CASE AUTH/3012/1/18

VOLUNTARY ADMISSION BY PIERRE FABRE

Failure to certify material

Pursuant to Case AUTH/2962/7/17, Pierre Fabre voluntarily admitted that it had identified certain breaches of the Code in material related to Toviaz (fesoterodine), a treatment for the symptoms of overactive bladder syndrome. The material at issue included that used at a cycle meeting in April 2017, a Toviaz slide set and an email, with attachments, sent to the representatives after the cycle meeting.

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 Pierre Fabre.

Pierre Fabre noted that a slide deck, 'Marketing Focus: Strategy for UK & ROI' presented at the cycle meeting and subsequently emailed to the representatives bore no code number or date of preparation and there was no disclaimer regarding its use or distribution. Pierre Fabre submitted that the slides had not been certified before use and that the information on one slide was unbalanced and misleading and not always capable of substantiation.

With regard to the framework for the cycle meeting, agenda and objectives, Pierre Fabre again noted the absence of a code number, date of preparation and certification.

Pierre Fabre submitted that the Toviaz 'Meetings in a box' slides used at the cycle meeting had also not been certified and nor had an email sent to the sales force after the cycle meeting.

Pierre Fabre noted that one of the documents sent with the email was a corporate presentation for use with health professionals. The presentation charted the company's history and a slide which detailed strategic partnerships in 2015 (some of which existed, *inter alia*, to further the development of new medicines) referred to possible therapeutic targets and a licensing opportunity. Pierre Fabre submitted that such information might encourage an audience to enquire about medicines in development/ commercial opportunities. Further the sales force briefing material for the presentation referred to the healthy product pipeline which might encourage representatives to pay particular attention to the slide. Pierre Fabre also submitted that another slide of the corporate presentation referred the audience to the company's global website for further information. Pierre Fabre stated that the website was thus not addressed to a UK audience. Pierre Fabre stated that the briefing material was not certified.

Pierre Fabre submitted that the breaches above collectively demonstrated a failure to understand, to apply and to comply with certification of materials used to brief representatives, and other breaches. Pierre Fabre stated that the breaches above reflected the errors and confusion of accountability for responsibility for compliance with the Code that occurred during a period of dysfunctional management.

Pierre Fabre submitted however, that there had been no breach of Clause 2 as there were no risks for patient safety and the breaches had not brought discredit upon, or reduced confidence in, the industry.

Pierre Fabre apologised unreservedly for the breaches above. The company was fully committed to maintaining high standards and to taking all steps to both remedy the failings identified. Pierre Fabre UK and Europe had learned from these failings and were taking all available steps to prevent recurrence.

The details response from Pierre Fabre is given below.

The Panel noted that the marketing focus slide deck used at the cycle meeting did not include a date of preparation or guidance as to how it was to be used by representatives. The email dated 2 May 2017 did not give any instructions about the use of this presentation which the Panel considered was briefing material for representatives as required by the Code. The Panel noted the failure to certify the presentation and ruled a breach of the Code.

With regard to the date of preparation the Panel noted that the Code referred to promotional material. It was not clear whether the marketing focus presentation was to be shown to health professionals. In the Panel's view, as the presentation was briefing material it would have been helpful to include a date of preparation but as there was no requirement for it do so. The Panel did not consider Clause 4.8 applied so no breach of that clause was ruled.

One slide was headed 'Decision Tree' with three sub headings including'Mirabegron is better tolerated than any anticholinergic' beneath which was the claim 'European Warning – CV risk'. Pierre Fabre stated that the material failed to balance this with the statement in the Toviaz summary of product characteristics (SPC) that it should be used with caution in patients with risk of QT prolongation. The Panel thus considered that the briefing material was misleading and not capable of substantiation as required; breaches of the Code were ruled. The briefing material advocated a course of action which would be likely to lead to a breach of the Code if the representatives used this statement.

With regard to the framework for the cycle meeting, agenda and objectives, the Panel considered that this constituted briefing material as it referred to the quantity and quality of calls by representatives on health professionals. The failure to certify such material meant that it did not comply with the relevant requirement of the Code. A breach of the Code was ruled.

With regard to the date of preparation the Panel noted its comments above regarding briefing material and again ruled no breach of the Code.

With regard to the Toviaz 'meetings in a box' slides, the Panel noted that they were not certified at the time of the April cycle meeting. They were certified on 5 May. The first slide of the presentation in April was marked 'Draft'. The Panel considered that the slides should have been certified prior to being presented at the cycle meeting. Their use at the cycle meeting would constitute briefing material for the representatives and, as previously, the failure to certify briefing material was ruled in breach of the Code.

With regard to the email sent after the cycle meeting, which provided certain documents to the representatives, the Panel noted that it was not certified and considered that it should have been as it constituted briefing material. A breach of the Code was ruled.

The company profile presentation was to be used with health professionals. It gave an overview of the company's history. One slide referred to partnerships which were to 'Develop and commercialize two novel molecules in oncology'. The briefing material instructed representatives to use the slides at meetings prior to the presentation of main product slides with the key messages that the company had patient interest at its core and it was steadily growing with a healthy product pipeline. It was for promotional use.

The Panel was concerned that the presentation included focus on strategic partnerships which referred to developing and commercialising two novel molecules in oncology.

The Panel considered that the presentation went beyond general comments about Pierre Fabre's interests in oncology. The slide would elicit questions about the pipeline. The briefing material for representatives gave no instructions about the response to such questions nor did it give much information about how the slides were to be used. The Panel considered that slide at issue promoted unlicensed medicines and a breach of the Code was ruled. This presentation had been certified.

The Panel noted that the briefing material for the presentation had not been certified as required by the Code. The briefing material and the company profile presentation advocated a course of action that would lead to a breach of the Code and thus the Panel ruled a breach of the Code.

The Panel noted Pierre Fabre's submission that another slide from the company profile presentation referred the audience to the global website (www.pierre-fabre.com) which was not addressed to a UK audience. Pierre Fabre cited one clause in this regard but provided no further details or the website content. The voluntary admission implied that the website had not been certified and thus the Panel ruled a breach of the Code.

The Panel noted its comments and rulings above and considered that Pierre Fabre had failed to maintain high standards. A breach of the Code was ruled.

The Panel noted its ruling above of a breach of the Code with regard to the promotion of unlicensed medicines, an activity likely to be in breach of Clause 2. The Panel noted that a robust certification procedure underpinned self-regulation. The Panel considered that in advertising a medicine prior to the grant of a marketing authorization and failing to certify material meant that Pierre Fabre had brought discredit upon or reduced confidence in the pharmaceutical industry and a breach of the Code was ruled.

Pursuant to Case AUTH/2962/7/17, Pierre Fabre Limited voluntarily admitted that it had identified certain breaches of the Code in material related to Toviaz (fesoterodine). Toviaz was indicated for the treatment of symptoms of overactive bladder syndrome. The marketing authorization holder was Pfizer Limited.

In September 2017 Pierre Fabre suspended all promotion of Toviaz in the UK pending the completion of steps being implemented by it in close consultation with Pfizer. The material at issue included that used at a cycle meeting in April 2017, a Toviaz slide set and an email, with attachments, sent to the representatives after the cycle meeting.

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 Pierre Fabre.

VOLUNTARY ADMISSION

Pierre Fabre noted that a slide deck, 'Marketing Focus: Strategy for UK & ROI' presented at the cycle meeting and subsequently emailed to the representatives bore no code number or date of preparation and there was no disclaimer regarding its use or distribution. Pierre Fabre submitted that the slides had not been certified before use in breach of Clause 14.1. The company also submitted that the information on slide 9 was unbalanced and misleading and not always capable of substantiation. Pierre Fabre admitted breaches of Clauses 7.2 and 7.4.

With regard to the framework for the cycle meeting, agenda and objectives, Pierre Fabre again noted the absence of a code number and date of preparation; the material had not been certified in breach of Clause 14.1.

Pierre Fabre provided two copies of Toviaz 'Meetings in a box' slides. The first copy was that used at the cycle meeting and the second copy was the one certified in May 2017, after the April meeting. As

the slides used at the April meeting had not been certified, Pierre Fabre admitted a breach of Clause 14.1.

Subsequent to the April cycle meeting, Pierre Fabre emailed the sales force and attached a number of documents. Pierre Fabre submitted that the email had not been certified, in breach of Clause 14.1.

Pierre Fabre noted that one of the documents sent with the email above was a corporate presentation for use with health professionals. The presentation charted the company's history and one slide detailed strategic partnerships in 2015; some of those partnerships existed, inter alia, to further the development of new medicines. The slide referred to possible therapeutic targets and a licensing opportunity. Pierre Fabre submitted that such information might encourage an audience to enquire about medicines in development/commercial opportunities. Pierre Fabre admitted breaches of Clauses 3.1 and 15.9.

Pierre Fabre stated that the sales force briefing material for the corporate presentation included key messages, one of which referred to the healthy product pipeline which might encourage representatives to pay particular attention to the slide discussed above. Further, Pierre Fabre also submitted that another slide in the presentation referred the audience to the company's global website for further information. Pierre Fabre stated that the website was thus not addressed to a UK audience. Pierre Fabre acknowledge a breach of Clause 14.1 in that the briefing material was not certified before use.

Pierre Fabre submitted that the breaches above collectively constituted a breach of Clause 9.1 as they demonstrated a failure to understand, to apply and to comply with certification of materials used to brief representatives, and other breaches. The breaches above also reflected the errors and confusion of accountability for responsibility for compliance with the Code that occurred during a period of dysfunctional management. Pierre Fabre submitted, however, that there had been no breach of Clause 2 as there were no risks for patient safety and the breaches had not brought discredit upon, or reduced confidence in, the industry.

Pierre Fabre stated that it was sharing the learnings of Case AUTH/2962/7/17 with all its UK and European staff and senior management would remind all staff to fulfil their obligations under the Code. Compliance with the spirit and letter of the Code and Pierre Fabre's code of ethics were fundamental to activities in the UK.

Pierre Fabre apologised unreservedly for the breaches above. The company was fully committed to maintaining high standards and to taking all steps to both remedy and prevent further recurrence of the failings identified. Its policies and procedures were under review and it had recently trained and tested employees on the Code and had learned from the failings detailed above and were taking all available steps to prevent recurrence. Pierre Fabre would continue to implement its remedial plan and to voluntarily admit any further breaches of the Code that were identified as promptly as practicable. These steps included withdrawal of all materials in breach of the Code, including those referred to above.

In considering this matter, Pierre Fabre was asked in addition to the clauses it had cited in its admission to respond in relation to the requirements of Clause 4.8 in relation to all points where a failure to include a date of preparation was included and to Clause 15.9 in relation to the sales force briefing for the company profile presentation. The company was also asked to respond to Clause 2 in relation to the collective admissions.

RESPONSE

April 2017 cycle meeting

Pierre Fabre stated that the April 2017 cycle meeting was scheduled by the then national sales director and was attended by all representatives. On 7 April 2017, separate meetings were held for each of the two UK regions.

Briefings at these meetings were provided verbally and in slide format. This followed detailed written training materials provided to sales representatives in November 2016 on the Code.

The materials presented at the April 2017 cycle meeting were created to inform representatives about the progress of promotion of Toviaz and to provide verbal briefings, supported by slide presentations.

The national sales manager and regional sales managers had provided draft content for these materials. Due to the absence on sick leave of the two individuals with significant experience of the Code, the slides were not finalised in time for review and certification by Pfizer, or for prior certification on Zinc by Pierre Fabre. The slides were presented on 6 April 2017 with limited support on both content and on the requirements of the Code. The medical director was not present at this meeting, and it was explained that the presentations were in draft form, with the understanding that the presentations would follow by email.

Materials were circulated on 2 May 2017 by email, after review and certification of some materials via the Zinc platform. The list of recipients of these materials was the same as stated on the email of 2 May 2017.

Promotion of Toviaz was suspended in September 2017 and had not recommenced. As part of an ongoing process by new Pierre Fabre Management to review and where relevant withdraw all materials and meetings conducted under previous management in 2017, all the materials at issue described in the voluntary admission were withdrawn on 21 December 2017. This process started in November 2017.

Agreement between Pfizer and Pierre Fabre in relation to the certification of materials

Pierre Fabre was responsible for the marketing and promotion of Toviaz in the UK, with Pfizer remaining the marketing authorization holder. Pfizer and Pierre Fabre must certify all Toviaz material in line with Clause 14 of the Code.

The presentations and email referred to in the voluntary admission were however not shared with Pfizer for review and certification. This breach of both the agreement with Pfizer and of the Code occurred due to a combination of time pressure and of the culture of previous management of Pierre Fabre.

Breaches of the Code

Pierre Fabre stated it had now identified breaches of Clauses 3.1, 4.8, 7.2, 7.4, 14.1, 15.9 and 9.1 of the Code. It submitted that these collective breaches did not constitute a breach of Clause 2 of the Code.

The company apologised unreservedly for these breaches and had implemented changes and significant remedial steps to prevent their recurrence.

With regard to slide 9 of the presentation, Pierre Fabre submitted that the statement 'European warning – CV risk' for mirabegron [Betmiga, marketed by Astellas] was not balanced, and so in breach of Clause 7.2 because Section 4.4 of the Toviaz summary of product characteristic (SPC) included the statement that 'Toviaz should be used with caution in patients with risk for QT prolongation'.

The slide should have been reviewed in accordance with local codes and procedures. In this instance, the slide was not reviewed in accordance with the Code.

Pierre Fabre stated that one slide of the Company Profile Presentation breached Clause 15.9. The company initially considered that Clause 15.9 was more relevant to the presentation. On reflection, it was acknowledged that the briefing document referred to all of the slides in the presentation, including the one at issue, and also referred to a 'healthy product pipeline' as a key message, and therefore also breached Clause 15.9 of the Code.

Pierre Fabre acknowledged that the slide deck presented at the April 2017 meeting and the agenda and objectives for that cycle meeting should have included a date of preparation. The company apologised for not noting these as separate breaches of Clause 4.8 above.

On reflection, however, Pierre Fabre submitted that the further breaches of the Code identified (Clause 15.9 and 4.8) fell under the scope of the admitted breach of Clause 9.1 of the Code, as they provided further examples of failure to maintain high standards.

Pierre Fabre Limited apologised for the breaches and submitted that it had learned from the errors and breaches and had taken a number of steps to remedy them and to prevent recurrence.

Pierre Fabre submitted that the breaches did not overall constitute a breach of Clause 2 of the Code. No risk for patient safety occurred as a result of the breaches, and that these individual and collective breaches had not brought discredit upon or reduced confidence in the industry.

PANEL RULING

Slide deck 'Marketing Focus: Strategy for UK and ROI'

The Panel noted that the slide deck 'Marketing Focus: Strategy for UK & ROI' did not include a date of preparation or guidance as to how it was to be used by representatives.

The email dated 2 May 2017 did not give any instructions about the use of this presentation which had been discussed at the cycle meeting.

The Panel noted that the presentation was briefing material for representatives as required by Clause 15.9 of the Code. The supplementary information to Clause 14.1 required that briefing material be certified. The Panel noted that failure to certify the presentation was in breach of Clause 14.1 and a breach of that Clause was ruled.

With regard to the date of preparation the Panel noted that Clause 4.8 referred to promotional material. It was not clear whether the marketing focus presentation was to be shown to health professionals. In the Panel's view as the presentation was briefing material it would have been helpful to include a date of preparation. However, there was no requirement for briefing material to include a date of preparation. In the circumstances the Panel did not consider Clause 4.8 applied so no breach of Clause 4.8 was ruled.

The slide headed 'Decision Tree' had three sub headings which included 'Mirabegron is better tolerated than any anticholinergic' beneath which was the claim 'European warning – CV risk'. Pierre Fabre stated that the material failed to balance this with the statement in the Toviaz SPC that it should be used with caution in patients with risk of QT prolongation.

The Panel considered that by failing to balance the statement the briefing material was misleading and not capable of substantiation as required by Clauses 7.2 and 7.4 and breaches of those Clauses were ruled. The briefing material advocated a course of action which would be likely to lead to a breach of the Code if the representatives used this statement.

Framework April Cycle Meeting

With regard to the framework for the cycle meeting, agenda and objectives, the Panel considered that this constituted briefing material as it referred to

the quantity and quality of calls by representatives on health professionals. The failure to certify such meant that it did not comply with the relevant requirement of Clause 14. A breach of Clause 14.1 was ruled as acknowledged by Pierre Fabre.

With regard to the date of preparation the Panel noted that Clause 4.8 referred to promotional material. In the Panel's view, as the material was, in effect briefing material, it would have been helpful to include a date of preparation but as there was no requirement for it to do so the Panel did not consider that Clause 4.8 applied so no breach of that clause was ruled.

Toviaz Meeting in a Box Slide Set

With regard to the Toviaz 'meetings in a box' slides, the Panel noted that they were not certified at the time of the April cycle meeting. They were certified on 5 May. The first slide of the presentation in April was marked 'Draft'.

The Panel considered that the slides should have been certified prior to being presented at the cycle meeting. Their use at the cycle meeting would constitute briefing material for the representatives and, as previously, the failure to certify briefing material was ruled in breach of Clause 14.1.

The Panel noted that the slides when presented to health professionals would then be promotional material rather than briefing material.

Email

With regard to the email dated 2 May 2017 which provided certain documents to the representatives, the Panel noted that it was not certified and considered that it should have been as it constituted briefing material. A breach of Clause 14.1 was ruled. The email could have given clearer guidance about the use of the various materials.

Two of the documents sent with the email in question (Toviaz Marketing Focus: strategy for UK and ROI, the company profile presentation and its briefing material) were the subject of the voluntary admission.

Company profile presentation and representatives briefing material

The company profile presentation was to be used with health professionals. It gave an overview of the company's history. One slide referred to partnerships which were to 'Develop and commercialize two novel molecules in oncology'. The briefing material instructed representatives to use the slides at meetings prior to the presentation of main product slides with the key messages that the company had patient interest at its core and it was steadily growing with a healthy product pipeline. It was for promotional use.

The Panel was concerned that the presentation included focus on strategic partnerships which referred to developing and commercialising two novel molecules in oncology.

The Panel considered that the presentation went beyond general comments about Pierre Fabre's interests in oncology. The slide about partnerships would elicit questions about the pipeline. The briefing material for representatives gave no instructions about the response to such questions nor did it give much information about how the slides were to be used.

The Panel considered that the slide at issue promoted unlicensed medicines and a breach of Clause 3.1 was ruled. This presentation had been certified.

The Panel noted that the briefing material for the presentation had not been certified as required by Clause 14.1. The briefing material and the company profile presentation advocated a course of action that would lead to a breach of the Code and thus the Panel ruled a breach of Clause 15.9 of the Code.

The Panel noted Pierre Fabre's submission that another slide from the same presentation referred the audience to the global website (www.pierre-fabre.com) which was not addressed to a UK audience. Pierre Fabre raised Clause 14.1 in this regard but provided no further details or the website content. The voluntary admission implied that the website had not been certified and thus the Panel ruled a breach of Clause 14.1.

Overall

The Panel noted its comments and rulings above and considered that Pierre Fabre had failed to maintain high standards. A breach of Clause 9.1 was ruled.

The Panel noted its ruling of a breach of Clause 3.1 which was listed as an example of activities that were likely to be in breach of Clause 2. The Panel noted that a robust certification procedure underpinned self-regulation. The Panel considered that in advertising a medicine prior to the grant of a marketing authorization and failing to certify material meant that Pierre Fabre had brought discredit upon or reduced confidence in the pharmaceutical industry and a breach of Clause 2 was ruled.

Voluntary admission received **18 January 2018**

Case completed **21 March 2018**