spreadsheet; during the process of de-identifying the data, some meetings with common titles but in fact separate events were mistakenly given the same meeting number. Therefore it looked like a small number of healthcare professionals had attended the same meeting more than once. An updated spreadsheet was provided.

Attendance at multiple advisory boards

With regard to attendance at multiple advisory boards, Novo Nordisk submitted that some healthcare professionals had attended more than one advisory board in a year. There were several reasons why this might occur. Each advisory board had a different focus and advice required, which was reflected in the objectives for the advisory board. However, there might be a limited number of specialists who were able to give advice about a particular topic. For example, if advice was required for market access and reimbursement for diabetes therapies in Wales, there might be one or two healthcare professionals who had the knowledge to give advice on this. The same healthcare professional might also be a clinical trial investigator who would then be part of a limited number of professionals who were able to give advice on a more scientific level at a different advisory board.

In addition, some therapy areas had a very limited number of specialists at this time (eg obesity). As obesity was a risk factor for type 2 diabetes, some diabetes specialists were also obesity specialists and therefore might be invited to advisory boards in both therapy areas. As stated in its initial response, some advisors also had key roles in multiple NHS and access committees at a national, regional or local level.

Novo Nordisk submitted that it applied robust selection criteria to identify those who were invited to attend advisory boards. Expertise in the subject matter of interest drove the identification process. Aligned with the industry practice, identification of experts was carried out through an external third party mapping, using desktop research and peer nomination. This approach enabled an objective identification process that was repeated every three years to ensure the most updated list of experts were available based on emerging research and practices.

Fair Market Value rates

In response to the question from the Panel about the differences in fair market value rates paid to certain individuals in earlier years compared to later years; two health professionals were highlighted, Novo Nordisk submitted that sometimes advisors were paid less than the maximum fair market value amount. This accounted for lower payments.

Novo Nordisk submitted that one of the health professionals attended an advisory board in 2013 and chaired the meeting; there was one hour preparation time in addition to the advisory board time (1+2 hours). The hourly rate was in line with the Fair Market Value rates in 2013. Whilst looking at the details of advisory board attendance and work for this health professional, Novo Nordisk discovered that he/she had also attended two other advisory boards in 2013. The company updated the spreadsheet to accurately reflect these details.

The other health professional was the chair of the advisory board meeting in 2013, and as such had to undertake preparation work. This was in addition to the 6 hours service at the advisory board meeting. Unfortunately, Novo Nordisk stated that it did not have the corresponding paperwork to show the preparation work – it was approximately five and a half years ago and it was thought that a Novo Nordisk employee might have deleted some information given he/she thought it would no longer ever be needed. Novo Nordisk would expect 1 or 2 hours preparation for this advisory board. Details of the hourly rate were provided based on a 2 hour preparation.

Advisory boards held at the embassy

Novo Nordisk provided the supporting documentation for the four meetings held at the embassy listing the advisors, their honoraria, and the fair market value rate per hour. Information regarding the subsistence for attendees and additional cost information was also provided.

In response to a further request for additional information Novo Nordisk provided copies of the minutes for the four meetings at the named embassy. There was no pre-reading for three of these meetings (2012, 2013 and 2015) and for the other (2014) the pre-reading consisted of a clinical paper (Buse *et al*, 2014) and summary of product characteristics (SPC) for Xultophy. Novo Nordisk provided a document detailing how the advice had been used. Three of the advisory boards were to gain advice on the Novo Nordisk portfolio and pipeline at a strategic level, discussing Phase 2 data in some cases. Novo Nordisk stated that the advice gained had led to changes in strategy and planning for the therapy areas in question.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the PMCPA stated that anonymous complaints would be accepted but that, like all other complaints, the complainant had the burden

of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant had provided no evidence to support his/her allegations and could not be contacted for more information. The PMCPA was not an investigatory body as such.

The Panel noted that it was acceptable for companies to pay health professionals and others for relevant advice. Nonetheless, the arrangements for such meetings had to comply with the Code, particularly Clause 23. To be considered a legitimate advisory board the choice and number of participants should stand up to independent scrutiny; each should be chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes of the advisory board. The number of participants should be limited so as to allow active participation by all. The agenda should allow adequate time for discussion. The number of meetings and the number of participants should be driven by need and not the invitees' willingness to attend. Invitations to participate should state the purpose of the advisory board meeting, the expected advisory role and the amount of work to be undertaken. If an honorarium was offered it should be made clear that it was a payment for such work and advice. Honoraria must be reasonable and reflect the fair market value of the time and effort involved.

The Panel noted that Clause 22.1 stated that hospitality must be strictly limited to the main purpose of the event and must be secondary to the purpose of the meeting, ie subsistence only. The level of subsistence offered must be appropriate and not out of proportion to the occasion. Clause 22.1 applied to scientific meetings, promotional meetings, scientific congresses and other such meetings and training. The supplementary information to Clause 22.1 also stated that a useful criterion in determining whether the arrangements for any meeting were acceptable was to apply the question 'Would you and your company be willing to have these arrangements generally known?'. The impression that was created by the arrangements for any meeting must always be kept in mind.

The Panel was concerned at the number of advisory board meetings at around 200 in 6 years. Companies needed to be very certain that each met the requirements of the Code, particularly the legitimate need for the services and the criteria for and number of consultants. The Panel was unsure whether there was always a justifiable need for similar advisory boards in different areas of the UK. However, the complainant had only provided limited information and no detailed allegations had been made in this regard.

The Panel was also concerned that there was a lack of pre-reading for some of the advisory boards, for example three of the four advisory boards held at the named embassy. The minutes/reports etc provided for some of the advisory boards showed some of the learnings gained. It was not always clear from the documentation that the focus was on obtaining

feedback. For some meetings the proportion of time on the agenda allocated to presentations did not appear to allow adequate time for discussion. Feedback from the participants should be the main focus of these meetings and only a small proportion of the time should be spent on company presentations. There were additional concerns about the advisory boards at the named embassy including the justification for the presence of the ambassador, the length of presentations compared to the time seeking advice (for example one meeting at the embassy the time allocated for presentations was just under two hours (not including the opening and concluding presentations) compared with just over two hours for feedback), the number of advisors and the ratio of Novo Nordisk staff to advisors at some meetings, and that dinner was provided despite the meetings starting at 11 or 12 including lunch and finishing between 5 and 6pm. The Panel queried whether it was usual for very senior Novo Nordisk staff to attend such an advisory board. Given all these concerns the Panel considered that Novo Nordisk had failed to maintain high standards in relation to the advisory boards in general and a breach of Clause 9.1 was ruled. (This clause was the same in codes since 2008).

The Panel noted that the complainant had provided no evidence with regard to the payments for attending advisory boards or that there was not a legitimate need for them. Although the Panel had concerns it did not consider that the complainant had shown on the balance of probabilities that the arrangements were unacceptable as alleged. The Panel ruled no breach of Clause 23.1 and consequently no breach of Clause 18.1. This ruling applied to the range of meetings since 2012, when the relevant clauses were 20.1 and 18.1 until the 2016 Code when the relevant clauses were 23.1 and 18.1)

Although the Panel had concerns it did not consider the complainant had shown on the balance of probabilities that the advisory boards were disguised promotion and no breach of Clause 12.1 was ruled. This ruling applied to the range of meetings since 2012. (This clause was the same in codes since 2008).

The Panel noted its concerns about some of the hospitality provided. Again the complainant was not clear about his/her concerns and had provided no evidence. Given the generality of the allegations, the Panel's view was that the complainant had not satisfied the burden of proof in relation to Clause 22. The Panel therefore ruled no breach of Clause 22.1. (This ruling applied to the range of meetings since 2012 when the relevant clause was 19.1 until the 2016 Code when the relevant clause was 22.1).

The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure.

Complaint received **7 November 2018**

Case completed **1 April 2019**

HEALTH PROFESSIONAL v BIOGEN IDEC

Imraldi Mailing

A hospital doctor complained that he/she had been inconvenienced by having to collect from the post office an Imraldi (adalimumab) mailing sent by Biogen Idec because the postman was unable to deliver the package to his/her home address as a signature was required. The complainant stated that this was unacceptable and an inappropriate marketing practice which constituted harassment. At least one other of his/her colleagues had also been put to considerable inconvenience by this practice.

The complainant stated that he/she had tried to ask the mailing company to remove him/her from its database and was awaiting a reply.

The detailed response from Biogen Idec is given below.

The Panel noted the complainant's submission that the Imraldi mailing was sent to his/her home address and that he/she had received information from pharmaceutical companies over the years to home and work addresses. The Panel noted Biogen Idec's submission that it had confirmed with the third-party mailing house that the addresses held on its database were those which had been provided by health professionals' themselves. The Panel noted the complainant's concern that the Imraldi mailing required a signature on receipt and he/she had to collect it from the post office which was considerably inconvenient.

Based on Biogen Idec's submission, it appeared to the Panel that the Imraldi mailing at issue was non-promotional additional Risk Management Materials (aRMMs) which Biogen Idec was required to send to targeted health professionals based on its legal and regulatory obligations. The Panel noted Biogen Idec's submission that the relevant pharmacovigilance guideline required it to track dissemination of the aRMMs and that by sending the materials by recorded delivery it allowed Biogen Idec to monitor whether the material at issue was actually received by the health professional.

The Panel acknowledged that extreme dissatisfaction was usually necessary on the part of an individual before he or she was moved to submit a complaint. The Panel noted it might be inconvenient for an individual to have to collect a package from the post office during office hours. However, in the Panel's view, that Biogen Idec wanted to track its dissemination of risk minimisation materials to ensure that it was received for compliance purposes was not unreasonable in this particular case. Taking everything into consideration, and noting its comments above, the Panel did not consider that sending the Imraldi mailing at issue by recorded

delivery was inappropriate marketing practice that constituted harassment as alleged. The Panel considered that Biogen Idec had not failed to maintain high standards in this regard and ruled no breach of the Code.

The Panel noted the complainant's comment that he/she had asked the mailing company to remove him/her from its database and was awaiting a reply. The Panel noted that the complainant wished to remain anonymous to Biogen Idec and had not provided details of when he/she had submitted the request to be removed from the mailing list. The Panel considered that the complainant had not discharged the burden of proof that Biogen Idec had failed to maintain high standards in this regard and no breach of the Code was ruled.

A hospital doctor complained that he/she had been inconvenienced by having to collect from the post office an Imraldi (adalimumab) mailing. Samsung Bioepis was the marketing authorisation holder for Imraldi. Biogen International GmbH was partnered with Samsung Bioepis for all Imraldi commercial activities, including required national regulatory activities. Biogen Idec Limited confirmed that it was responsible for the Imraldi mailing at issue which solely featured the Biogen company logo.

COMPLAINT

The complainant submitted that his/her complaint was prompted by the receipt of a packet of commercial/marketing information from a company that used a database (kept by a named mailing company) to access his/her details. A photograph of the Imraldi material at issue was provided by the complainant. The postman was unable to deliver the package to the complainant's home address as a signature was required. The complainant stated that he/she then had to go to considerable inconvenience to pick the package up from the post office five miles away on a busy high street in office hours. This was unacceptable; at least one other of his/her rheumatology colleagues had also been put to considerable inconvenience by this practice.

The complainant noted that he/she had received information from pharmaceutical companies over the years to both his/her home and work addresses in this way, but the post labels originating from the mailing company now stated as a special instruction that the package 'cannot be left without a signature'. This was the case for a recent package delivered to work which put busy secretaries under unnecessary pressure.

The complainant considered that this was an inappropriate marketing practice which constituted harassment.

The complainant stated that he/she had tried to ask (by telephone and email) the mailing company to remove him/her from its database and was awaiting a reply.

When writing to Biogen Idec, the Authority asked it to consider the requirements of Clause 9.1 of the Code.

RESPONSE

Biogen Idec explained that the materials at issue were additional Risk Management Materials (aRMMs) that were required as a condition of the Imraldi marketing authorisation to be disseminated to health professionals before launch. The mailing was carried out on behalf of Biogen by a third-party medical mailing specialist.

Biogen Idec stated that it understood that the complaint did not relate to the content of the mailing, but rather the method by which the mailing was sent, in particular, that it required a signature upon receipt which caused inconvenience due to the complainant having to collect it from the post office.

Biogen Idec noted that the complainant referred to information from other pharmaceutical companies being delivered using recorded delivery/courier and had referred to another recent example delivered to the complainant's work which required a signature and appeared unrelated to the Imraldi mailing. As such, Biogen Idec submitted that the mailing method it used for the Imraldi mailing at issue was, at the very least, not unique practice and that this was not surprising considering the published guidelines on good pharmacovigilance practices.

Biogen Idec noted that the complainant referred to receipt of 'commercial/marketing information'. Biogen Idec submitted that the Imraldi mailing in question was neither commercial nor marketing information, but legally mandated information concerning aRMMs.

Biogen Idec submitted that the launch of Imraldi required the company to post aRMMs to relevant health professionals with information about the medicine. It was a condition of the product licence to provide these risk mitigation materials to target health professional specialities who would use the product, and this was mandated by the European Medicines Agency (EMA). The aRMMs were agreed with the Pharmacovigilance Risk Assessment Committee under the EU Risk Management Plan, and subsequently approved by the EMA's Committee for Medicinal Products for Human Use.

The content of the aRMMs also must be, and was, approved nationally by each National Competent Authority, such as the Medicines and Healthcare products Regulatory Agency (MHRA) and distributed to the target health professionals before launching the product. Furthermore, a list of health professional specialities to be targeted with the aRMMs information, based on the approved indications for use, was sent to the MHRA for its review, modification and approval at national level. The MHRA approved the aRMMs for the UK

on 31 July 2018 and requested that the target list included the following: homecare providers and hospital pharmacists, rheumatology, dermatology, gastroenterology, ophthalmology, and specialist rheumatology paediatric clinical nurse specialists and nurse consultants.

Biogen Idec noted that the Imraldi mailing was thus not a form of advertising (and not direct marketing materials under the Privacy and Electronic Communications (EC Directive) Regulations 2003), but legally mandated materials that were sent to targeted health professionals in compliance with the company's regulatory obligations. It also clearly did not constitute harassment, although this specific allegation appeared to concern receipt of mailings generally and was not a complaint about the Imraldi mailing specifically.

As noted above, Biogen Idec engaged a medical mailing specialist, to administer the mailing of the aRMMs across Europe. The mailing company administered a database of practising health professionals' contact information, which it updated and checked regularly. The mailing company identified the health professionals in its database to whom the aRMMs should be disseminated, based on the MHRA approved target list, and printed and disseminated the materials on behalf of Biogen Idec.

In relation to the specific complaint that the aRMMs were sent by recorded delivery rather than ordinary mail, Biogen Idec noted that the relevant pharmacovigilance guideline required it to track dissemination of the aRMMs. In particular, the Heads of Medicines Agencies and EMA's Guideline on good pharmacovigilance practices (GVP) Module XVI – Risk minimisation measures: selection of tools and effectiveness indicators (Rev 2) effective as at 31 March 2017, specifically provided as follows:

'XVI.B.4.1.1. Reaching the target population

When risk minimisation measures involve the provision of information and guidance to healthcare professionals and/or patients by means of educational tools, measures of distribution **and receipt** should be used to acquire basic information or implementation. These metrics should focus on assessing whether the materials were delivered to the target audience and **whether they were actually received by the target population** (emphasis added).'

Biogen Idec submitted that sending the aRMMs by recorded delivery allowed it to track its compliance with providing this information to health professionals and confirming whether they were actually received. It also allowed Biogen Idec in the future, should it be necessary, to prove compliance with its regulatory obligations and best practice guidelines to any regulatory authority (such as the MHRA) which might request information/proof in this regard.

In Biogen Idec's view, distribution of aRMMs information by recorded delivery was wholly consistent with the maintenance of high standards in the pharmaceutical industry, and in any event,

could not reasonably be considered to be in breach of maintaining high standards under Clause 9.1 of the Code.

Biogen Idec stated that it was not its practice to send materials to home addresses and if it happened on this occasion, Biogen Idec confirmed with the mailing company that the addresses held on its database were those which had been provided by the health professionals themselves. Biogen Idec was committed to compliance with the General Data Protection (GDPR) regulations and ensuring that any supplier or vendors it used were GDPR compliant. Accordingly, if the complainant wished to amend his/her mailing address or be removed from any mailing list, Biogen Idec recommended that he/she contacted the mailing company directly to carry out such changes.

Biogen Idec stated that it would be unlikely that the complainant would have known that the letter was from a pharmaceutical company before he/she went to pick it up as the third-party medical mailing specialist used plain envelopes. The packages included return addresses however, it was unlikely that the sender or nature of the materials would be known prior to receiving them.

For the reasons outlined above, Biogen Idec considered that it had upheld high standards as per Clause 9.1 and denied that a breach of the Code had been identified.

PANEL RULING

The Panel noted that Samsung Bioepis was the marketing authorisation holder for Imraldi and according to Biogen Idec's submission it was partnered with Samsung Bioepis for all commercial activities for Imraldi, including required national regulatory activities. The Panel noted that Biogen Idec Limited confirmed that it was responsible for the Imraldi mailing at issue.

The Panel noted the complainant's submission that the Imraldi mailing was sent to his/her home address and that he/she had received information from pharmaceutical companies over the years to home and work addresses. The Panel noted Biogen Idec's submission that it had confirmed with the third-party mailing house that the addresses held on its database were those which had been provided by health professionals' themselves. The Panel noted the complainant's concern that the Imraldi mailing required a signature on receipt and he/she had to collect it from the post office which was considerably inconvenient.

The Panel noted that the complainant had referred to the instruction 'cannot be left without a signature' on the labels used by the third-party mailing house in question and in this regard referred to another recent

package delivered to his/her work address which also required a signature and put busy secretaries under unnecessary pressure. It appeared to the Panel that this package was unrelated to the Imraldi mailing at issue; the complainant had provided no further information regarding the content of the other package and the Panel had no information before it with regard to which medicine it related to and subsequently whether Biogen Idec was the responsible pharmaceutical company. The Panel therefore could make no ruling on the package delivered to the complainant's work and considered only the Imraldi mailing delivered to his/her home.

Based on Biogen Idec's submission, it appeared to the Panel that the Imraldi mailing at issue was non-promotional additional Risk Management Materials (aRMMs) which Biogen Idec was required to send to targeted health professionals based on its legal and regulatory obligations. The Panel noted Biogen Idec's submission that the relevant pharmacovigilance guideline required it to track dissemination of the aRMMs and that by sending the materials by recorded delivery it allowed Biogen Idec to monitor whether the material at issue was actually received by the health professional.

The Panel acknowledged that extreme dissatisfaction was usually necessary on the part of an individual before he or she was moved to submit a complaint. The Panel noted it might be inconvenient for an individual to have to collect a package from the post office during office hours. However, in the Panel's view, that Biogen Idec wanted to track its dissemination of risk minimisation materials to ensure that it was received for compliance purposes was not unreasonable in this particular case. Taking everything into consideration, and noting its comments above, the Panel did not consider that sending the Imraldi mailing at issue by recorded delivery was inappropriate marketing practice that constituted harassment as alleged. The Panel considered that Biogen Idec had not failed to maintain high standards in this regard and ruled no breach of Clause 9.1.

The Panel noted the complainant's comment that he/she had asked the mailing company to remove him/her from its database and was awaiting a reply. The Panel noted that the complainant wished to remain anonymous to Biogen Idec and had not provided details of when he/she had submitted the request to be removed from the mailing list. The Panel considered that the complainant had not discharged the burden of proof that Biogen Idec had failed to maintain high standards in this regard and no breach of Clause 9.1 was ruled.

Complaint received **7 November 2018**

Case completed **28 March 2019**

COMPLAINANT v ALLIANCE PHARMACEUTICALS

Promotion of Xonvea on LinkedIn

A complainant who described him/herself as a concerned UK health professional complained about a post from Alliance Pharmaceuticals received on his/her LinkedIn feed.

The post announced that Alliance Pharmaceuticals had launched Xonvea (doxylamine succinate 10mg/ pyridoxine hydrochloride 10mg) and described it as a new treatment indicated for nausea and vomiting of pregnancy (NVP) where conservative management had failed. The post included the brand name in logo format and linked to a press release headed 'Xonvea launch in the UK'. The opening paragraph stated that Alliance Pharma plc, 'announces that it has today launched Xonvea, its prescription product for the treatment of nausea and vomiting of pregnancy (NVP), in the UK. Xonvea is a new licensed medicine available in the UK for women with NVP where conservative management has failed'.

The complainant alleged that the post had been sent to all followers of the website and had been further disseminated by UK based employees liking the announcement. The complainant was concerned that it was an example of blatant promotion to the public.

The detailed response from Alliance is given below.

The Panel noted that the post at issue, which included a link to a press release was posted to the Alliance Pharmaceuticals Limited section on the LinkedIn site at the time Xonvea was launched in the UK. In the Panel's view, the two could not reasonably be separated and in that regard both elements were considered together.

The Panel noted Alliance Pharmaceuticals' submission that the post was newsworthy and would only be visible to LinkedIn users who had chosen to follow the company which included approximately 4000 users. During the uploading process the size of the Xonvea logo in the LinkedIn post was significantly increased. The Panel noted Alliance Pharmaceuticals' submission that this unintended change meant that the post could be considered promotional in nature, as would an Alliance employee liking it.

The Panel noted that the LinkedIn post announced to readers that Alliance Pharmaceuticals had launched Xonvea and described it as a new treatment indicated for nausea and vomiting of pregnancy (NVP) where conservative management had failed. The post linked to a press release which was headed Xonvea launch in the UK. The press release included a statement that 'there is no other licensed treatment for nausea and vomiting of pregnancy in the UK so this is excellent news

for patients and clinicians as it fulfils a significant unmet medical need' and 'Xonvea's combination of doxylamine and pyridoxine is recommended as a first-line pharmacotherapy in the USA and Canada and has been prescribed to over 33 million women in more than 40 years'. The Panel considered that these statements constituted product claims and could encourage members of the public to ask their health professional to prescribe a prescription only medicine. The Panel did not agree with Alliance Pharmaceuticals' view that it was simply the change in the size of the product logo on the LinkedIn post that meant the post was promotional.

Turning to the second allegation, the Panel noted Alliance Pharmaceuticals' submission that the post was also 'liked' by at least one Alliance UK employee and would therefore be seen by his/her followers on the LinkedIn site. The Panel considered it was likely that the Alliance employee's connections would include members of the public.

The Panel considered that, on the balance of probabilities, the Alliance Pharmaceuticals' LinkedIn account followers and the Alliance employees' connections to whom the post had been disseminated by virtue of the employees' 'like' would include members of the public.

The Panel considered that a prescription only medicine had been promoted to the public and might encourage members of the public to ask their health professionals to prescribe it. Breaches of the Code were ruled in relation to both the original LinkedIn post and associated press release on Alliance Pharmaceuticals' LinkedIn account and the further dissemination of this content due to Alliance Pharmaceuticals' employees' like of the post. The Panel considered that high standards had not been maintained and ruled a breach of the Code.

The Panel was concerned that the guidance in the company-wide email which was sent at the time of the Xonvea launch appeared to encourage 'liking' of a Xonvea social media post. The Panel considered that Alliance had failed to maintain high standards in this regard and a breach of the Code was ruled.

The Panel noted its comments and rulings above and, on balance, considered the circumstances did not warrant a ruling of a breach of Clause 2 which was used as a sign of particular censure.

A complainant who described him/herself as a concerned UK health professional complained about a post from Alliance Pharmaceuticals (ref AL/3484/10.18/0.001) received on his/her LinkedIn feed.

The post announced that Alliance Pharmaceuticals had launched Xonvea (doxylamine succinate 10mg/ pyridoxine hydrochloride 10mg) and described it as a new treatment indicated for nausea and vomiting of pregnancy (NVP) where conservative management had failed. The post included the brand name in logo format. The post linked to a press release which was headed 'Xonvea launch in the UK'. The opening paragraph stated that Alliance Pharma plc, 'announces that it has today launched Xonvea, its prescription product for the treatment of nausea and vomiting of pregnancy (NVP), in the UK. Xonvea is a new licensed medicine available in the UK for women with NVP where conservative management has failed'.

COMPLAINT

The complainant alleged that the advertisement and linked press release appeared in his/her LinkedIn feed and that the post had been sent to all followers of the website and had been further disseminated by UK based employees liking the announcement.

The complainant was concerned that it was an example of blatant promotion to the public.

When writing to Alliance Pharmaceuticals, the Authority asked it to consider the requirements of Clauses 2, 9.1, 26.1 and 26.2 of the Code.

RESPONSE

Alliance Pharmaceuticals submitted that the item was posted to the Alliance Pharmaceuticals Limited corporate website homepage and to LinkedIn as part of its corporate PR campaign at the time of launch of Xonvea in the UK. Alliance Pharmaceuticals did not consider that the certified content of the LinkedIn post or associated press release were promotional in nature; the content was based on a public press release with no promotional claims. It was posted to the Alliance Pharmaceuticals Limited section on the LinkedIn site as it was newsworthy and would have only been visible to LinkedIn users who had chosen to follow the company, currently approximately 4000 users. It would not have been visible to the whole LinkedIn community as per the complaint.

Alliance Pharmaceuticals submitted that its investigation, however, showed that the content which appeared on LinkedIn was significantly different to the approved final form which was unintentional. According to Alliance Pharmaceuticals the Xonvea logo was significantly increased in size during the uploading process which the company accepted could inadvertently create a different impression to some readers viewing the content.

Alliance Pharmaceuticals was currently reviewing its procedures to determine what corrective and preventative actions could be put in place to avoid a recurrence of the error. Alliance Pharmaceuticals intended to have an additional review (similar to printed hard copy) with any dynamic content to make absolutely sure that the online content was exactly what was intended at the approval stage.

Alliance Pharmaceuticals submitted that as per the complaint, the post was 'liked' by at least one Alliance employee and therefore seen by their followers on the LinkedIn site. LinkedIn was not able to share the data retrospectively because of the General Data Protection Regulation (GDPR) and Alliance Pharmaceuticals could therefore not investigate it any further. Alliance Pharmaceuticals explained that had the content been entirely non-promotional as intended, it did not believe that liking the post would have had any significant impact as the material was intended to be suitable for the public. Furthermore, at the time of the launch an email was sent company-wide providing guidance regarding how the company should manage social media activity including guidance on liking, sharing and commenting.

The messages beneath the post were written by two external advertising agencies, who had worked with Alliance previously, but had not worked on the Xonvea brand in at least the last three years.

Alliance Pharmaceuticals submitted that its current copy approval standard operating procedure (SOP) discussed how to approach the approval of digital media content. The company was already in the process of expanding on that with a specific SOP intended to provide more robust guidance to its teams regarding appropriate management of digital and social media. A current draft of the procedure to ensure staff had the appropriate guidance in this area was provided.

With regards to the clauses it was asked to consider, Alliance Pharmaceuticals stated that:

- Because of the dynamic nature of LinkedIn there had been a change to the certified final form of the item and the company accepted a breach of Clause 14.1.
- Although it was the company's intention that the post was to be a suitable corporate announcement of the launch of its product in the UK, it accepted that the change in the final form might have inadvertently given a different impression. Alliance Pharmaceuticals acknowledged that the final form would therefore be considered promotional in nature, as would an Alliance employee liking the post and it accepted a breach of Clause 26.1.
- It accepted that the change in the final form which led to inadvertent promotion to the public meant that the company had not maintained high standards in breach of Clause 9.1.
- Other than the change in size of the logo, the content was an appropriate simple announcement of the product launch linked to a press release that was also balanced and factual; it did not make any claims, nor did it raise unfounded hopes of successful treatment or encourage members of the public to ask for Xonvea. Alliance Pharmaceuticals therefore denied a breach of Clause 26.2.
- It had considered the examples of activities which were given as likely to be a breach of Clause 2 in the 2016 Code. Alliance Pharmaceuticals emphasised that there was no suggestion that

it had prejudiced patient safety or public health and it therefore did not consider the matter was sufficient to be considered a breach of Clause 2.

Alliance Pharmaceuticals submitted that in summary, although the item was intended to be part of a non-promotional PR campaign at the launch of its new product, it accepted that a mistake during the uploading process and the dynamic nature of LinkedIn led the company to inadvertently promote to members of the public. The company submitted that it would take steps to ensure its copy approval process was updated to prevent a recurrence and it was finalising its new social media policy to ensure its staff had up to date guidance on Code compliance in this challenging area.

As part of its ongoing revalidation of its processes Alliance Pharmaceuticals had engaged with compliance companies to audit its existing copy approval processes. Depending on the outcome of that audit it proposed to make further refinements to its copy approval processes.

PANEL RULING

The Panel noted that LinkedIn was different to some other social media platforms in that it was a business and employment-orientated network and was primarily, although not exclusively, associated with an individual's professional heritage and current employment and interests. In the pharmaceutical industry, the Panel noted that an individual's network might, albeit not exclusively, be directly or indirectly associated with the healthcare industry.

The Panel noted that the complainant's allegations referred to both Alliance Pharmaceuticals' post on its LinkedIn account and the further dissemination of the content by its UK based employees liking the post. The Panel noted that material could be disseminated or highlighted by an individual on LinkedIn in a number of ways, including by posting, sharing, commenting or liking. The Panel further noted that the nature of LinkedIn was such that posts could be broadly and quickly disseminated making them available to other LinkedIn users.

The Panel further noted that there was no complaint about the comments written beneath the post by two agencies who had previously worked with Alliance. One of these comments stated, 'Congratulations a first. At last a product that can make a huge difference during pregnancy'. The Panel noted that companies were responsible for the acts and omissions of their third-party agencies. Alliance Pharmaceuticals' submitted that neither agency had worked on the Xonvea brand in at least the last 3 years. The Panel was unclear whether the agencies still worked with Alliance Pharmaceuticals in any capacity but did not consider this further as there was no relevant allegation.

The Panel noted that the post at issue, which included a link to a press release (both of which were referred to by the complainant), was posted to the Alliance Pharmaceuticals Limited section on the LinkedIn site as part of its corporate PR

campaign at the time Xonvea was launched in the UK. In the Panel's view given the LinkedIn post was inextricably linked to the press release, the two could not reasonably be separated and in that regard both elements were considered together.

The Panel noted Alliance Pharmaceuticals' submission that the post was newsworthy and would only be visible to LinkedIn users who had chosen to follow the company which included approximately 4000 users.

The Panel noted the company's submission that during the uploading process to the Alliance Pharmaceuticals Ltd LinkedIn account, the size of the Xonvea logo in the LinkedIn post was significantly increased. The Panel noted Alliance Pharmaceuticals' submission that this unintended change meant that the post could be considered promotional in nature, as would an Alliance employee liking it.

With regard to Alliance Pharmaceuticals' admission of a breach of Clause 14.1 because the final form of the LinkedIn post was different to what had been certified, there did not appear to be an allegation in this regard and hence this clause had not been raised by the case preparation manager. The Panel could, therefore, make no ruling in this regard. In the Panel's view, a robust certification procedure underpinned self-regulation and it was concerned that it appeared that Alliance Pharmaceuticals only became aware of this matter on notification of the complaint rather than as a result of its own due diligence.

The Panel noted Alliance Pharmaceuticals' submission that, other than the change in the size of the Xonvea logo, it considered the LinkedIn post was a non-promotional corporate announcement of the launch of its product in the UK and that had the content been entirely non-promotional as intended, liking the post would not have had any significant impact as the material was intended to be suitable for the public. This was reflected in the description of the intended audience in the approval certificate of the post and associated press release. The Panel further noted Alliance Pharmaceuticals' submission that the press release was balanced, factual, made no claims and did not raise unfounded hopes of successful treatment or encourage members of the public to ask for Xonvea.

The Panel noted that the supplementary information to Clause 26.2 allowed information to be made available in order to inform shareholders, the Stock Exchange and the like by way of annual reports and announcements etc which may relate to both existing medicines and those not yet marketed. Such information must be factual and presented in a balanced way. Business press releases should identify the business importance of the information. The Panel queried whether Alliance Pharmaceutical's intended post and press release was appropriate for an audience that would likely extend beyond the relevant media and financial and investment community as would, on the balance of probabilities, likely be the case with regards to Alliance Pharmaceutical's 4000 LinkedIn followers.

The Panel noted that the LinkedIn post announced to readers that Alliance Pharmaceuticals had launched Xonvea (doxylamine succinate 10mg/pyridoxine hydrochloride 10mg) and described it as a new treatment indicated for nausea and vomiting of pregnancy (NVP) where conservative management had failed. The post linked to a press release which was headed Xonvea launch in the UK. The press release similarly covered the launch of Xonvea in the UK and included a statement from Alliance Pharmaceuticals' CEO that 'there is no other licensed treatment for nausea and vomiting of pregnancy in the UK so this is excellent news for patients and clinicians as it fulfils a significant unmet medical need'. The press release further stated 'Xonvea's combination of doxylamine and pyridoxine is recommended as a first-line pharmacotherapy in the USA and Canada and has been prescribed to over 33 million women in more than 40 years'. The Panel considered that these statements constituted product claims and could encourage members of the public to ask their health professional to prescribe a prescription only medicine. The Panel did not agree with Alliance Pharmaceuticals' view that it was simply the change in the size of the product logo on the LinkedIn post that meant the post was promotional.

Turning to the second allegation, the Panel noted Alliance Pharmaceuticals' submission that the post was also 'liked' by at least one Alliance UK employee and would therefore be seen by his/her followers on the LinkedIn site. The Panel considered it was likely that the Alliance employee's connections would include members of the public.

The Panel understood that if an individual 'liked' a post it increased the likelihood that the post would appear in his/her connections LinkedIn feeds thereby disseminating the material. In the Panel's view, activity conducted on social media that could potentially alert one's connections to the activity might be considered proactive dissemination of material. In addition, an individual's activity and associated content might appear in the individual's list of activities on his/her LinkedIn profile page which was visible to his/her connections; an individual's profile page was also potentially visible to others outside his/her network depending on the individual's security settings. In the Panel's view the act of liking the material amounted to proactive dissemination of the material.

In the Panel's view, it was of course not unacceptable for company employees to use personal LinkedIn accounts and the Code would not automatically apply to all activity on a personal account; whether the Code applied would be determined on a case-by-case basis taking into account all the circumstances including: the content, any direct or indirect reference to a product, how the information was disseminated on LinkedIn, the company's role in relation to the availability of the content and whether such activity was directed or encouraged by the company. If activity was found to be within the scope of the Code, the company would be held responsible.

The Panel noted that Clause 26.1 prohibited the promotion of prescription only medicines to the public. Clause 26.2 stated that information about prescription only medicines which was made available either directly or indirectly to the public must be factual, presented in a balanced way, must not raise unfounded hopes of successful treatment and must not encourage members of the public to ask their health professional to prescribe a specific prescription only medicine.

The Panel noted its comments above and considered that, on the balance of probabilities, the Alliance Pharmaceuticals' LinkedIn account followers and the Alliance employees' connections to whom the post had been disseminated by virtue of the employees' 'like' would include members of the public. The Panel noted the product claims within the press release and the branded logo in the LinkedIn post.

The Panel considered that a prescription only medicine had been promoted to the public and might encourage members of the public to ask their health professionals to prescribe it. Breaches of Clauses 26.1 and 26.2 were ruled in relation to both the original LinkedIn post and associated press release on Alliance Pharmaceuticals' LinkedIn account and the further dissemination of this content due to Alliance Pharmaceuticals' employees' like of the post. The Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel was mindful of the complex issues that had to be addressed by companies when advising staff about social media use. The increasing use of social media, both in the personal and business capacity, presented compliance challenges. In addition, many social media platforms used algorithms and had settings which individuals and companies might not be fully aware of. In the Panel's view, companies should remain vigilant and ensure that they took reasonable steps to highlight the potential compliance issues that might arise from interacting on social media including 'liking' certain posts on LinkedIn given such posts could thereby potentially be pushed to their connections' feeds. The Panel was aware that the types of activity performed by the Alliance Pharmaceuticals' employees on LinkedIn was not uncommon across the industry. In the Panel's view, employees might feel inclined to endorse posts that were published by their company's corporate social media team or which related to their company and depending on the content such activity may or may not fall within the scope of the Code. It was therefore critical that companies provided clear and tailored guidance for its employees which was regularly reviewed.

The Panel noted Alliance Pharmaceuticals' submission that at the time of launch, an email was sent company-wide regarding how the company should manage social media activity, including guidance on liking, sharing and commenting. The Panel noted that the email included:

'Xonvea is a prescription-only medicine and as such we are not able to promote this to the

general public – this would include comments and shares on social media. For this reason please can I kindly ask that you abide by the following in terms of your social media accounts: 1. You are able to like a Xonvea related post.’

The Panel was concerned that the guidance in the company-wide email which was sent at the time of the Xonvea launch appeared to encourage ‘liking’ of a Xonvea social media post. The Panel considered that Alliance had failed to maintain high standards in this regard and a breach of Clause 9.1 was ruled.

The Panel noted its comments and rulings above and, on balance, considered the circumstances did not warrant a ruling of a breach of Clause 2 which was used as a sign of particular censure.

Complaint received **29 November 2018**

Case completed **20 March 2019**

VOLUNTARY ADMISSION BY MERCK SHARP & DOHME

Failure to provide prescribing information and certify an advertisement

Merck Sharp & Dohme voluntarily admitted that an advertisement for Keytruda (pembrolizumab) did not contain prescribing information. Keytruda was indicated for, *inter alia*, advanced melanoma in adults.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Merck Sharp & Dohme.

Merck Sharp & Dohme explained that the advertisement at issue had been displayed at a scientific congress, held in the UK in October 2018. The advertisement had been developed and certified for use with the congress programme app only. As part of the sponsorship package of the congress Merck Sharp & Dohme was also offered the placement of the company logo in the registration area. The congress organisers inadvertently printed the digital advertisement intended for the app instead of the company logo and placed it on a pillar just after the registration area (before the exhibition area). Consequently, the printed advertisement only contained a link to prescribing information, as it was intended to be viewed in digital format, and so full prescribing information was not provided.

At 14:30 on the second day of the conference, an employee noticed the error and immediately informed the Merck Sharp and Dohme team and requested that the congress representative immediately remove and destroy the poster, which was completed by 14.45.

The response from Merck Sharp & Dohme is given below.

The Panel noted that it was a well-established principle that a company was responsible for the acts or omissions of its agents or third parties. Merck Sharp & Dohme was thus responsible for the placement of the Keytruda advertisement at issue in the congress registration area by the congress organisers.

The Panel noted that the advertisement in question did not include prescribing information as required by the Code and a breach was ruled accordingly as acknowledged by Merck Sharp & Dohme.

The Panel further noted that the advertisement had not been certified for such use and a breach of the Code was ruled as acknowledged by Merck Sharp & Dohme.

The Panel noted that Merck Sharp & Dohme had clearly stated in emails to the congress organisers that only the Merck Sharp & Dohme logo was to be placed on the pillar. The Panel noted the corrective

action promptly taken by Merck Sharp & Dohme once it became aware of the error. The Panel considered that Merck Sharp & Dohme had been badly let down by the congress organisers. Overall the Panel considered that Merck Sharp & Dohme had not failed to maintain high standards and no breach of the Code was ruled.

Merck Sharp & Dohme voluntarily admitted that an advertisement (ONCO-1269798-0000) for Keytruda (pembrolizumab) displayed in a conference registration area, did not contain prescribing information. Keytruda was indicated for, *inter alia*, advanced melanoma in adults.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Merck Sharp & Dohme.

VOLUNTARY ADMISSION

Merck Sharp & Dohme explained that the advertisement at issue had been displayed at a global melanoma scientific congress held in the UK in October 2018. The advertisement had been developed and certified for use with the congress programme app only. The congress programme was only available as an app and access was only provided during registration. As part of the sponsorship package of the congress Merck Sharp & Dohme was also offered the placement of the company logo in the registration area. The congress organisers inadvertently printed the digital advertisement intended for the app instead of the company logo and placed it on a pillar just after the registration area (before the exhibition area). Consequently, the printed advertisement only contained a link to prescribing information, as it was intended to be viewed in digital format, and so full prescribing information was not provided.

Merck Sharp & Dohme explained that it was a sponsor of the congress which included in the offering: a full-page colour advertisement for mobile app and a company branded pillar. Merck Sharp & Dohme Global was responsible for the development of materials and all required documentation was provided to Merck Sharp & Dohme UK for review and approval, together with a checklist of all materials. On 24 October 2018 Merck Sharp & Dohme Global emailed the congress organisers to ask them to upload the digital advertisement to the congress programme app and print the Merck Sharp & Dohme logo alone for the pillar. Although the digital advertisement was correctly uploaded to the congress programme app it was also printed in error by the congress organisers and placed on the pillar which was intended for the Merck Sharp & Dohme logo.

The printed advertisement placed on the pillar stated 'tap here for prescribing information' as per the certified digital advertisement, and therefore, prescribing information could not be accessed. As the Merck Sharp & Dohme logo in isolation did not require certification nor examination under the Code it was not passed back to the medical signatory on site for review and approval of the printed document prior to placement.

The opening session of the congress was at 17:30 on 24 October. From 17:30, all head office staff were engaged in speaker rehearsals and final logistical preparations in relation to a promotional meeting to be held at lunchtime on 25 October 2018. At 14:30 on 25 October, an employee noticed the printing error and immediately informed the Merck Sharp & Dohme internal team and requested that the congress representative immediately remove and destroy the poster. This was completed by 14:45. The congress organisers confirmed by email that the poster had been removed and destroyed as soon as it had been brought to their attention and acknowledged responsibility for the incorrect printing.

With regards to possible breaches of the Code, Merck Sharp & Dohme referred to the following: Clause 4.1 – no prescribing information was available on a printed advertisement. The intention was that this was a digital advertisement for use on a mobile app and the prescribing information was available one-click away, in digital form. The digital advertisement was incorrectly printed by the congress organisers and placed on the pillar instead of the Merck Sharp & Dohme corporate logo.

Clause 14.1 – the pillar wrap was not certified in printed final form. As per the description of the job bag, there was no intention to print the digital advertisement for the app. The description of the job bag for the digital advertisement (ONCO-1269798-0000) stated: 'MSD advert for [congress] program which will be available to all attendees. The program will be available as an app and will not be printed'.

Clause 9.1 – as no prescribing information had been provided, the Panel might wish to consider whether high standards had been maintained. However, Merck Sharp & Dohme firmly believed that high standards had been maintained throughout and that this was an isolated incident caused by an unfortunate error in printing by the congress organisers, which they freely admitted. Merck Sharp & Dohme acknowledged that the actions by third parties still fell under its responsibility, however the company had operated responsibly, ethically and professionally throughout and had taken corrective

action as soon as the mistake was identified.

In summary, Merck Sharp & Dohme considered that its internal processes were not at fault. The digital form was certified, and it was clear from the job summary that it was for a digital advertisement and not to be printed. There was clear documentation that only the corporate logo, which did not require certification or examination, should be on the pillar.

RESPONSE

Merck Sharp & Dohme had no further comments.

PANEL RULING

The Panel noted that it was a well-established principle that a company was responsible for the acts or omissions of its agents or third parties. If this were not the case companies would be able to rely on such acts or omissions as a means of circumventing the requirements of the Code. Merck Sharp & Dohme was thus responsible for the placement of the Keytruda advertisement at issue in the congress registration area by the congress organisers.

The Panel noted that the advertisement in question did not include prescribing information as required by Clause 4.1 and a breach was ruled accordingly as acknowledged by Merck Sharp & Dohme.

The Panel further noted that the advertisement had not been certified for such use and a breach of Clause 14.1 was ruled as acknowledged by Merck Sharp & Dohme.

The Panel noted that the congress organisers had inadvertently printed the digital advertisement intended for the congress programme app instead of the company logo and placed it on a pillar just after the registration area. The Panel noted that Merck Sharp & Dohme had clearly stated in emails to the congress organisers that only the Merck Sharp & Dohme logo was to be placed on the pillar. The Panel noted the corrective action promptly taken by Merck Sharp & Dohme once it became aware of the error. The Panel considered that Merck Sharp & Dohme had been badly let down by the congress organisers. Overall the Panel considered that Merck Sharp & Dohme had not failed to maintain high standards and no breach of Clause 9.1 was ruled.

Voluntary admission received	30 November 2018
Case completed	21 February 2018

ANONYMOUS, NON-CONTACTABLE v NAPP

Use of social media to advertise meetings

An anonymous, non-contactable complainant who described him/herself as a concerned health professional complained that advertisements for meetings, sponsored by pharmaceutical companies, including Napp, on Facebook and Twitter did not include sponsorship statements.

According to the complainant, this was notable from Facebook notifications and the meeting advertisements themselves. The complainant further alleged that these advertisements were reaching the public.

The complainant provided a copy of material which referred to a diabetes specialist nurse meeting which appeared to be one of a series and noted that Napp was even hosting one of the meetings.

The detailed response from Napp is given below.

The Panel noted that a group of diabetes specialist nurses (DSNs) appeared to be planning to hold nine meetings in different areas of England over a week in 2019. None of the meetings had taken place at the time the complaint was received or considered.

The Panel noted that the complainant provided no Twitter postings in support of his/her allegations but had provided what appeared to be a post on Facebook which gave the date and location of one meeting.

The Panel noted Napp's submission that it was not sponsoring the meeting advertised in the post provided by the complainant. The Panel, therefore, ruled no breach of the Code in relation to the post provided by the complainant for that meeting.

The Panel noted that Napp provided a similar Facebook post for another meeting, which listed Napp's offices as the venue for the meeting. The Panel noted Napp's submission that it had agreed to sponsor the meeting and had also decided to sponsor (venue payment and appropriate refreshments) six of the nine DSN meetings. The arrangements were planned to be similar.

The Panel noted that the agenda for the meeting at Napp's offices stated 'This has been solely produced by the [group of DSNs]. The funding for the printing and venue has been provided through sponsorship by Napp Pharmaceuticals'. It further stated that Napp would have an exhibition stand outside the meeting room.

The Panel noted Napp's submission that it was a 'hands-off' sponsorship of a third party organised non-promotional and educational meeting and that Napp had had no involvement in the organisation of the meeting. The Panel considered that whilst

the agenda of the meeting detailed Napp's involvement in sponsorship of the meeting, each item had to stand alone. The Panel considered that although Napp's office was listed as the venue on the Facebook post advertising the meeting, Napp's sponsorship was not clear from that post and the Panel, therefore, ruled a breach of the Code which was appealed by Napp.

The Appeal Board noted the Napp sponsorship agreement for the meeting at issue signed by a nurse on behalf of the group of DSNs which stated that 'The Recipient has confirmed that in all materials or publications which arise from or are used in connection with Activities (including invites and agendas), Napp's Sponsorship of the Activities will be declared by displaying the following statement 'Supported by sponsorship from Napp Pharmaceuticals Limited'. The declaration of sponsorship must be sufficiently prominent to ensure readers are aware of it at the outset'.

The Appeal Board noted Napp's submission that the arrangements were an arms-length sponsorship of a third party organised non-promotional educational meeting and that the group of DSNs were not a third party engaged by, or acting on behalf of, Napp. Napp had approved the agenda which included its sponsorship declaration and that its offices were the venue for the meeting. The Appeal Board noted Napp's submission that it had no knowledge of the Facebook post detailing the meeting at issue prior to receiving the complaint.

The Appeal Board noted Napp's submission that according to the information provided to it from the group of DSNs if 'Event' or 'Invite' were clicked within the Facebook post at issue the link included the declaration of Napp's sponsorship.

The Appeal Board noted that the agenda included the sponsorship statement and listed Napp's offices as the venue and that the Facebook post gave Napp's address under the heading 'Details'. The Appeal Board considered, in the particular circumstances of this case, that the group of DSNs had not included a declaration of Napp's sponsorship on the Facebook post at issue at the outset, despite Napp's sponsorship agreement, did not amount to a breach of the Code. The Appeal Board, therefore, ruled no breach of that clause. The appeal was successful.

The Panel noted the complainant's allegation that the meeting advertisements were reaching the public. The Panel noted Napp's submission that the group of DSNs confirmed that the posts appeared on its open Facebook page which could be accessed by anyone in addition to its closed Facebook group which was for registered diabetes

specialists only. The two Facebook posts stated that the events were for health professionals only and neither made reference to any prescription only medicine. The Panel noted Napp's submission that it would pay for the printing of the agenda but would not be involved in any further promotion of the meeting. Advertisements including any social media advertisements for the meetings were done by DSNs.

As noted above, Napp had no involvement with regard to the first meeting. Without considering the responsibility of Napp in relation to the post for the second meeting at Napp's offices, it was clear to the Panel that the complainant had not provided any evidence to show that Napp had advertised a prescription only medicine to the public in relation to its involvement with the meetings. No breaches of the Code were ruled.

The Panel noted that the complainant stated that there was no evidence of certified meetings. There was no requirement under the Code for meetings in the UK to be certified. The Panel therefore ruled no breach of the Code.

With regard to Napp hosting one of the meetings, the complainant did not specifically state what were the concerns. The Panel did not consider that the complainant had provided any evidence to show that holding the meeting at Napp's offices was inappropriate and, based on the narrow allegation, no breach of the Code was ruled.

The Panel noted that the complainant listed a number of other clauses but provided few or no details of why, in his/her view, Napp was in breach of those clauses. It was not for the Panel to make out a complainant's allegations. The Panel, therefore, ruled no breaches of the Code.

The Panel noted its comments and rulings above and did not consider, in the circumstances of this case, that Napp had failed to maintain high standards. No breach of the Code was ruled.

The Panel noted that a ruling of a breach of Clause 2 of the Code was a sign of particular censure and reserved for such. In that regard, the Panel did not consider that the matter warranted such a ruling and so no breach of Clause 2 was ruled.

An anonymous, non-contactable complainant who described him/herself as a concerned health professional complained about advertisements for meetings, sponsored by pharmaceutical companies, including Napp, on Facebook and Twitter.

COMPLAINT

The complainant alleged that advertisements for meetings that were being sponsored by pharmaceutical companies, including Napp, on Twitter and Facebook did not include sponsorship statements. According to the complainant, this was notable from Facebook notifications and the meeting advertisements themselves. The complainant further alleged that these advertisements were reaching the public.

The complainant stated that, in particular, and most notable, was that Napp was even hosting one of the meetings.

The complainant provided a copy of material which referred to a diabetes specialist nurse meeting which appeared to be one of a series. The description referred to diabetes health professionals with a love of diabetes care and that the meeting was a fabulous networking and learning opportunity where experienced professionals and people with diabetes would inform and inspire with new skills and innovations in diabetes care.

The complainant alleged that Napp was in breach of the following clauses:

- Clause 2 – bringing discredit to the industry
- Clause 4 – prescribing information (lack of in promotional materials)
- Clause 9 – high standards and suitability
- Clause 11 – distribution of materials
- Clause 12 – disguised promotion
- Clause 14 – certification – no evidence of certified meetings
- Clause 18 – inducements and appropriate payments of officials
- Clause 19 – medical educational goods and services
- Clause 20 – joint working
- Clause 22 – meetings, hospitality and sponsorship
- Clause 23 – the use of consultants
- Clause 24 – transfer of value to health professionals
- Clause 26 – relations with the public and media
- Clause 28 – internet.

RESPONSE

Napp noted that the complainant provided no Twitter posting and the 'advert' provided made no mention of Napp. Napp did note, however, that the complainant noticed from the Facebook notifications and meeting advertisements that there were no sponsorship statements.

Napp stated that the meetings at issue were of a group of DSNs that had a large number of members in its Facebook group. This was a closed group whose membership consisted solely of health professionals. According to its website, 'The aim of the [group of DSNs] is to share best practice to improve outcomes for people with diabetes ... and to connect DSNs to provide a support network of specialists'. Napp submitted that it had no partnership or past relationship with this DSN group and only became aware of its existence when one of Napp's representatives was approached by a local DSN to seek funding to support a meeting in February 2019. Napp viewed this as the provision of sponsorship for a third party organised non-promotional and educational meeting. Napp followed its internal compliance processes as per its relevant standard operating procedure (SOP) and relevant sales force training. The sales force used a computer-based customer relationship management (CRM) system and as part of it were trained on compliance advice relating to third party sponsorship meeting requirements/agreements.

The appropriate completed and signed (by the third-party specialist nurse) sponsorship form was reviewed and examined by two medical signatories. Napp submitted that high standards were, therefore, maintained as per Clause 9.1. Clear declaration of Napp's involvement and sponsorship were on the agenda (copy provided), as per Clauses 9.10 and 22.4. Napp submitted that it would pay for the printing of the agenda but would not be involved in any further promotion of the meeting and would not distribute the printed agendas to any of the health professionals.

Napp submitted that the meeting was to be held in one of the meeting rooms at Napp's offices as venue support. Napp submitted that the meeting facility was appropriate as per Clause 22.1: there would be no entertainment, it was an appropriately sized dedicated private meeting room, a reasonable light lunch would be provided, and there was ample parking. There would be a separate area for an exhibition stand promoting Invokana (canagliflozin) manned by two representatives. The stand would be in a private area outside the meeting room, away from other Napp staff and any members of the public. Napp noted that towards the end of the meeting, the meeting agenda involved a presentation by a diabetic patient, and it had been highlighted to the group of DSNs that it must keep the patient speaker away from the promotional stand. No-one from Napp would attend the meeting presentations. Napp submitted that it had no involvement in the development of the agenda or selection of the speakers and associated presentations. This meeting was solely organised by the group of DSNs; Napp had no involvement in the organisation of the meeting and, in that regard, Napp referred to the declaration on the February 4 agenda. Napp submitted that since agreeing to sponsor the meeting, it had decided to sponsor (venue payment and appropriate refreshments) six of the nine meetings. The arrangements were planned to be similar and aligned to Napp's SOPs and approval process as explained above.

Napp reiterated that it had provided a hands-off sponsorship only as a way of meeting support to help fund the group of DSN's meeting and had not been involved in any promotion of the events, including any social media advertisements. Napp had no knowledge of Facebook and Twitter postings until it was notified of the complaint. Napp staff have had no involvement at all in these postings. The postings were made solely by members of the group of DSNs, who were independent health professionals.

Napp stated that once it knew about these postings, it telephoned and emailed members of the group of DSNs to gain further information about the postings and provide additional advice about Code compliance, for example, Napp asked the group of DSNs to make more prominent that the meetings were for health professionals only and solely organised by the group of DSNs. Relevant correspondence was provided. Napp submitted that the postings on Facebook could be accessed by anyone due to the public nature of Facebook.

However, the postings did not promote any medicines and clearly stated that the event was for health professionals only.

The DSNs confirmed that 'these are on our closed Facebook group which is for registered diabetes specialists HCPs only! They are also on our open Facebook group which is mainly for practice and community nurses in diabetes'. The correspondence also confirmed that Napp was not sponsoring the meeting in the post provided by the complainant; an unrelated company was sponsoring that meeting.

Napp provided a copy of its Corporate and Code guidance document on Social Media and the signed agreement for the third-party meeting sponsorship to acknowledge the presence of a promotional stand at the meeting.

Napp submitted that the following clauses were not relevant as follows:

Clause 4 – No promotional material had been distributed for Napp medicines (prescribing information would, of course, be available from the promotional stand at the meetings).

Clause 11 – Napp had not, and would not, be distributing any material, eg meeting agenda flyers.

Clause 12 – There would be no promotion at the meeting, apart from at a promotional stand outside the meeting which was stated on the agenda, so this was not disguised.

Clause 14 – The meetings were third party, non-promotional meetings examined by two medical final signatories rather than certified.

Clause 18 – There were no inducements, gifts or payments being paid to health professionals as part of the non-promotional educational meetings in question.

Clause 19 – There was no provision of medical and educational goods and services. This was a third party 'hands-off' sponsorship.

Clause 20 – This was not a joint working initiative and there was no joint working between Napp and the group of DSNs.

Clause 23 – Health professionals were not being used as advisors or consultants at the meetings. Napp was not involved in the selection or payment of any of the speakers.

Clause 24 – The events had not yet happened and, therefore, no transfers of value had happened. They would be captured once incurred as per disclosure requirements for sponsorships of third party events.

Clause 26 – There would be no advertising of prescription only medicines to members of the public and no evidence of this had been provided by the complainant.

In summary, Napp submitted that it had provided a comprehensive account of its involvement in the DSN group meetings and had explained how it had maintained high standards (Clause 9.1) and made clear its involvement in the agenda (Clauses 9.10 and 22.4). Napp submitted that the meeting arrangements concerning appropriate venues and hospitality would meet the requirements of Clause 22.1. Napp submitted that its activities had not brought discredit upon, or reduced confidence in, the

pharmaceutical industry, so it firmly believed that it had upheld the highest standards as per Clause 2.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable; the Panel was, therefore, unable to contact him/her to ask for more information. The Panel noted that as set out in the introduction to the Constitution and Procedure, complainants had the burden of proving their complaint on the balance of probabilities. Anonymous complaints were accepted and, like all complaints, judged on the evidence provided by the parties.

The Panel noted that a group of DSNs appeared to be planning to hold nine meetings in different areas of England over a week in February 2019. None of the meetings had taken place at the time the complaint was received or considered.

The Panel noted that the complainant provided no Twitter postings in support of his/her allegations but had provided what appeared to be a post on Facebook from the group of DSNs which was headed Diabetes Specialist Nurse [group] and gave the date and location of a meeting. The Panel had no details with regard to the content to be presented at the meeting.

The Panel noted that Clause 22.4 stated that when meetings were sponsored by pharmaceutical companies, that fact must be disclosed in all of the papers relating to the meetings and in any published proceedings. The declaration of sponsorship must be sufficiently prominent to ensure that readers were aware of it at the outset.

The Panel noted Napp's submission that it was not sponsoring the meeting advertised in the post provided by the complainant. The Panel, therefore, ruled no breach of Clause 22.4 in relation to the post provided by the complainant for that meeting.

The Panel noted that Napp provided a similar Facebook post for the meeting which listed Napp's offices as the venue. The Panel noted Napp's submission that it had agreed to sponsor this meeting and had also decided to sponsor (venue payment and appropriate refreshments) six of the nine meetings. The arrangements were planned to be similar.

The Panel noted that the agenda for the meeting stated 'This has been solely produced by the [group of DSNs]. The funding for the printing and venue has been provided through sponsorship by Napp Pharmaceuticals'. It further stated that Napp would have an exhibition stand outside the meeting room.

The Panel noted Napp's submission that it was a 'hands-off' sponsorship of a third party organised non-promotional and educational meeting and that Napp had had no involvement in the organisation of the meeting. The Panel considered that whilst the agenda of the meeting detailed Napp's involvement in sponsorship of the meeting, each item had to

standalone. The Panel considered that although Napp's office was listed as the venue on the Facebook post advertising the Cambridge meeting, Napp's sponsorship was not clear from that post and the Panel, therefore, ruled a breach of Clause 22.4.

The Panel noted that Napp provided the agenda for a third meeting which stated, *inter alia*, that the venue and catering for the event had been sponsored by Napp and Napp had had no input in to the agenda items for this meeting. Napp had also stated that it was sponsoring a number of other meetings. The Panel, however, did not have copies of the Facebook posts for those meetings and, therefore, could make no rulings in that regard.

The Panel noted the complainant's allegation that the meeting advertisements were reaching the public. The Panel noted that the complainant had raised Clause 26 but had not provided detailed reasons. Clause 26.1 included that prescription only medicines must not be advertised to the public. The Panel noted Napp's submission that the group of DSNs confirmed that the posts appeared on its open Facebook page which could be accessed by anyone in addition to its closed Facebook group which was for registered diabetes specialists only. The two Facebook posts stated that the events were for health professionals only and neither made reference to any prescription only medicine. The Panel noted Napp's submission that it would pay for the printing of the agenda but would not be involved in any further promotion of the meeting. Advertisements for the meetings including any social media advertisements were done by DSNs.

As noted above, Napp had no involvement with regard to the first meeting. Without considering the responsibility of Napp in relation to the post for the meeting at Napp's offices, it was clear to the Panel that the complainant had not provided any evidence to show that Napp had advertised a prescription only medicine to the public in relation to its involvement with the group of DSN's meetings. No breach of Clauses 26.1 and 28.1 were ruled.

The Panel noted that when quoting Clause 14 the complainant stated that there was no evidence of certified meetings. There was no requirement under the Code for meetings in the UK to be certified.

The supplementary information to Clause 22.1 included that all meetings which were planned were checked to see that they complied with the Code and meetings which involved travel outside the UK must be formally certified as set out in Clause 14.2. The Panel noted Napp's submission that the appropriate completed and signed (by the third-party specialist nurse) sponsorship form was reviewed and examined by two medical signatories. The Panel noted Napp's submission that all 9 of the meetings were to be held in the UK. The Panel, therefore, ruled no breach of Clause 14.2. With regard to Napp hosting one of the meetings, the complainant did not specifically state what were the concerns. The Panel noted that Clause 22.1 and its supplementary information stated, *inter alia*, that meetings must be held in appropriate

venues conducive to the main purpose of the event. With any meeting, certain basic principles applied including that the venue must be appropriate and conducive to the main purpose of the meeting; lavish, extravagant or deluxe venues must not be used, companies must not sponsor or organise entertainment (such as sporting or leisure events) and companies should avoid using venues that are renowned for their entertainment facilities. The Panel did not consider that the complainant had provided any evidence to show that holding the meeting at Napp's offices was inappropriate and, based on the narrow allegation, no breach of Clause 22.1 was ruled.

The Panel noted that the complainant listed a number of other clauses but provided few or no details of why, in his/her view, Napp was in breach of those clauses. It was not for the Panel to make out a complainant's allegations. The Panel was unsure which materials were at issue in relation to the alleged breaches of Clauses 4, 11 and 12. Napp submitted that Clauses 18, 19, 20, 23 and 24 were not relevant, including that the meetings had not happened, and it was not involved in the selection or payment of speakers. The Panel, therefore, ruled no breach of Clauses 4, 11, 12, 18, 19, 20, 23 and 24 of the Code.

The Panel noted its comments and rulings above and did not consider, in the circumstances of this case, that Napp had failed to maintain high standards. No breach of Clause 9.1 was ruled.

The Panel noted that a ruling of a breach of Clause 2 of the Code was a sign of particular censure and reserved for such. In that regard, the Panel did not consider that the matter warranted such a ruling and so no breach of Clause 2 was ruled.

APPEAL BY NAPP

Napp noted that the complainant listed several Code clauses but provided no details as to why Napp was in breach of those clauses, the majority of which were irrelevant to the activity or this complaint. The complainant drew attention to the Facebook and Twitter advertisements for meetings that were being sponsored by pharmaceutical companies, including Napp Pharmaceuticals, which meant that the complainant was aware of Napp's sponsorship of the meetings. The complainant went on to state that Napp Pharmaceuticals was even hosting one of the meetings and that these meetings were being advertised across Facebook and Twitter and also reaching the public. Napp submitted that it was important to note that it was not found in breach of the clauses related to these allegations. However, for the appeal, Napp would focus on Clause 22.4.

As explained previously, Napp submitted that it had absolutely no knowledge of the Facebook or other social media postings until this was brought to its attention through receipt of the complaint. The group of DSNs were not a third-party agency for which Napp would be responsible for their activities. Napp played no part in the arrangements, nor the decision by the group of DSNs to post these

meetings on Facebook. Napp was not aware of the way the group of DSNs advertised its meetings and neither was it consulted by it before its decision to do so. Furthermore, the sponsorship agreements form for Napp, and signed by the group of DSNs, clearly stated 'The Recipient has confirmed that in all materials or publications which arise from or are used in connection with Activities (including invites and agendas), Napp's Sponsorship of the Activities will be declared by displaying the following statement 'Supported by sponsorship from Napp Pharmaceuticals Limited'. The declaration of sponsorship must be sufficiently prominent to ensure readers are aware of it at the outset'.

Napp submitted that according to the information sent to it by the group of DSNs, it did what they thought was right by not overtly advertising Napp's name to ensure only interested health professions would have access to the event details and the agenda. The group of DSNs was cautious not to mention Napp's name in the first screen view of their postings and hence the need to click on the 'Event' or 'Invite', which then had the wording of the declaration of sponsorship which accurately reflected Napp's involvement. Napp submitted that it had a robust process in place for the approval of third-party educational meetings including its SOPs and training given to staff about third parties and social media.

Napp stated it was not involved directly or indirectly with the posting on Facebook, and this should substantiate the fact that it was not responsible for the wording of the postings. Napp was only aware of the proposed meeting agenda which was approved as part of the 'arm's length' sponsorship request. This meeting agenda clearly stated the extent of Napp's sponsorship and the declaration was sufficiently prominent to ensure that readers were aware of it at the onset. Napp had no knowledge, control or influence over the Facebook postings. Since Napp was not aware of the postings, there was no way of reviewing these postings. Nevertheless, the postings, albeit printed after the Panel's ruling, stated 'Events have been solely organised by the [group of DSNs] and sponsored through funding by pharmaceutical companies'.

Napp noted that the PMCPA advice on 'Arm's length arrangements and unrestricted grants' stated:

'...it is possible for a company to sponsor material, produced by a third party, which mentioned its own products, and not be liable under the Code for its contents, but only if, *inter alia*, there had been a strictly arm's length arrangement between the parties. In practical terms the arrangements must be such that there could be no possibility that the pharmaceutical company had been able to exert any influence or control over the final content of the material.'

The above advice also stated that the factors which might mean there had not been a strictly arm's length arrangement would include, but not be restricted to:

- Initiation of the material, or the concept for it, by the pharmaceutical company (Napp submitted that it was not involved in the initiation of the Facebook posting or the agenda)
- Influence from the pharmaceutical company on the content/balance/scope of the material (Napp submitted that it did not influence the content of the Facebook posting or help produce it)
- Choice/or direct payment of the authors by the pharmaceutical company (Napp submitted that it did not pay any authors or any of the DSNs who wrote the posting)
- Influence from the pharmaceutical company on the list of persons to whom the material was sent. (Napp submitted that it was not involved and was unaware of list of persons the posting was sent).

Napp stated that the above consideration would apply to sponsorship of health professional meetings or events by pharmaceutical companies.

Napp submitted that it was an established requirement of the Code that companies would be held responsible under the Code for all third parties which undertook work on their behalf, whether engaged directly or indirectly. The group of DSNs was an NHS group and was not a third party engaged by or acting on behalf of Napp. Therefore, Napp was not responsible for the activities of the group of DSNs especially in this case which was without its knowledge.

That said, Napp submitted that pharmaceutical companies should not interfere with the arrangements of meetings organised by independent parties such as those organised by health professionals to avoid the accusations of influencing the arrangements or content of such meetings. Close involvement in aspects of such meetings could be perceived as controlling the meeting arrangements or programme. Napp should not be held liable or responsible for the activities of health professionals which was beyond its control and more importantly beyond the remit of a hands-off sponsorship.

Napp submitted that working with health professionals to fund educational meetings such as the group of DSN's meetings (which sought to share best practice in diabetes care and inform health professionals about skills in diabetes care) could bring significant benefits to patients. The role of the group of DSNs was hugely important in ensuring high-quality diabetes patient care. A ruling of a breach of Clause 22.4 in this case would not seek to encourage such initiatives which Napp was sure was not the PMCPA's intention.

In summary, Napp submitted that it had provided a comprehensive account of its involvement in the group of DSN's meetings and addressed its appeal of the Panel's ruling of Clause 22.4. Napp had explained how it was not involved in the arrangements of the meetings organised by the DSNs, including the decision to post the meetings on social media. Napp made clear its involvement in the agenda for the meetings which was simply to provide funding for the meetings without which would have been challenging for the group of DSN's

meetings to run. Napp appealed the breach of Clause 22.4 based on the above.

FURTHER PANEL CONSIDERATION

Following receipt of the appeal from Napp an error was identified in that three of the five enclosed pages provided by the complainant were not provided by the Case Preparation Manager to either Napp when it was notified of the complaint, or to the Panel as an enclosure attached to the original complaint. Two of the three pages at issue were provided by Napp in its response to the complaint and were, therefore, provided to the Panel. The third page listed geographical venues and links for four meetings and a statement that two were to be confirmed very soon (no URL link but a hashtag was stated). This third page was not provided to the Panel and therefore the Panel did not look at the links.

When the PMCPA became aware of this matter the omitted material was provided to Napp with a provisional view that the page in question had not affected the ultimate outcome of the matter or prejudiced Napp in any way and the appeal should proceed in the usual way. Napp was asked for its comments and stated that it had no significant additional comment at this stage but as it was appealing the Panel's ruling Napp reserved judgement on whether or not this could affect the outcome.

On reviewing the omitted material, the members of the Panel agreed that Napp was not disadvantaged by the Panel's failure to review the omitted information. The Panel's ruling of a breach of Clause 22.4 was clearly only in relation to the meeting held at Napp's offices. It could be argued that the failure to clearly indicate which of the meetings listed in the omitted information were sponsored by Napp might be covered by the complainant's very general allegations in this regard. The anonymous, non-contactable complainant might be disadvantaged. However, if the Appeal Board upheld the Panel's ruling of a breach of Clause 22.4 in relation to the meeting referred to in the information considered by the Panel, then the requisite undertaking would cover similar breaches of the Code including potentially those other meetings listed on the page in question. In these circumstances the appeal in relation to the meeting should go ahead.

APPEAL BOARD RULING

The Appeal Board noted that Clause 22.4 stated that when meetings were sponsored by pharmaceutical companies, that fact must be disclosed in all of the papers relating to the meetings and in any published proceedings. The declaration of sponsorship must be sufficiently prominent to ensure that readers were aware of it at the outset.

The Appeal Board noted the Napp sponsorship agreement for the meeting at issue signed by the group of DSNs stated that 'The Recipient has confirmed that in all materials or publications which arise from or are used in connection with Activities (including invites and agendas), Napp's Sponsorship

of the Activities will be declared by displaying the following statement 'Supported by sponsorship from Napp Pharmaceuticals Limited'. The declaration of sponsorship must be sufficiently prominent to ensure readers are aware of it at the outset'.

The Appeal Board noted Napp's submission that the arrangements were an arms-length sponsorship of a third party organised non-promotional educational meeting and that the group of DSNs was not a third party engaged by, or acting on behalf of, Napp. Napp had approved the agenda which included its sponsorship declaration and that its offices were the venue for the meeting. The Appeal Board noted Napp's submission that it had no knowledge of the Facebook post detailing the meeting at issue prior to receiving the complaint.

The Appeal Board noted Napp's submission that according to the information provided to it from the group of DSNs that if 'Event' or 'Invite' were clicked within the Facebook post at issue the link included the declaration of Napp's sponsorship. A copy of the

Facebook post provided by Napp dated 4 February, which was after the Panel ruling and, therefore, not the subject of the complaint, now stated that 'Events have been solely organised by the group of DSNs and sponsored through funding by pharmaceutical companies'.

The Appeal Board noted that the agenda included the sponsorship statement and listed Napp's offices as the venue and that the Facebook post gave Napp's address under the heading 'Details'. The Appeal Board considered, in the particular circumstances of this case, that the group of DSNs had not included a declaration of Napp's sponsorship on the Facebook page at issue at the outset, despite Napp's sponsorship agreement, did not amount to a breach of Clause 22.4. The Appeal Board, therefore, ruled no breach of that clause. The appeal was successful.

Complaint received	6 December 2018
Case completed	13 March 2019

ANONYMOUS, NON-CONTACTABLE v SANOFI

Use of social media to advertise meetings

An anonymous, non-contactable complainant who described him/herself as a concerned health professional complained about advertisements for meetings sponsored by pharmaceutical companies, including Sanofi, on Facebook and Twitter and alleged various breaches of the Code including failure to include sponsorship statements and that the advertisements were reaching the public.

The detailed response from Sanofi is given below.

The Panel noted Sanofi's submission that it had decided not to sponsor what appeared to be the meetings at issue. No evidence had been provided by the complainant to support his/her allegation of Sanofi's involvement. The Panel considered that on the information before it, as Sanofi had no involvement with the meeting(s) there could be no breach of the Code as alleged and no breaches of the Code were ruled.

An anonymous, non-contactable complainant who described him/herself as a concerned health professional complained about advertisements for meetings sponsored by pharmaceutical companies including Sanofi on Facebook and Twitter.

COMPLAINT

The complainant alleged that advertisements for meetings that were being sponsored by pharmaceutical companies, including Sanofi, on Twitter and Facebook did not include sponsorship statements. According to the complainant, this was notable from Facebook notifications and the meeting advertisements themselves. The complainant further alleged that these advertisements were reaching the public.

The complainant provided a copy of material which referred to a diabetes specialist nurse meeting on Tuesday, 5 February which appeared to be one of a series. The description referred to diabetes health professionals with a love of diabetes care and that the meeting was a fabulous networking and learning opportunity where experienced professionals and people with diabetes would inform and inspire with new skills and innovations in diabetes care.

The complainant alleged that Sanofi was in breach of the following clauses:

- Clause 2 – bringing discredit to the industry
- Clause 4 – prescribing information (lack of in promotional materials)
- Clause 9 – high standards and suitability
- Clause 11 – distribution of materials
- Clause 12 – disguised promotion
- Clause 14 – certification – no evidence of certified meetings

- Clause 18 – inducements and appropriate payments of officials
- Clause 19 – medical educational goods and services
- Clause 20 – joint working
- Clause 22 – meetings, hospitality and sponsorship
- Clause 23 – the use of consultants
- Clause 24 – transfer of value to health professionals
- Clause 26 – relations with the public and media
- Clause 28 – internet.

RESPONSE

Sanofi confirmed that it was not involved with the sponsorship of the meeting referred to in the advertisement provided by the complainant or any other meetings being run by that group of diabetes specialist nurses; it was, therefore, unable to answer the majority of the questions raised by the Authority. Sanofi submitted that it understood that it had been contacted as a result of being directly named by the complainant but Sanofi did not consider that there was evidence of a case against it.

Sanofi stated it was aware of a collaboration of diabetes specialist nurses (DSNs) led by a number of individual DSNs who had collectively set up the group. Sanofi understood that the aim of the group was to support and share best practice between DSNs across the country. In terms of Sanofi's relationship with the group, Sanofi submitted details of its individual business relationships with certain DSNs through its sales team in terms of representative/customers. In addition, some DSNs had previously been contracted to speak at various Sanofi meetings and one of them at national Sanofi-led promotional meetings and had attended the European Association for the Study of Diabetes (EASD) with Sanofi as a sponsored delegate.

Sanofi submitted that it was approached by the group early in 2018 with a request to sponsor a series of meetings called the 'Stronger Together' tour as part of 'National DSN week' 4-8 February 2019. Given the date on the information provided by the complainant, it was likely that the meeting in question was part of that series. Sanofi had decided not to sponsor the meetings.

PANEL RULING

The Panel noted Sanofi's submission that it had decided not to sponsor the series of meetings called the 'Stronger Together' tour as part of 'National DSN week' 4-8 February 2019 which appeared to be the meetings at issue in the complaint. No evidence had been provided by the complainant to support his/her allegation of Sanofi's involvement. The Panel

considered that on the information before it, as Sanofi had no involvement with the meeting(s) there could be no breach of the Code as alleged. The Panel therefore ruled no breach of Clauses 2, 4, 9, 11, 12, 14, 18, 19, 20, 22, 23, 24, 26 and 28.

Complaint received **12 December 2018**

Case completed **18 January 2019**

COMPLAINANT v SHIELD

Information about Feraccru

A complainant who described him/herself as a concerned UK health professional, complained about the answers to frequently asked questions (FAQs) on the Feraccru (ferric maltol) website. Feraccru, was indicated for the treatment of iron deficiency in adults.

The complainant noted the following FAQ and answer:

‘Can Feraccru be used in patients with Hb<9.5g/dL?’

Feraccru should not be used in IBD [inflammatory bowel disease] patients with haemoglobin <9.5g/dL. We have not studied the use of Feraccru in these patients. However, our phase 3 CKD study included patients with haemoglobin levels as low as 8g/dL.’

The complainant stated that the first line was correct. The second line appeared to reassure - especially the use of the word ‘however’ - data in Phase 3 trials did not mean one could advocate use beyond the data in the summary of product characteristics (SPC).

The complainant was even more worried about a FAQ on pregnancy:

‘Is Feraccru suitable for patients that are pregnant or breastfeeding?’

We do not have any clinical data in this population. A benefit/risk assessment should be made before prescribing Feraccru.’

The complainant referred to the SPC which used much stronger language:

‘Pregnancy
There are no data from the use of Feraccru in pregnant women. Ferric maltol is not systemically available.

Definitive animal studies are not available for maltol with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Feraccru during pregnancy.

Breastfeeding
Ferric maltol is not available systemically and is therefore unlikely to pass into the mother’s milk. No clinical studies are available to date. As a precautionary measure, it is preferable to avoid the use of Feraccru during breast-feeding.’

The complainant was concerned that Shield had many flaws on its other website and it appeared that the company was encouraging the use of its

product in several groups which was against the licensed indication.

The detailed response from Shield is given below.

The Panel noted that Feraccru was indicated in adults for the treatment of iron deficiency. Section 4.4 of the SPC, special warnings and precautions for use, stated that Feraccru should not be used in patients with IBD flare or in IBD patients with haemoglobin (Hb) <9.5g/dL. Section 5.1 of the SPC referred to data from IBD studies which included IBD patients with the lower limit of haemoglobin. The SPC did not mention a lower limit for haemoglobin in other groups of patients.

The Panel noted the answer to the question on the Shield website referred to data in patients with chronic kidney disease (CKD) with haemoglobin as low as 8g/dl. The Panel noted that the SPC made no specific mention of CKD. The Panel was unsure of the impact of the statement in the SPC that Feraccru had not been studied in patients with impaired renal and/or hepatic function.

The Panel did not consider that the response on the Shield website advocated use of the medicine beyond the SPC given the broad indication for Feraccru and no breach of the Code was ruled. The response could have been better worded but, in the Panel’s view, it was not misleading and the Panel therefore ruled no breaches of the Code.

The Panel noted that the response to the question on the Shield website in relation to use in pregnancy or breast feeding, did not include all the relevant information from the SPC. It was made clear that there was no clinical data in this population. The response was referenced to the SPC and PIL; readers were not specifically referred to the statements in the SPC and PIL for further information as stated by Shield.

The Panel noted that health professionals would make a benefit/risk assessment before prescribing any medicine, particularly so in patients who were pregnant or breastfeeding. The Panel considered that to omit from the answer very relevant additional information from the SPC that as a precautionary measure it was preferable to avoid the use of Feraccru during pregnancy and breastfeeding was misleading. Full information had not been provided. The Panel also considered that the answer to the FAQ on the Shield website was inconsistent with information in the SPC. The Panel therefore ruled breaches of the Code which were upheld on appeal by Shield. It was important that health professionals could rely upon the industry for accurate, complete information about its medicines. The Panel did not consider that high standards had

been maintained and ruled a breach of the Code which was upheld on appeal by Shield. The Panel did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 which was reserved as a sign of particular censure.

A complainant who described him/herself as a concerned UK health professional, complained about the answers to frequently asked questions (FAQs) on the Feraccru (ferric maltol) website. Feraccru, was indicated for the treatment of iron deficiency in adults.

COMPLAINT

The complainant noted the following FAQ and answer:

‘Can Feraccru be used in patients with Hb<9.5g/dL?

Feraccru should not be used in IBD [inflammatory bowel disease] patients with haemoglobin <9.5g/dL. We have not studied the use of Feraccru in these patients. However, our phase 3 CKD study included patients with haemoglobin levels as low as 8g/dL.’

The complainant stated that the first line was correct. The second line appeared to reassure - especially the use of the word ‘however’ - data in Phase 3 trials did not mean one could advocate use beyond the data in the summary of product characteristics (SPC).

The complainant was even more worried about a FAQ on pregnancy:

‘Is Feraccru suitable for patients that are pregnant or breastfeeding?

We do not have any clinical data in this population. A benefit/risk assessment should be made before prescribing Feraccru.’

The complainant referred to the SPC which used much stronger language:

‘Pregnancy
There are no data from the use of Feraccru in pregnant women. Ferric maltol is not systemically available.

Definitive animal studies are not available for maltol with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Feraccru during pregnancy.

Breastfeeding
Ferric maltol is not available systemically and is therefore unlikely to pass into the mother’s milk. No clinical studies are available to date. As a precautionary measure, it is preferable to avoid the use of Feraccru during breast-feeding.’

The complainant stated that it was quite concerning that Shield had many flaws on its other website and it appeared that the company was encouraging the use of its product in several groups which was against the licensed indication.

In writing to Shield the Authority drew attention to Clauses 2, 3.2, 7.2 and 9.1.

RESPONSE

Shield stated that as the complainant was anonymous, it was not possible to assess if he/she was a health professional and therefore whether access to the health professional section of the website was appropriate.

With regard to the FAQ about use of the medicine in patients with haemoglobin levels below 9.5g/dl, Shield submitted that Feraccru was indicated in adults for the treatment of iron deficiency. There was no specific lower level of haemoglobin specified, however Section 4.4 of the SPC provided information that limited the use of Feraccru in patients with Inflammatory Bowel Disease (IBD) to those with a Hb level >9.5g/dl. This limit reflected the study population from the original studies of Feraccru. A subsequent study in CKD patients included those with a Hb level as low as 8g/dl. The information reflected the full body of data available for Feraccru, was entirely consistent with the licensed indication and provided additional information to allow rational and appropriate use of Feraccru. Shield denied a breach of Clauses 3.2, 7.2 or 9.1.

With regard to the second issue raised by the complainant, the FAQ referring to the use of Feraccru in patients who were pregnant or breastfeeding, Shield referred to the answer on the website and that the response referred readers to the SPC and PIL for further information. Shield also referred to the relevant sections in the SPC and submitted that the SPC did not prohibit the use of Feraccru in either pregnancy or breast feeding. As was the case for most new medicines, there was no data available in these populations and therefore it was preferable to avoid use unless the benefit outweighed any risk as judged by the treating physician.

Ferric maltol was not systemically available and iron was a physiological substance required by mother and infants.

Shield submitted that the response to the FAQ was not misleading, it was consistent with the SPC, referred the reader to the SPC and PIL to provide further information and did not encourage off label use. Shield denied a breach of Clause 3.2 or 7.2.

In light of the above, Shield submitted that there was also no evidence of a breach of Clause 2.

PANEL RULING

The Panel noted that Feraccru was indicated in adults for the treatment of iron deficiency. Section 4.4 of the SPC, special warnings and precautions for use, stated that Feraccru should not be used in patients with IBD flare or in IBD patients with haemoglobin (Hb) <9.5g/dL. Section 5.1 of the SPC referred to data from IBD studies which included IBD patients with the lower limit of haemoglobin. The SPC did not mention a lower limit for haemoglobin in other groups of patients.

The Panel noted the answer to the question on the Shield website referred to data in patients with chronic kidney disease (CKD) with haemoglobin as low as 8g/dl. The Panel noted that the SPC made no specific mention of CKD. The Panel was unsure of the impact of the statement in the SPC that Feraccru had not been studied in patients with impaired renal and/or hepatic function. The Panel noted that Clause 3.2 stated that the promotion of a medicine must be in accordance with the particulars listed in its SPC. This clause did not prohibit companies from providing information not included in a SPC if that information was not inconsistent with the particulars listed in the SPC.

The Panel did not consider that the response on the Shield website advocated use of the medicine beyond the SPC given the broad indication for Feraccru and no breach of Clause 3.2 was ruled. The response could have been better worded but, in the Panel's view, it was not misleading and the Panel therefore ruled no breach of Clause 7.2. The Panel consequently ruled no breach of Clauses 9.1 and 2.

The Panel noted that the response to the question on the Shield website in relation to use in pregnancy or breast feeding, did not include all the relevant information from the SPC. It was made clear that there was no clinical data in this population. The response was referenced to the SPC and PIL; readers were not specifically referred to the statements in the SPC and PIL for further information as stated by Shield.

The Panel noted that health professionals would make a benefit/risk assessment before prescribing any medicine, particularly so in patients who were pregnant or breastfeeding. The Panel considered that to omit from the answer very relevant additional information from the SPC that as a precautionary measure it was preferable to avoid the use of Feraccru during pregnancy and breastfeeding was misleading. Full information had not been provided. The Panel also considered that the answer to the FAQ on the Shield website was inconsistent with information in the SPC. The Panel therefore ruled breaches of Clauses 7.2 and 3.2 of the Code. It was important that health professionals could rely upon the industry for accurate, complete information about its medicines. The Panel did not consider that high standards had been maintained and ruled a breach of Clause 9.1. The Panel did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 which was reserved as a sign of particular censure.

APPEAL BY SHIELD

Shield noted that the Panel's ruling of breaches of Clauses 3.2, 7.2 and 9.1 of the Code related to the information it had provided on the FAQ section of its website regarding Feraccru, specifically in relation to the suitability of Feraccru for patients who were pregnant or breast-feeding. This information was set out below:

'FAQ:

Is Feraccru suitable for patients that are pregnant or breastfeeding?

Response:

We do not have any clinical data in this population. A benefit/risk assessment should be made before prescribing Feraccru'

Shield noted that its response to the question was accompanied by a footnote, which directed the reader to the SPC and the PIL. The Panel had concluded that Shield's website did not include all the relevant information from the SPC and was therefore misleading in breach of Clause 7.2. In doing so, the Panel appeared to have placed significant reliance on the fact that the following text from the SPC was not repeated in the FAQ section on the website: 'As a precautionary measure, it is preferable to avoid the use of Feraccru during pregnancy [and] breast-feeding.' The Panel had also concluded that the response was inconsistent with information in the SPC, in breach of Clause 3.2. Further, in view of the rulings above, the Panel had ruled a breach of Clause 9.1.

Shield stated that iron deficiency was a significant health issue in pregnancy and when breast-feeding. Oral iron salts were commonly used but had poor bioavailability and were often poorly tolerated. Women were therefore frequently left iron deficient throughout their pregnancy leading to increased complication during partus and the puerperium. Given the challenges of iron replacement faced by health professionals, Shield had received many questions around the potential use of Feraccru in pregnancy and breastfeeding.

Shield submitted that it promoted Feraccru as a second line therapy and as an alternative to IV iron and it was also positioned as such on formularies in the NHS.

In Shield's view that it was reasonable to assume that a health professional accessing Shield's website to search for a question as to whether Feraccru could be used in pregnancy had a reason to do so, such as they had found other preparations to be ineffective or the patient was intolerant.

Shield submitted that the information provided for Feraccru through Shield's FAQ section was in accordance with the terms of its marketing authorisation and was consistent with the particulars listed in its SPC. The information provided was balanced, fair, objective, unambiguous and conveyed meaning of the wording in the SPC.

Shield submitted that it was important to place the use of the 'precautionary measure' in the appropriate context. The words 'as a precautionary measure' were reasonably understood to mean that, in the absence of an appropriate medical assessment, it was preferable to avoid use of Feraccru during breast-feeding. Information was provided to ensure the health professional recognised the lack of data for patients who were pregnant or who were breast feeding. It was Shield's belief that a

reasonable health professional would interpret the fact that there was no data from the use of pregnant women or in breast feeding to mean, inherently, that alternative products should be used if possible. However, the additional statement 'A benefit/risk assessment should be made before prescribing Feraccru', easily directed the attention of the health professional to the SPC and PIL and ensured that any decision on prescribing was made after a full benefit/risk assessment was carried out to consider the patient's individual circumstances, and any decision was made having considered the full contents of the SPC and PIL. For these reasons, Shield did not accept that its response was inconsistent with the information in the SPC and could not be found in breach of Clause 3.2.

Shield noted that the Panel ruled that omitting the precautionary statement from its response to the FAQ rendered it misleading (Clause 7.2) and inconsistent with the information in the SPC (Clause 3.2). To do so was to place disproportionate importance on the precautionary statement and ignored other essential information in the SPC which was necessary to consider when carrying out a balanced assessment. Indeed, had Shield chosen, for example, only to use some of the language around lack of ferric maltol systemically, or the fact that it was unlikely to be found in breast milk in its response, then Shield could have been accused of 'cherry picking' from the SPC and could rightly have been found to be in breach of Clause 7.2 for this reason.

Shield submitted that if the only additional statement in the SPC were to be that it was preferable to avoid the use of Feraccru at all in pregnancy and breastfeeding then a health professional could consider that they ought never to use Feraccru in such a situation. As was clear from the rest of the contents of the SPC, it would be erroneous to make a blanket decision not to prescribe Feraccru to women who were pregnant or breast-feeding. Such an error in judgement could lead to a failure to prescribe in the appropriate circumstances and might lead to women not receiving a treatment that could provide benefit to them and their infant.

Shield submitted that it followed that to take the precautionary statement out of context, and to misinterpret it so as to find Shield in breach of the Code, was unreasonable and perverse in the context of Clause 7.2.

Shield submitted that there was nothing in the response that conflicted with the full SPC in the sense that there could reasonably be said to be any 'encouraging' (to quote the complainant) of the use of Feraccru. Instead, the response to the question ensured that the fact that no data was available in pregnancy and breast-feeding was clear and directed the health professional to read the full SPC and assess the individual patient circumstances before making a prescribing decision. Shield did not accept that ensuring rational prescribing was in any way failing to maintain high standards and therefore there should be no finding of breach of Clause 9.1.

Shield submitted that it had acted in accordance with industry standards and promoted its products in a consistent manner and in accordance with the marketing authorisations. On no reasonable interpretation could it be said to have failed in respect of its accuracy, fairness and objectivity in the way in which it had provided information to the relevant health professional. No element of this case involved Shield preventing the information which would permit a health professional to make a fair, complete and accurate assessment of each individual patient from being readily available.

Shield submitted that the basis of the complaint was premised on a disagreement about the way certain information was provided to health professionals. This appeal set out the good reasons for the approach adopted in its response to the FAQ and the way in which that interacted with the SPC. It also highlighted why the position adopted by the Panel was flawed and if upheld could put patients at risk of not receiving medicines that could benefit them. Shield stood by the approach it had adopted, which ensured that patient safety was paramount and allowed health professionals to make a fully informed decision when prescribing Feraccru.

COMMENTS FROM THE COMPLAINANT

The complainant noted that given that this matter had already been viewed by industry experts he/she would not add any further value.

APPEAL BOARD RULING

The Appeal Board noted that the FAQ on Shield's Feraccru website for health professionals stated, 'Is Feraccru suitable for patients that are pregnant or breastfeeding?' and the drop-down response stated 'We do not have any clinical data in this population. A benefit/risk assessment should be made before prescribing Feraccru ^{1,4}'. The superscript 1 and 4 were linked to a separate page that contained a list of references including the SPC (at position 1) and PIL (at position 4) for Feraccru. There was no mention on the page containing the FAQ to indicate what the superscript 1 and 4 were referring to. The SPC and PIL were included as unnumbered links at the bottom of the page along with other documents.

The Appeal Board noted Section 4.6 of the Feraccru SPC referred to the absence of data from the use of Feraccru in pregnant women and that ferric maltol was not systemically available. It also stated that 'Definitive animal studies are not available for maltol with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Feraccru during pregnancy', and 'As a precautionary measure, it is preferable to avoid the use of Feraccru during breast-feeding'. The Appeal Board noted there was a difference between the absence of data and the absence of definitive data.

The Appeal Board noted the company's submission at the appeal that a risk/benefit assessment would include a detailed examination of the entire SPC and consideration of each patient's particular circumstances.

The Appeal Board considered that in terms of a health professional making a prescribing decision, the response to the FAQ was neutral; whereas the SPC included a specific precautionary measure that it was preferable to avoid the use of Feracru during pregnancy [and] breast-feeding. The Appeal Board noted that the warning would be included in the SPC for a reason and failure to include it in the FAQ response was misleading. Consequently, the Appeal Board considered that the response to the FAQ at issue was misleading and inconsistent with the SPC and it upheld the Panel's rulings of breaches of Clauses 7.2 and 3.2. A prescriber

reading the response to the FAQ might not be aware of the precautionary measure in the SPC. It was important that health professionals could rely upon the industry for accurate and complete information about its medicines. The Appeal Board upheld the Panel's ruling of a breach of Clause 9.1. The appeal was unsuccessful.

Complaint received **17 December 2018**

Case completed **2 April 2019**

COMPLAINANT v ASTELLAS

Promotion of Betmiga

A contactable complainant who described him/herself as a concerned health professional complained about a Betmiga (mirabegron) advertisement issued by Astellas Pharmaceuticals.

Betmiga was indicated for the symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence in adults with overactive bladder (OAB) syndrome.

The complainant stated that the headline 'More OAB patients stay on treatment with BETMIGA than with antimuscarinics' was interesting since antimuscarinics were often unpopular due to side effects.

The complainant stated that it was very poor to have Chapple *et al* (2017) as the sole reference. This stated, 'Limitations include the retrospective design, use of prescription records to estimate outcomes, and inability to capture reasons for discontinuation'. These 'massive caveats' were not mentioned in the advertisement and it was also not clear whether the treatment was used in patients who were contra-indicated, such as uncontrolled hypertension, or other at-risk groups such as limited liver or kidney function.

The complainant stated that the Betmiga summary of product characteristics (SPC) mentioned nothing about being better than antimuscarinics and as far as he/she could see there was no prospective study that had been undertaken against all antimuscarinics.

The complainant alleged that this was extremely misleading and used very weak data which could easily lead to inappropriate use of Betmiga.

The detailed response from Astellas is given below.

The Panel noted that the advertisement depicted two men and a woman walking together in a field, with the woman walking on a highlighted path. A dotted line pointed to the woman with the boxed statement 'Her 6th hike since the day she started BETMIGA'. At the top of the page in a box, in larger font, was the headline claim, 'More OAB patients stay on treatment with BETMIGA than with antimuscarinics', referenced to Chapple *et al* (2017). In the bottom right-hand corner of the picture was the Betmiga logo with the statement 'Treatment they can keep taking is treatment that can keep working'. Below the picture was the text:

'When an antimuscarinic fails because of side effects or poor efficacy, prescribing another may be of minimal benefit [referenced to Chancellor *et al* (2016)]. So why not take a different path?'

BETMIGA is in another class, relaxing the bladder via β 3-adrenoreceptors [referenced to the Betmiga SPC]. It can be just as effective as an antimuscarinic but it doesn't have the same side-effect profile [referenced to Maman *et al* (2014)]. The result: more patients still taking their treatment at the 12 month mark' [referenced to Chapple *et al* (2017)].

The Panel noted that the Code did not prohibit the use of retrospective observational studies that utilised prescription records to estimate outcomes as a means of substantiating a claim provided that the claim complied with the requirements of the Code. Context was important.

The Panel noted the text below the picture and within the advertisement as set out above, including, *inter alia*, the use of the connector 'The result' and considered that it implied that the reason more Betmiga patients were still taking their treatment at 12 months was because it had a favourable side-effect profile compared to antimuscarinics. This, in the Panel's view, was not evident from Chapple *et al* which was unable to examine the reasons for discontinuation as these data were not contained in the database. The Panel noted the caution expressed by the study authors, 'Mirabegron provides an alternative treatment option for OAB with the potential to increase treatment persistence'. The Panel noted the limitations of the study including, *inter alia*, the use of prescription-event rather than patient-derived data to estimate outcomes. The Panel noted that the claim in question was unqualified and thus did not fairly reflect the study.

The Panel considered that insufficient information about the study had been provided in the advertisement to enable the reader to meaningfully assess the claim in question and form their own opinion of the therapeutic value of the medicine in relation to treatment persistence. The Panel considered that the claim was misleading, exaggerated and not capable of substantiation. Breaches of the Code were ruled.

A contactable complainant who described him/herself as a concerned health professional complained about a Betmiga (mirabegron) advertisement (ref BET18035UKa) issued by Astellas Pharmaceuticals Limited and published in the December 2018 edition of Pulse magazine.

Betmiga was indicated for the symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence in adults with overactive bladder (OAB) syndrome.

COMPLAINT

The complainant stated that the headline 'More OAB patients stay on treatment with BETMIGA than with antimuscarinics' was interesting since antimuscarinics were often unpopular due to side effects.

The complainant stated that it was very poor to have Chapple *et al* (2017) as the sole reference. It stated, 'Limitations include the retrospective design, use of prescription records to estimate outcomes, and inability to capture reasons for discontinuation'. These 'massive caveats' were not mentioned in the advertisement and it was also not clear whether the treatment was used in patients who were contra-indicated, such as uncontrolled hypertension, or other at-risk groups such as limited liver or kidney function.

The complainant stated that this might be OK if all the other evidence said the same but the Betmiga summary of product characteristics (SPC) mentioned nothing about being better than antimuscarinics and as far as he/she could see there was no prospective study that had been undertaken against all antimuscarinics.

The complainant alleged that this was extremely misleading and used very weak data which could easily lead to inappropriate use of Betmiga. He/she thought that this fell below the standards the MHRA required let alone the ABPI.

In writing to Astellas attention was drawn to the requirements of Clauses 7.2, 7.4 and 7.10 of the Code.

RESPONSE

Astellas stated that it took very seriously all allegations of non-compliance with any regulations, including the Code, and had conducted a comprehensive investigation in order to address all points raised by the complainant.

Astellas disagreed that the claim 'More OAB patients stay on treatment with Betmiga than with antimuscarinics' was misleading and could not be substantiated. Astellas also denied that the reference used to substantiate the claim was poor.

Chapple *et al* (2017) was a retrospective, longitudinal, observational study of anonymised data from the UK Clinical Practice Research Datalink (CPRD) GOLD database. The objective of the study was to compare persistence and adherence with mirabegron versus tolterodine extended release (ER) and other antimuscarinics in routine clinical practice over a 12-month period. The primary end point was persistence (time to discontinuation); secondary endpoints included 12-month persistence rates and adherence.

CPRD was a real-world research service supporting retrospective and prospective public health and clinical studies. CPRD was jointly sponsored by the Medicines and Healthcare products Regulatory Agency (MHRA) and the National Institute for Health

Research (NIHR), as part of the Department of Health and Social Care. CPRD collected de-identified patient data from a network of GP practices across the UK. Primary care data were linked to a range of other health related data to provide a longitudinal, representative UK population health dataset. The data encompassed over 35 million patient lives, including 10 million currently registered patients.

Astellas submitted that for more than 30 years, research using CPRD data and services had informed clinical guidance and best practice, resulting in over 2,000 peer-reviewed publications investigating drug safety, use of medicines, effectiveness of health policy, health care delivery and disease risk factors. The CPRD primary care database was thus a rich source of health data for research, including data on demographics, symptoms, tests, diagnoses, therapies, health-related behaviours and referrals to secondary care.

Chapple *et al*, included 21,966 patients, and was published in a peer-reviewed journal, European Urology, the official journal of the European Association of Urology (EAU) which was currently read by more than 20,000 urologists globally. Impact factors were used to measure the credibility of a journal by calculating the number of times selected articles were cited within the last few years; the higher the impact factor, the more highly ranked the journal. Only 1.7% of journals had an impact factor greater than 10. European Urology had an impact factor of 17.581. In addition, Chapple *et al* had been cited in other scientific articles 35 times, many of which were published in international journals.

Chapple *et al* concluded that 'Persistence and adherence were statistically significantly greater with mirabegron than with tolterodine ER and other antimuscarinics prescribed for OAB in the UK'.

With the above in mind, Astellas submitted that the claim at issue was an unambiguous statement of fact, substantiated by Chapple *et al*, a publication of research data from a comprehensive database, published in a highly reputable journal. The claim was therefore consistent with the requirements of Clauses 7.2 and 7.4. The claim did not in any way exaggerate the qualities of the medicine and was thus not in breach of Clause 7.10.

Clarity of Study Limitations

Astellas stated it was important to note that the advertisement was about patients' persistence with treatment. Retrospective database investigations were universally accepted to be the best way to assess a patient's persistence with a treatment. Any prospective study would change compliance rates; it was human nature to behave differently when being observed. In addition, the ABPI guidance Demonstrating Value with Real World Data recognised the value of retrospective data in that regard.

Given this, Astellas submitted it was not necessary to include the limitations of the study in the advertisement itself. Astellas did not consider that

omitting this information rendered the advertisement misleading and disagreed that the advertisement was in breach of Clause 7.2 in that regard.

Inference that Betmiga is 'Better' than Antimuscarinics

With regard to the complainant's statement that there was nothing in the Betmiga summary of product characteristics (SPC) about Betmiga being 'better' than antimuscarinics, Astellas did not consider that there was any direct or implied claim in the advertisement at issue of superior efficacy for Betmiga vs antimuscarinic medicines. The advertisement was about persistence in, and adherence by, patients in their treatment and this was reflected in:

- The headline claim ('More OAB patients stay on treatment with Betmiga than with antimuscarinics');
- The imagery of a patient being able to conduct normal activities such as going on a hike;
- The text underneath the image which referred to taking a different path with Betmiga if a patient discontinued an antimuscarinic ('**It can be just as effective** as an antimuscarinic, but it doesn't have the same side-effect profile'; emphasis added by Astellas).

Astellas therefore disagreed that there were any claims of superior efficacy and denied a breach of Clauses 7.2 and 7.4. There was no claim or other information about Betmiga that could be considered exaggerated in this regard and Astellas denied a breach of Clause 7.10.

Inappropriate Use of Betmiga

With regard to the allegation that the advertisement might lead to clinicians using Betmiga inappropriately, Astellas noted that no further explanation was provided by the complainant. The advertisement evidently and prominently stated the indication for Betmiga, and the contraindications and warnings were clearly laid out in the prescribing information. Astellas therefore denied a breach of Clause 7.10 in this regard.

MHRA Standards

With regard to the allegation that the advertisement fell below the standards of the MHRA, Astellas submitted it was important to highlight that the claim at issue, supported by Chapple *et al*, had been vetted by the MHRA which had no comments on the claim. Astellas recognised that the Code reflected and extended beyond the law. Astellas submitted that the fact that this vetting had occurred should help to reassure the complainant.

PANEL RULING

The Panel noted the complainant's allegation that the advertisement fell below standards that the MHRA required. The Panel noted Astellas' submission that the claim at issue, supported by Chapple *et al* (2017), had been vetted by the MHRA. The Panel

was unclear if the advertisement at issue had been vetted by the MHRA or just the claim 'More OAB patients stay on treatment with Betmiga than with antimuscarinics'. Astellas made no submission in that regard but referred to vetting of the claim. The Panel could only consider the matter under the Code.

The Panel noted from the approval certificate that the advertisement in question was intended as a double page spread in Pulse. It depicted two men and a woman walking together in a field, with the woman walking on a highlighted path. A dotted line pointed to the woman with the boxed statement 'Her 6th hike since the day she started BETMIGA'. At the top of the page in a box, in larger font, was the headline claim, 'More OAB patients stay on treatment with BETMIGA than with antimuscarinics', referenced to Chapple *et al* (2017). In the bottom right-hand corner of the picture was the Betmiga logo with the statement 'Treatment they can keep taking is treatment that can keep working'. Below the picture was the text:

'When an antimuscarinic fails because of side effects or poor efficacy, prescribing another may be of minimal benefit [referenced to Chancellor *et al* (2016)]. So why not take a different path? BETMIGA is in another class, relaxing the bladder via β 3-adrenoreceptors [referenced to the Betmiga SPC]. It can be just as effective as an antimuscarinic but it doesn't have the same side-effect profile [referenced to Maman *et al* (2014)]. The result: more patients still taking their treatment at the 12 month mark' [referenced to Chapple *et al* (2017)].

The Panel noted the complainant's allegation that it was poor for Chapple *et al* to be the sole reference for the headline claim and he/she referred to the limitations of the study as described in the paper which were not mentioned in the advertisement. The Panel further noted the complainant's statement that the Betmiga SPC did not mention that it was 'better' than antimuscarinics and there had been no prospective studies against all antimuscarinics.

The Panel noted Astellas' submission that Chapple *et al* was a retrospective, longitudinal, observational study of anonymised data from a recognised UK database, included 21,966 patients, was published in a peer-reviewed journal and had been cited in other scientific articles. The Panel noted Astellas' submission that Chapple *et al* concluded, 'Persistence and adherence were statistically significantly greater with mirabegron than with tolterodine ER and other antimuscarinics prescribed for OAB in the UK'. The Panel further noted Astellas' submission that there was no direct or implied claim of superior efficacy for Betmiga versus antimuscarinic medicines in the advertisement at issue.

In the Panel's view, the acceptability of the headline claim 'More OAB patients stay on treatment with BETMIGA than with antimuscarinics' should be considered within the context of the advertisement.

The Panel did not agree that it was not necessary to have the limitations of the study in the advertisement because, in Astellas' view, retrospective database

investigations were universally accepted to be the best way to assess a patient's persistence with treatment. The Panel noted that the Code did not prohibit the use of retrospective observational studies that utilised prescription records to estimate outcomes as a means of substantiating a claim provided that the claim complied with the requirements of the Code including Clauses 7.2 and 7.4. Context was important.

The Panel noted the text below the picture and within the advertisement as set out above, including, *inter alia*, the use of the connector 'The result' and considered that it implied that the reason more Betmiga patients were still taking their treatment at 12 months was because it had a favourable side-effect profile compared to antimuscarinics. This, in the Panel's view, was not evident from Chapple *et al* which was unable to examine the reasons for discontinuation as these data were not contained in the database. The Panel noted the caution expressed by the study authors, 'Mirabegron provides an alternative treatment option for OAB with the **potential** to increase treatment persistence' (emphasis added). The Panel noted the limitations of the study including, *inter alia*, the use of prescription-event rather than patient-derived data to estimate outcomes. The Panel noted that the claim in question was unqualified and thus did not fairly reflect the study.

The Panel noted its comments above and considered that insufficient information about the study had been provided in the advertisement to enable the reader to meaningfully assess the claim in question and form their own opinion of the therapeutic value of the medicine in relation to treatment persistence. The Panel considered that the claim was misleading in this regard and a breach of Clause 7.2 was ruled.

The Panel noted that Clause 7.4 stated any information, claim or comparison must be capable of substantiation. The Panel noted its comments above and considered that the misleading implication that the difference in treatment persistence between Betmiga and antimuscarinics was as a result of their different side-effect profiles was not capable of substantiation and thus ruled a breach of Clause 7.4.

In the Panel's view, the claim in question within the context of the advertisement, and on the balance of probabilities, exaggerated Betmiga's properties in relation to treatment persistence and side effects and therefore did not encourage the rational use of Betmiga and a breach of Clause 7.10 was ruled.

Complaint received **18 December 2018**

Case completed **3 April 2019**

COMPLAINANT v SANOFI

Online advertisement

A complaint was received from an individual of unknown professional status, who complained about an online advertisement for Praluent (alirocumab) placed by Sanofi in the HSJ (Health Service Journal). Praluent was a lipid lowering agent. The advertisement in question was headed 'Advertorial: PCSK9 inhibitors – Recognising innovation in cholesterol treatment to help address a UK health burden' and discussed the use of Praluent. Prescribing information for Praluent was included.

The complainant was surprised to find the advertisement in an online journal with information on how to prescribe. The complainant was concerned that members of the public could subscribe to the HSJ [Health Service Journal] and so the website was not a suitable medium for an article about the benefits of prescribing a specific medicine.

The complainant noted that each reference had a hyperlink and queried whether Sanofi had permission from each of the website owners to create these hyperlinks eg, with the National Institute for Health and Care Excellence (NICE) or the British Heart Foundation. The complainant stated that he/she had been unable to find or access some of the references through the links provided.

The complainant noted that the material in question appeared to focus on the clinical aspects of treatment which he/she considered was more appropriate for doctors and not for the mixed readership of the HSJ.

The detailed response from Sanofi is given below.

The Panel noted that the Code covered the promotion of medicines to health professionals and to other relevant decision makers. These were defined as particularly those with an NHS role who could influence in any way the administration, consumption, prescription, purchase, recommendation, sale, supply or use of any medicine but who were not health professionals. The Panel also noted previous cases involving advertising in the HSJ which was a specialist professional journal not aimed at the general public. In the Panel's view it was acceptable for companies to advertise medicines in the HSJ provided the advertisement was appropriate for the audience. The Panel considered that this also applied to the HSJ website where the advertisement in question had been placed.

The Panel noted the information provided by Sanofi about the target audience for the material in question, the website readership statistics and that the HSJ was intended for healthcare leaders or others who had a direct or indirect role in decision making within the NHS.

The content of the advertisement was broad and included information on the economic impact of cardiovascular disease, efficacy, side effects, tolerability and NICE recommendations. There was no mention of costs in the body of the advertisement; the only mention was in the prescribing information which included the list price of Praluent. The Panel did not consider that the inclusion of clinical content and references to clinical evidence meant that the advertisement was not tailored to the HSJ website audience.

On balance, the Panel was satisfied that the advertisement was sufficiently tailored to the HSJ audience and in that regard the audience could reasonably be assumed to have an interest in it. The Panel therefore ruled no breach of the Code in this regard.

The Panel did not consider that the advertisement for Praluent on the HSJ website was an advertisement to the public who subscribed to the HSJ as alleged. The HSJ was for those with a role in healthcare including health professionals. The Panel therefore ruled no breach in this regard.

The Panel noted the complainant stated that he/she had not been able to access the references. The links were not working. It was not clear whether the complainant had asked Sanofi to supply the references. Sanofi had not responded to this point nor had it responded as to whether it had permission from each of the website owners to create these hyperlinks. The Panel considered that if links were used in advertisements then they should work. The Code required substantiation to be provided on request and on the information available to the Panel there had been no request.

Given its rulings above the Panel considered that there had not been a failure to maintain high standards and ruled no breach of the Code.

An individual of unknown professional status complained about an online advertisement for Praluent (alirocumab) placed by Sanofi in the HSJ (Health Service Journal). Praluent was a lipid lowering agent. The advertisement in question was headed 'Advertorial: PCSK9 inhibitors – Recognising innovation in cholesterol treatment to help address a UK health burden' and discussed the use of Praluent. Prescribing information for Praluent was included. The piece was dated 25 June 2018.

COMPLAINT

The complainant stated that he/she was surprised to find the advertisement in an online journal with information on how to prescribe. The complainant was concerned that members of the public could

subscribe to the HSJ [Health Service Journal] and so he/she did not consider that the website was a suitable medium for an article about the benefits of prescribing a specific medicine.

The complainant noted that each reference had a hyperlink and queried whether Sanofi had permission from each of the website owners to create these hyperlinks eg, with the National Institute for Health and Care Excellence (NICE) or the British Heart Foundation. The complainant stated that he/she had been unable to find or access some of the references through the links provided.

The complainant noted that the material in question appeared to focus on the clinical aspects of treatment which he/she considered more appropriate for doctors and not for the mixed readership of the HSJ.

When writing to Sanofi, the Authority asked it to consider the requirements of Clauses 9.1, 11.1, 26.1 and 26.2 of the 2016 Code.

RESPONSE

Sanofi stated that the advertorial in question was posted on the HSJ website rather than being included in an online journal.

In relation to the target audience for the advertorial, the HSJ website showed 18% of its readers were commissioners, 20% were from the private sector, 32% were healthcare providers and 27% were involved in commissioning.

Sanofi noted that the HSJ website and HSJ logo contained the wording 'For Healthcare Leaders' which indicated to the audience that the website was intended for healthcare leaders or others who had a direct or indirect role in decision-making within the NHS.

Sanofi submitted that the inclusion of pharmaceutical company advertising in the HSJ had previously been considered (Case AUTH/2058/10/07, Cases AUTH/2426/8/11 and AUTH/2427/8/11) when the Panel concluded that it did not accept that an advertisement in the HSJ constituted *per se* an advertisement to the public and it also 'considered that the publication was an acceptable vehicle for the advertisement of prescription only medicines' (Cases AUTH/2426/8/11 and AUTH/2427/8/11). In Case AUTH/2058/10/07 the Panel's view was that 'it was acceptable for companies to advertise medicines in the HSJ provided the advertisement was appropriate for the audience'.

Sanofi submitted that the placement of the advertisement on the HSJ website did not constitute promotion to the public and as such it denied breaches of Clauses 26.1 and 26.2.

The content of the advertisement was tailored to an audience of clinical and non-clinical health professionals and other relevant decision makers in line with the readership of the HSJ website. As such Sanofi denied a breach of Clause 11.1.

The advertisement highlighted the disease burden as an introductory statement and preface which made relevant reading for the clinicians and non-clinical decision makers alike. The first part of the advertisement was entirely dedicated to highlighting the disease burden; it explained the impact of cardiovascular disease in general on morbidity and mortality, healthcare and economic costs and discussed the relevant social impact. This section also discussed the current therapies used for lipid lowering and the societal impact on cardiovascular disease with specific reference to LDL C and cholesterol levels. It highlighted the clinical unmet need in optimum lipid management with specific focus on familial hypercholesterolemia which related to the impact on society, economic framework and healthcare. The sections on disease burden, unmet need and economic/social impact were of greater relevance to the non-clinical decision makers involving commissioners and policy makers who might be unaware of these aspects of the disease burden or unmet need especially with regards to Praluent. In Sanofi's view, this information would be of significant relevance in their decision making process.

Sanofi submitted that the second part of the advertisement looked at the clinical efficacy measure for Praluent in general and mentioned the relevant clinical evidence that related to the unmet need and disease burden which was highlighted in the first part of the advertisement. Whilst this was clinical data it was of significant relevance to the non-clinical decision makers since it crucially helped provide a plug in response to the level of unmet need that was highlighted. The commissioners and policy makers needed to be informed of the clinical efficacy of Praluent while responding to the challenge of the unmet clinical need in their local and regional environments.

This was of even more importance while considering the gap in uptake in the NICE recommended population that had been highlighted in the second part of the advertisement.

In conclusion, Sanofi refuted any breach of Clauses 11.1, 26.1 or 26.2 and thus of Clause 9.1.

PANEL RULING

The Panel noted that the Code covered the promotion of medicines to health professionals and to other relevant decision makers. These were defined as particularly those with an NHS role who could influence in any way the administration, consumption, prescription, purchase, recommendation, sale, supply or use of any medicine but who were not health professionals. The Panel also noted previous cases involving advertising in the HSJ. The HSJ was a specialist professional journal and was not aimed at the general public. In the Panel's view it was acceptable for companies to advertise medicines in the HSJ provided the advertisement was appropriate for the audience. The Panel considered that this also applied to the HSJ website where the advertisement in question had been placed.

Clause 11.1 required that promotional material should only be sent or distributed to those categories of persons whose need for, or interest in, the particular information could reasonably be assumed. The supplementary information to Clause 11.1 stated that promotional material should be tailored to the audience to whom it was directed.

The Panel noted the information provided by Sanofi about the target audience for the material in question, the website readership statistics and that the HSJ was intended for healthcare leaders or others who had a direct or indirect role in decision making within the NHS.

The content of the advertisement was broad and included information on the economic impact of cardiovascular disease, efficacy, side effects, tolerability and NICE recommendations. There was no mention of costs in the body of the advertisement; the only mention was in the prescribing information which included the list price of Praluent. The Panel did not consider that the inclusion of clinical content and references to clinical evidence meant that the advertisement was not tailored to the HSJ website audience.

On balance, the Panel was satisfied that the advertisement was sufficiently tailored to the HSJ audience and in that regard the audience could reasonably be assumed to have an interest in it. The Panel ruled no breach of Clause 11.1.

The Panel did not consider that the advertisement for Praluent on the HSJ website was an advertisement to the public who subscribed to the HSJ as alleged. The HSJ was for those with a role in healthcare including health professionals. The Panel therefore ruled no breach of Clauses 26.1 and 26.2.

The Panel noted the complainant stated that he/she had not been able to access the references. The links were not working. It was not clear whether the complainant had asked Sanofi to supply the references. Sanofi had not responded to this point nor had it responded as to whether it had permission from each of the website owners to create these hyperlinks. The Panel considered that if links were used in advertisements then they should work. The Code required substantiation to be provided on request and on the information available to the Panel there had been no request. Sanofi was welcome to send the references to the PMCPA for it to send them to the complainant.

Given its rulings above the Panel considered that there had not been a failure to maintain high standards and ruled no breach of Clause 9.1.

Complaint received **7 January 2019**

Case completed **24 April 2019**

TILLOTTS v FERRING

Failure to withdraw material

Tillotts Pharma UK complained that Ferring Pharmaceuticals Ltd had failed to honour an inter-company agreement to withdraw a Cortiment (budesonide prolonged release tablets) leavepiece. Cortiment was indicated in adults for the induction of remission in patients with mild to moderate active ulcerative colitis where 5 ASA treatment was not sufficient. The leavepiece was entitled 'Guidance on Prescribing Cortiment by brand' and included the claim relating to Cortiment that 'Generic budesonides lack this unique [multimatrix] MMX structure'.

Tillotts initiated inter-company dialogue with Ferring and objected, *inter alia*, to the use of the term 'generic budesonides' in the leavepiece at issue. As there were no generic oral budesonides available in the UK, the term was inaccurate and misleading and Tillotts asked that the material be withdrawn.

Tillotts was thus concerned to note that three weeks later the leavepiece in question was distributed from the Ferring stand at the Scottish Society of Gastroenterology (SSG) meeting in November 2018. This clearly meant that the term 'generic' had not been revised in future promotional activity as Ferring stated it would be.

Tillotts wrote to Ferring on 17 December to ask why the material had been used at the SSG meeting. There had either been a failure of Ferring's withdrawal process, or a change in Ferring's commitment to withdraw the material. In its response of 20 December, Ferring confirmed that the leavepiece had been withdrawn as of 18 December and replaced with a new piece.

Tillotts noted that although neither the Code nor the letter from Ferring of 25 October set a timeline for withdrawal of material, to allow nearly 8 weeks to pass was unacceptable and demonstrated a failure to maintain high standards. Tillotts also alleged that use of the material at one promotional event, and possibly others, during this eight week period was also a failure to maintain high standards.

The detailed response from Ferring is given below.

The Panel noted that although undertakings given during the course of inter-company dialogue were not covered by the Code and were thus not subject to the requirements of the Code, it was important that companies complied with such undertakings. Failing to implement an inter-company undertaking might indicate that previous inter-company dialogue had ultimately been unsuccessful.

The Panel noted that Ferring had informed Tillotts that it agreed to withdraw the material. The

Panel considered, in the circumstances, it was not unreasonable for Tillotts to assume that the leavepiece had been withdrawn. This had not happened until some weeks later. The Panel might be sympathetic to the submission that Ferring was waiting for comment from Tillotts regarding another matter it had raised before changing the leavepiece if Ferring had made this clear to Tillotts. The Panel disagreed with Ferring's submission about the use of the claim 'generic budesonides lack this ... structure'. In the Panel's view, the claim was misleading as oral budesonide was not available as a generic in the UK. The term 'generic' had a particular meaning in relation to medicines. The Panel considered, therefore, that high standards had not been maintained and a breach of the 2016 Code was ruled. The Panel considered that this ruling covered both the failure to withdraw the leavepiece and its continued use.

Tillotts Pharma UK Limited complained that Ferring Pharmaceuticals Ltd had failed to honour an inter-company agreement to withdraw a Cortiment (budesonide prolonged release tablets) leavepiece (ref COR/2078/2017/UK). Cortiment was indicated in adults for the induction of remission in patients with mild to moderate active ulcerative colitis where 5 ASA treatment was not sufficient. The leavepiece was entitled 'Guidance on Prescribing Cortiment by brand' and included the claim relating to Cortiment that 'Generic budesonides lack this unique [multimatrix] MMX structure'.

COMPLAINT

Tillotts explained that on 16 October 2018 it initiated inter-company dialogue with Ferring and objected, *inter alia*, to the use of the term 'generic budesonides' in the leavepiece at issue. As there were no generic oral budesonides available in the UK, the term was inaccurate and misleading and Tillotts asked that the material be withdrawn. The letter named the four brands available in the UK.

The response from Ferring dated 25 October included:

'We acknowledge your statement in relation to the use of the term 'generic' and shall revise this in future promotional activity.

We confirm withdrawal of the leave piece in question and replacement of the term generic with another term.'

Tillotts was thus concerned to note that three weeks later the leavepiece in question was distributed from the Ferring stand at the Scottish Society of Gastroenterology (SSG) meeting held 14-16 November. This clearly meant that the term 'generic'

had not been revised in future promotional activity as Ferring stated it would be.

Tillotts wrote to Ferring on 17 December to ask why the material had been used at the SSG meeting. There had either been a failure of Ferring's withdrawal process, or a change in Ferring's commitment to withdraw the material. In its response of 20 December, Ferring confirmed that the leavepiece had been withdrawn as of 18 December and replaced with a new piece with the specified changes. Ferring did not, however, explain why the leavepiece had been used at the SSG meeting as requested.

Tillotts noted that although neither the Code nor the letter from Ferring of 25 October set a timeline for withdrawal of material, to allow nearly 8 weeks to pass was unacceptable and demonstrated a failure to maintain high standards in breach of Clause 9.1. Tillotts also alleged that use of the material at one promotional event, and possibly others, during this eight week period was also in breach of Clause 9.1, as Ferring had stated that use of the term 'generic' with regard to budesonide products would be revised in future promotional activity.

RESPONSE

Ferring denied breaches of Clause 9.1. The company submitted that in the spirit of goodwill, it offered to amend the material in relation to the word 'generic' although it did not accept that its use was inappropriate. Ferring noted that Tillotts did not acknowledge receipt of Ferring's response or acknowledge its counter arguments and as no timeframe had been stated in Ferring's letter of 25 October, Ferring allowed for sufficient time to elapse before taking action. The obvious consideration was that Tillotts might require further action in relation to a second point which had also been discussed. Ferring would not want to change the material twice in a short space of time if Tillotts raised further points (which could often be the case in inter-company exchanges).

Ferring stated that in a genuine grammatical error, its letter of 25 October implied that the material had been withdrawn. The letter referred to revising future promotional activity and stated:

'We confirm withdrawal of the leave piece in question and replacement of the term generic with another term.'

but should have stated:

'We confirm our willingness to withdraw the leave piece in question and replacement of the term generic with another term.'

Ferring apologised for the confusion caused.

In the absence of a response from Tillotts, Ferring stated that it continued with business as usual, including the dissemination of material for use at the SSG meeting. Ferring noted that it responded to

Tillotts on 25 October; material was sent to the SSG meeting 2 weeks later so that it could be used at the meeting (14-16 November). Ferring noted that at that point, it had not received any response from Tillotts.

Ferring submitted that it waited 7 weeks for a response from Tillotts and it took the unilateral decision on 18 December to withdraw the leavepiece in question. The withdrawal notice (copy provided) was issued by Ferring before the receipt of the letter from Tillotts (dated 17 December, received 20 December). Ferring submitted that its withdrawal email clearly denoted the procedure that needed to be followed and aligned with its standard operating procedure (SOP) on the management of promotional materials (copy provided).

Ferring responded to Tillotts on 20 December to acknowledge receipt of the letter and confirmed when the leavepiece in question was actually withdrawn. Ferring noted that it never provided a timeframe for withdrawal of the material in question. The difference of opinion in relation to the term 'generic' was not a patient safety issue. Ferring did not consider that in the circumstances, the timelines involved in the withdrawal were inappropriate and the company denied a breach of Clause 9.1. Ferring further denied the alleged breach of Clause 9.1 in relation to the continued use of the leavepiece.

PANEL RULING

The Panel noted that although undertakings given by companies during the course of inter-company dialogue were not covered by the Code and were thus not subject to the requirements of the Code, it was important that companies complied with such undertakings. Failing to implement an inter-company undertaking might indicate that previous inter-company dialogue had ultimately been unsuccessful.

The Panel noted that Ferring had informed Tillotts that it agreed to withdraw the material. The Panel considered, in the circumstances, it was not unreasonable for Tillotts to assume that the leavepiece had been withdrawn. This had not happened until some weeks later. The Panel might be sympathetic to the submission that Ferring was waiting for comment from Tillotts regarding another matter it had raised before changing the leavepiece if Ferring had made this clear to Tillotts. The Panel disagreed with Ferring's submission about the use of the claim 'generic budesonides lack this ... structure'. In the Panel's view, the claim was misleading as oral budesonide was not available as a generic in the UK. The term 'generic' had a particular meaning in relation to medicines. The Panel considered, therefore, that high standards had not been maintained and a breach of Clause 9.1 was ruled. The Panel considered that this ruling covered both the failure to withdraw the leavepiece and its continued use.

Complaint received **7 January 2019**

Case completed **19 March 2019**

COMPLAINANT v ENDO VENTURES

Promotion of Fluoxetine

A complainant who described him/herself as a concerned UK health professional, complained about an advertisement for fluoxetine issued by Endo Ventures. Fluoxetine's indications included the treatment of major depressive episodes in adults. The advertisement included a claim for fluoxetine 'for treatment of depressive illness'.

The complainant alleged that 'depressive illness' as referred to in the advertisement was broader than the licensed indications.

The detailed response from Endo Ventures is given below.

The Panel noted that fluoxetine was indicated for adults for major depressive episodes, obsessive-compulsive disorder or bulimia nervosa and for children and adolescents aged 8 years and above for moderate to severe major depressive episodes. The Panel noted that these indications were given in the prescribing information in the advertisement as were details about the age range for use of the medicine. The first mention of an indication was in the advertisement where the claim 'for treatment of depressive illness' appeared below the product name. The Panel considered that the claim was not an accurate reflection of any of the fluoxetine indications and was therefore inconsistent with the SPC. The Panel ruled a breach of the Code as acknowledged by Endo Ventures.

The Panel considered that high standards had not been maintained and ruled a further breach.

A complainant who described him/herself as a concerned UK health professional, complained about an advertisement for fluoxetine (ref FLUO 0010/2018) which was placed in Pulse by Endo Ventures Ltd. Fluoxetine's indications included the treatment of major depressive episodes in adults. The advertisement included a claim for fluoxetine 'for treatment of depressive illness'.

COMPLAINT

The complainant alleged that 'depressive illness' as referred to in the advertisement was broader than the licensed indications which were:

'Adults:
Major depressive episodes
Obsessive-compulsive disorder
Bulimia nervosa: Fluoxetine is indicated as a complement to psychotherapy for the reduction of binge-eating and purging activity.'

Children and Adolescents aged 8 years and above: Moderate to severe major depressive episode, if depression is unresponsive to psychological therapy after 4-6 sessions. Antidepressant medication should be offered to a child or young person with moderate to severe depression only in combination with a concurrent psychological therapy.'

The complainant alleged that the advertisement appeared to promote fluoxetine off-licence both in terms of the age of the individual as well as the severity of the depression.

When writing to Endo Ventures, the Authority asked it to consider the requirements of Clauses 3.2 and 9.1 of the 2016 Code.

RESPONSE

Endo Ventures explained that to ensure compliance with the Code and MHRA Blue Guide, it had engaged the services of a third party to advise it with regard to promotional activities and, in particular, to provide medical approval for promotional materials including advertisements. A copy of the approval certificate, signed by the third party, was provided.

On receipt of the complaint, the third party signatory reviewed the advertisement and acknowledged that the claim 'for treatment of depressive illness', in isolation, could be considered as too broad a representation of the indication. However, the full licensed indications, as listed in the summary of product characteristics (SPC), were included as an integral part of the advertisement in the prescribing information on the same page.

Regarding the advertisement as a whole, it was clear that there was no intent to promote off-label. However, in consideration of this feedback, Endo Ventures had immediately withdrawn all future advertisements using the claim at issue and undertook that future advertisements would contain a modified statement of the indication, for example, 'for the treatment of major depressive episodes in adults'.

In response to the complainant's comment that the advertisement appeared to promote the product off-label both in terms of the age of the individuals and the severity of depression, Endo Ventures repeated that it had no intention to promote off-label, and the text extracted by the complainant from the prescribing information was a true representation of the indications in the SPC. A side-by-side comparison of the text in the SPC and prescribing information was as follows:

SPC	Prescribing Information
<p>4.1 Therapeutic indications Adults:</p> <p>Major depressive episodes.</p> <p>Obsessive-compulsive disorder.</p> <p>Bulimia nervosa: Fluoxetine is indicated as a complement of psychotherapy for the reduction of binge-eating and purging activity.</p> <p>Children and Adolescents Aged 8 Years and Above:</p> <p>Moderate to severe major depressive episode, if depression is unresponsive to psychological therapy after 4-6 sessions. Antidepressant medication should be offered to a child or young person with moderate to severe depression only in combination with a concurrent psychological therapy.</p>	<p>Indication: Adults:</p> <p>Major depressive episodes,</p> <p>Obsessive-compulsive disorder (OCD),</p> <p>Bulimia nervosa as a complement of psychotherapy for the reduction of binge-eating and purging activity.</p> <p>Children and Adolescents Aged 8 Years and Above:</p> <p>Moderate to severe major depressive episode, if depression is unresponsive to psychological therapy after 4-6 sessions (in combination with a concurrent psychological therapy).</p>

The company submitted that the clinical meaning of the text in the prescribing information was identical to the SPC.

In conclusion, Endo Ventures stated that it had followed due process in clearing the advertisement through its internal review process via an established external regulatory consultancy, which approved the advertisement at issue. Endo Ventures' intention had always been to operate in compliance with the Code. Following receipt of the complaint and having reviewed the objection with regards to the claim 'for treatment of depressive illness', Endo Ventures agreed to amend this to 'for the treatment of major depressive episodes in adults' in all future versions of this advertisement.

PANEL RULING

The Panel noted that fluoxetine was indicated for adults for major depressive episodes, obsessive-compulsive disorder or bulimia nervosa and for children and adolescents aged 8 years and above for moderate to severe major depressive episodes. The Panel noted that these indications were given in the prescribing information in the advertisement as were details about the age range for use of the medicine. The first mention of an indication was in the advertisement where the claim 'for treatment of depressive illness' appeared below the product name. The Panel considered that the claim was not an accurate reflection of any of the fluoxetine indications and was therefore inconsistent with the SPC. The Panel ruled a breach of Clause 3.2 as acknowledged by Endo Ventures.

The Panel considered that high standards had not been maintained and ruled a breach of Clause 9.1.

Complaint received **9 January 2019**

Case completed **30 April 2019**

CODE OF PRACTICE REVIEW – May 2019

Cases in which a breach of the Code was ruled are indexed in **bold type**.

AUTH/3010/1/18	Bristol-Myers Squibb and Pfizer v Daiichi-Sankyo	Promotion of Lixiana	Breach Clause 2 Two breaches Clauses 7.2, 7.10 and 9.1	Appeal by respondent Required by Appeal Board to issue a corrective statement. Recovery of item required by Appeal Board	Page 4
AUTH/3014/1/18	Anonymous, non-contactable health professional v GW Pharmaceuticals	Promotion of Epidiolex	Breach Clauses 2, 3.1 and 9.1	No appeal	Page 28
AUTH/3024/3/18	Anonymous, hospital consultant non-contactable v GW Pharmaceuticals	Promotion of Epidiolex	No breach	No appeal	Page 33
AUTH/3026/3/18	Anonymous non-contactable v Sanofi	Promotion of Toujeo and Lantus	Breach Clauses 9.1 and 15.9	No appeal	Page 40
AUTH/3028/3/18	Ex-employee v AbbVie	Promotion of a poster and use of case studies	Breach Clauses 9.1, 9.10 and 14.1	Appeal by complainant	Page 45
AUTH/3029/4/18	Complainant v GW Pharmaceuticals	Arrangements for a meeting, alleged promotion of Epidiolex and unapproved slides	No breach	No appeal	Page 58
AUTH/3034/4/18	General practitioner v AstraZeneca	Patient engagement webpages	Breach Clauses 4.1 and 4.5	No appeal	Page 66
AUTH/3035/4/18	Anonymous health professional v Bayer	Promotion of Xarelto	Breach Clauses 2, 7.2, 7.4 and 9.1	No appeal	Page 70
AUTH/3038/4/18	Health professional v Novartis	Conduct of an employee on LinkedIn	Breach Clause 9.1 Two Breaches Clause 14.1, 26.1 and 26.2	No appeal	Page 74
AUTH/3048/6/18	Bial Pharma v Profile Pharma	Promotion of Xadago	Breach Clauses 7.2 and 7.3	No appeal	Page 82
AUTH/3050/6/18	Anonymous, non-contactable v Abbvie	Promotion of Synagis	No breach	No appeal	Page 87

AUTH/3051/6/18	Anonymous, contactable v Alexion	Promotional material advertised on LinkedIn	Two breaches Clause 9.1	No appeal	Page 90
AUTH/3054/7/18	Anonymous, non-contactable v PharmaMar	Meeting in Madrid	Breach Clauses 9.1 and 22.2	No appeal	Page 96
AUTH/3056/8/18	Ex-employee v GlaxoSmithKline	Activities of GlaxoSmithKline	Two breaches Clause 3.2, 7.2 and 9.1	No appeal	Page 100
AUTH/3057/8/18	Clinical Commissioning Group v Novo Nordisk	Conduct of a representative	No breach	No appeal	Page 115
AUTH/3058/8/18 and AUTH/3060/8/18	Pharmacists v Proveca	Letter regarding the supply of unlicensed and off-label glycopyrronium	Breaches Clauses 2, 8.2, 9.1 and 9.5 (AUTH/3058/8/18) Breaches Clauses 2 and 9.1 (AUTH/3060/8/18)	No appeal by respondent	Page 119
AUTH/3059/8/18	Anonymous non-contactable v Lundbeck	Company webpage and certification of promotional material	Three breaches Clause 14.1 Breaches Clauses 14.4, 26.1, 26.2 and 28.3	No appeal	Page 140
AUTH/3061/8/18	Health professional v Ferring	Conduct of a representative	No breach	No appeal	Page 145
AUTH/3062/8/18	Health professional v Sanofi	Toujeo leaflet	Breach Clauses 7.2 and 7.3	No appeal	Page 150
AUTH/3063/9/18	Voluntary admission by Dr Falk	Promotion to the public via YouTube	Breaches Clauses 9.1, 14.1, 26.1 and 26.2	No appeal	Page 155
AUTH/3066/9/18	Head of Medicines Optimisation v GlaxoSmithKline	List price reduction claims	Breaches Clauses 7.1, 7.2, 7.4, 7.5 and 9.1	No appeal	Page 158
AUTH/3103/10/18	Anonymous non-contactable v Ipsen	Promotion of Cabozmetyx	Breach Clause 3.2	No appeal	Page 163
AUTH/3104/10/18	Anonymous, non-contactable health professional v Merck Serono	Terms of trade	No breach	No appeal	Page 171
AUTH/3105/10/18	Pharmacy Team Leader v Eli Lilly	Compassionate supply of Olumiant	No Breach	No appeal	Page 173
AUTH/3106/10/18	Voluntary Admission by Janssen	Use of out-of-date Prescribing information	Two breaches Clause 4.1	No appeal	Page 177

AUTH/3107/10/18	Complainant v Daiichi-Sankyo	Promotion to the public	Breaches Clauses 9.1, 26.1 and 28.1	No appeal	Page 181
AUTH/3108/10/18	Complainant v Mitsubishi Tanabe	Promotion to the public	Breaches Clauses 9.1, 26.1 and 28.1	No appeal	Page 184
AUTH/3110/10/18	Anonymous v Napp	Colour of inverted triangle symbol	Breach Clause 9.1	No appeal	Page 191
AUTH/3111/10/18	Complainant v Pfizer	Legibility of prescribing information	No Breach	No appeal	Page 193
AUTH/3113/11/18	Ex-employee v Novartis	Medical Representative Examination	No breach	No appeal	Page 196
AUTH/3115/11/18	Anonymous, non-contactable Health professional v Novo Nordisk	Advisory boards	Breach Clause 9.1	No appeal	Page 198
AUTH/3121/11/18	Health professional v Biogen	Imraldi mailing	No Breach	No appeal	Page 203
AUTH/3126/11/18	Complainant v Alliance	Promotion of Xonvea on LinkedIn	Two breaches Clause 9.1 Breaches Clauses 26.1 and 26.2	No appeal	Page 206
AUTH/3127/12/18	Voluntary admission by Merck Sharp & Dohme	Failure to provide prescribing information and certify an advertisement	Breaches Clauses 4.1 and 14.1	No appeal	Page 211
AUTH/3131/12/18	Anonymous, non-contactable v Napp	Use of social media to advertise meetings	No breach	Appeal by respondent	Page 213
AUTH/3132/12/18	Anonymous, non-contactable v Sanofi	Use of social media to advertise meetings	No breach	No appeal	Page 220
AUTH/3134/12/18	Complainant v Shield	Information about Feraccru	Breaches Clauses 3.2, 7.2 and 9.1	Appeal by respondent	Page 222
AUTH/3135/12/18	Complainant v Astellas	Promotion of Betmiga	Breaches Clauses 7.2, 7.4 and 7.10	No appeal	Page 227
AUTH/3142/1/19	Complainant v Sanofi	Online advertisement	No Breach	No appeal	Page 231
AUTH/3143/1/19	Tillotts Pharma v Ferring	Failure to withdrawal material	Breach Clause 9.1	No appeal	Page 234
AUTH/3149/1/19	Anonymous v Endo Ventures	Promotion of Fluoxetine	Breaches Clauses 3.2 and 9.1	No appeal	Page 236

The Prescription Medicines Code of Practice Authority was established by the Association of the British Pharmaceutical Industry (ABPI) in 1993 to operate the Code of Practice for the Pharmaceutical Industry at arm's length from the ABPI itself. Compliance with the Code is obligatory for ABPI member companies and, in addition, over sixty non member companies have voluntarily agreed to comply with the Code and to accept the jurisdiction of the Authority.

The Code covers the advertising of medicines to health professionals and other relevant decision makers and also covers information about prescription only medicines made available to the public.

It covers:

- journal and direct mail advertising
- the activities of representatives, including any printed or electronic material used by them
- the supply of samples
- the provision of inducements in connection with the promotion of medicines and inducements to prescribe, supply, administer, recommend, buy or sell medicines by the gift, offer or promise of any benefit or bonus, whether in money or in kind
- the provision of hospitality
- the organisation of promotional meetings
- the sponsorship of scientific and other meetings, including payment of travelling and accommodation expenses
- the sponsorship of attendance at meetings organised by third parties
- all other sales promotion in whatever form, such as participation in exhibitions, the use of audio or video-recordings in any format, broadcast media, non-print media, the Internet, interactive data systems, social media and the like.

It also covers:

- the provision of information on prescription only medicines to the public either directly or indirectly, including by means of the Internet
- relationships with patient organisations
- disclosure of transfers of value to health professionals and organisations
- joint working between the NHS and pharmaceutical companies

- the use of consultants
- non-interventional studies of marketed medicines
- the provision of items for patients
- the provision of medical and educational goods and services
- grants, donations and benefits in kind to institutions.

Complaints submitted under the Code are considered by the Code of Practice Panel which consists of three of the four members of the Code of Practice Authority acting with the assistance of independent expert advisers where appropriate. One member of the Panel acts as case preparation manager for a particular case and that member does not participate and is not present when the Panel considers it.

Both complainants and respondents may appeal to the Code of Practice Appeal Board against rulings made by the Panel. The Code of Practice Appeal Board is chaired by an independent legally qualified Chairman, Mr William Harbage QC, and includes independent members from outside the industry. Independent members, including the Chairman, must be in a majority when matters are considered by the Appeal Board.

In each case where a breach of the Code is ruled, the company concerned must give an undertaking that the practice in question has ceased forthwith and that all possible steps have been taken to avoid a similar breach in the future. An undertaking must be accompanied by details of the action taken to implement the ruling. Additional sanctions are imposed in serious cases.

Further information about the Authority and the Code can be found at www.pmcpa.org.uk

Complaints under the Code should be sent to the Director of the Prescription Medicines Code of Practice Authority, 7th Floor, Southside, 105 Victoria St, London SW1E 6QT

telephone 020 7747 8880
facsimile 020 7747 8881
by email to: complaints@pmcpa.org.uk.