CASE AUTH/2444/10/11

GENERAL PRACTITIONER v BOEHRINGER INGELHEIM

Pradaxa website

A general practitioner complained about a Pradaxa (dabigatran) website created by Boehringer Ingelheim.

The complainant questioned whether access to the medical content for health professionals was sufficiently rigorous to restrict access only to health professionals. The complainant alleged that the arrangements were such that Boehringer Ingelheim clearly intended to facilitate the promotion of Pradaxa to the public.

The detailed response from Boehringer Ingelheim is given below.

The Panel noted that supplementary information to the Code stated that unless access to promotional material about prescription only medicines was limited to health professionals and appropriate administrative staff, a pharmaceutical company 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 front page of the website in question had two clearly labelled sections; one 'For UK healthcare professionals' and the other 'For patients and public'. The section for health professionals stated that 'If you are a UK health professional and would like more information on Pradaxa ... please click here'. The next screen referred to educational packs and required a choice between the two indications. The health professional part of the site was clearly promotional. The banner at the top of each page stated, inter alia, 'For UK healthcare professionals only'.

The Panel noted that the patient and public section of the website contained a short product overview and access to the Pradaxa patient information leaflets (PILs) and summaries of product characteristics (SPCs) via a link to the electronic medicines compendium (eMC).

The Panel considered that the amount of information in the public and patient section was on the limits of acceptability in order to avoid that audience needing to access material intended for health professionals. The sections for health professionals and for patients/public were clearly separated and labelled such that the intended audience for each was clear. On balance the Panel did not consider that the open access nature of the material for health professionals meant that prescription only medicines were being advertised to the public as alleged and ruled no breach of the Code which was upheld on appeal from the complainant.

The complainant noted that the first reference to the indication of stroke prevention in atrial fibrillation did not specify that this only referred to 150/110mg doses of Pradaxa and did not include the 75mg dose. The hyperlinked content was similar. This omission was misleading and clinically relevant.

The Panel noted that the recommended dose of Pradaxa for the prevention of stroke and systemic embolism in certain patients was 150mg twice daily (110mg twice daily in patients aged 80 or over). These dose recommendations could be accessed by clicking on a 'Dose' tab. The Panel did not consider that the failure to refer to the 75mg dose in the section clearly marked 'Stroke prevention in atrial fibrillation' was misleading as alleged. No breach was ruled.

The complainant noted that the location of the prescribing information was only clarified after prominent claims for Pradaxa.

The Panel noted that the first page of the site, following confirmation that the reader was a UK health professional, referred to the licensed indications but did not indicate where the prescribing information could be found. The reader had to click on the relevant indication before reaching the page which contained a link to the prescribing information. In the Panel's view, the prescribing information should have appeared on the page that referred to the licensed indications for Pradaxa which followed confirmation of the reader as a health professional. This part of the site was promotional and thus a breach was ruled.

A general practitioner complained about the Pradaxa (dabigatran) website (Pradaxa.co.uk) created by Boehringer Ingelheim Limited.

Pradaxa was indicated for primary prevention of venous thromboembolic events in adults who had undergone elective total hip or total knee replacement surgery. It was also indicated for the prevention of stroke and systemic embolism in certain adult patients.

Boehringer Ingelheim was asked to consider Clauses 4.6, 7.2, 22.1, 22.2 and 24.1 of the Code.

1 Access to the website

COMPLAINT

The complainant questioned whether the access to the medical content for health professionals was sufficiently rigorous to restrict access only to health professionals and queried whether it should require General Medical Council (GMC) or other such

registration details, as was the case with many other pharmaceutical company websites. The complainant alleged that the arrangements were such that Boehringer Ingelheim clearly intended to facilitate the promotion of Pradaxa to the public.

RESPONSE

Boehringer Ingelheim submitted that the main purpose of the website was to provide health professionals with factual information, including access to prescribing information and the educational pack, about the use of Pradaxa in stroke prevention in atrial fibrillation (SPAF). The public part of the site also provided information for patients, including the patient information leaflet (PIL) and summary of product characteristics (SPC). The health professional and public sites could be accessed without any special permission (this was not a restricted site) but the health professional had to click once to confirm they were a health professional and then there was a pop-up which required them to reconfirm this.

The Pradaxa marketing access authorization and agreement with the Medicines and Healthcare products Regulatory Agency (MHRA) required Boehringer Ingelheim to make copies of the educational pack (ref DBG 2653) (consisting of the prescriber guide for stroke prevention in atrial fibrillation (ref DBG 2466), SPCs and Pradaxa patient alert card (ref DBG 2464)) available to all health professionals. The communication plan for the educational pack was agreed with the MHRA and included making downloadable versions available on the health professional side of the Pradaxa.co.uk website. Boehringer Ingelheim submitted that if access to the site was further restricted beyond the click to confirm health professional status that would defeat one of the most important purposes of the site – health professionals could be hindered in gaining instant access to the educational pack. Restricting access would also break the company's agreement with the MHRA.

There was information available for patients on the website and it was clear from the landing site which part of the website was for the public. The public was very clearly signposted to the appropriate part of the site. The main information on the public part of the site was the PIL and SPC. This information was provided so that patients had sufficient information easily available on the site to answer their questions and were therefore not tempted to enter the health professional part of the site (a requirement of Clause 24.1). Boehringer Ingelheim knew that medicines guides were sometimes also made available for patients on company websites. With a new anticoagulant such as Pradaxa the company considered that such a guide in a therapy area undergoing considerable change because of new medicines could easily be considered contentious, undermine the advice from the prescribing physician and PIL, and also risk being seen as disparaging to warfarin (or other new oral anticoagulants as they became available). There was however a brief clinical overview about anticoagulants in general. Possible side effects of anticoagulants were also explained with advice for what to be aware of in terms of bleeding and bruising and patients were advised to report any side effects. There was also information on the yellow card reporting scheme, Boehringer Drug Safety, advice to discuss side effects with the GP and possible support available from NHS Direct and their local pharmacist.

On the home page there was a clear button, 'For UK healthcare professionals', and another, 'For patients and the public'. When a health professional tried to enter the relevant section of the site a further pop up button asked for confirmation they were a UK health professional. There was no requirement for a GMC number on the 'For UK healthcare professionals' button because Boehringer Ingelheim intended the site to be easily accessible to health professionals other than doctors, especially pharmacists and nurses, who needed copies of the educational pack, prescribing information and SPC. There was no robust list of pharmacists and nurses available, comparable to the GMC list, to use to limit access to the site in a formal way.

The supplementary information to Clause 24.1 explained that when access to a website was not restricted there must be adequate information available for members of the public to avoid them choosing to access materials for health professionals. Boehringer Ingelheim stated that this meant that there did not automatically need to be restricted access.

There did not appear to be any universal standard in the UK relating to access to websites by health professionals. Some companies required a health professional to register or enter his/her GMC number to access a site but others did not.

Boehringer Ingelheim considered that when introducing a new anticoagulant it had a responsibility to provide health professionals with information about it so that they understood the medicine properly and were able to use it safely and appropriately in the right patient groups, with the right follow-up care, and were aware of adverse events and risks of treatment. With a great deal of unregulated information available on the Internet it was especially important that material was well referenced, balanced and non-promotional. This was Boehringer Ingelheim's intention with the website.

Boehringer Ingelheim submitted that the website was balanced and informative and complied with the Code, particularly Clause 7.2. The SPC should be the main source of information for any prescriber but the registration study (RE-LY) was also of interest and a link to a summary of the study was included in the clinical evidence section of the website. Providing a completely inclusive short summary of a major study was challenging and so at the end of the document three clearly visible hyperlinks provided access to the original publication in the New England Journal of Medicine, the article in the same journal about newly identified clinical events, and the supplementary

appendix which was just a few pages long but provided a useful summary of all of the main outcome measures in the intent to treat population. Boehringer Ingelheim hoped that by providing all of this data as easily accessible original publications it could be seen that it its intention had been to inform, not mislead.

Boehringer Ingelheim hoped that it had demonstrated that it was aware of the requirements of Code, particularly Clauses 7.2, 22.1, 22.2, and 24.1, and had complied with these requirements.

PANEL RULING

The Panel noted that the supplementary information to Clause 24.1 stated that unless access to promotional material about prescription only medicines was limited to health professionals and appropriate administrative staff, 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 front page of the website in question had two clearly labelled sections; one entitled 'For UK healthcare professionals' and the other entitled 'For patients and public'. The section for health professionals stated that 'If you are a UK health professional and would like more information on Pradaxa…. please click here'. The next screen referred to the educational packs and required readers to choose between the stroke indication or the indication relating to hip/knee replacement surgery. The health professional part of the site was clearly promotional and included the educational pack, information on the mode of action, dosage and administration of the medicine. The banner at the top of each page stated 'For UK healthcare professionals only' and gave brief details of the stroke indication.

The Panel noted that the patient and public section of the website contained a short product overview for each indication and access to the PILs and SPCs for the product, via a link to the electronic medicines compendium (eMC).

The Panel considered that the information provided in the patient and public section of the website was limited, but nevertheless it was provided. The Panel queried whether the information in the public and patient section was sufficient to avoid the intended audience needing to access material intended for health professionals. The Panel considered that it was on the limits of acceptability in this regard. The sections for health professionals and for patients/public were clearly separated and labelled such that the intended audience for each section was clear, as set out in the supplementary information to Clause 24.1. On balance the Panel did not consider that the open access nature of the material for health professionals meant that prescription only medicines were being advertised to the public as alleged and ruled no breach of Clause 22.1. The Panel noted that there was no complaint about the content of the site merely the arrangements for accessing material intended for health professionals thus the Panel ruled no breach of Clause 22.2.

The Panel noted its rulings of no breach of the Code in relation to the arrangements for accessing the site and thus ruled no breach of Clause 24.1 in this regard.

APPEAL BY THE COMPLAINANT

The complainant appreciated the Panel's perspective with regard to its rulings of no breach of Clauses 22.1 and 22.2, but considered that these rulings should be referred to the Appeal Board. The complainant stated that it was evident that the product information was provided to the public and alleged that the relative 'insufficiency' of the information and content provided in the public section, compared with that for health professionals, was not appropriate or consistent with that required under Clause 22.2.

The consequence of this insufficiency of information was that it necessitated those members of the public who needed more information to, naturally and reasonably, refer to the associated content intended for health professionals. The unrestricted and close proximity of the hyperlink access to the health professionals' content clearly and intentionally helped facilitate this; the net effect was the promotion of Pradaxa to the public.

Although the complainant had not appealed the ruling of no breach of Clause 24.1, it appeared that the Panel's ruling in that regard was consequential to its rulings of no breach of Clauses 22.1 and 22.2. Boehringer Ingelheim was thus asked to address this point in its response to the appeal.

COMMENTS FROM BOEHRINGER INGELHEIM

Boehringer Ingelheim noted that the first page of the Pradaxa website had clearly marked separate entry tabs for the public and for health professionals. The open access nature of the materials for health professionals was consistent with the Code. There was no current requirement for restricted access to websites intended for health professionals. The demarcation between the sites for the public and health professionals was clear and a member of the public could not access the health professional site by accident. Because Pradaxa was a new medicine with an MHRA approved educational pack it was especially important that health professionals could easily access this material in addition to the SPC, PIL and prescribing information. Restricted access would have been likely to impair easy access to these essential materials by health professionals. Open access to company websites in this way was also consistent with current UK practice in the pharmaceutical industry. The variety of different health professionals who required access to the site was also extensive and included doctors, nurses and pharmacists. Restricting access would have been very challenging if not impossible because

identification listings for other health professionals, comparable to GMC numbers for doctors, were currently not universally available or standardised.

Boehringer Ingelheim noted that the Code specified which materials should be provided as a library resource for the public. The SPC and PIL were UK-specific and provided extensive information which was sufficient for interested members of the public who wanted to read more about the medicine. Although the public assessment report (PAR) was available, Boehringer Ingelheim submitted that it was not necessary or desirable to include this as a reference because the extent of the information then provided, in this instance, could obfuscate the most important information from a patient perspective, namely the PIL. The PIL provided the European Medicines Agency (EMA) website address so an interested member of the public could access the EMA site and would be made aware that further information was available to them if required. The correct emphasis was given in the PIL and the advice to consult the general practitioner or pharmacist for further information was the best advice, particularly in this instance when there had been a recent extension to the product licence. In general other companies did not currently reference the PAR. There was no obligation to refer to the PAR, although providing it could be consistent with good clinical practice. In this instance Boehringer Ingelheim submitted that providing the PAR in addition to the PIL and SPC would have been excessive and potentially confusing.

Boehringer Ingelheim submitted that for medicines in an established class, medicines guides were sometimes made available for the public by UK companies. As Pradaxa was the first of the new anticoagulants to gain a licence for stroke prevention in atrial fibrillation, Boehringer Ingelheim did not think that a medicines guide was currently practical. It would have been very difficult to provide a medicines guide which did not detract from the PIL or SPC and avoided any additional product claims. As the product class expanded and clinical experience increased a medicines guide could be appropriate and Boehringer Ingelheim would keep this under review.

In conclusion, Boehringer Ingelheim agreed with the Panel's rulings and denied breaches of Clauses 22.1, 22.2 and 24.1.

FINAL COMMENTS FROM THE COMPLAINANT

The complainant stated that it appeared that Boehringer Ingelheim had contrived many reasons for not having provided the necessary extent of information that would have been considered appropriately balanced and relevant to consumers; as was questioned by the Panel. Had this not occurred alongside the provision of the more detailed and promotional information aimed at health professionals then the question of balance would not have arisen or been a problem. Whilst the complainant conceded that restricting the health professional content might have been difficult for the reasons outlined it was still incumbent on the company to ensure that the consumer content was appropriately balanced and informative such that it did not effectively drive those who needed more to simply click on the conveniently and closely placed link to the health professional content.

The complainant stated that the provision of product information to consumers via the Internet must and could be better managed. It was bad enough that the ABPI had no remit over the many questionable materials, directly accessible to UK patients and consumers, that were promoted by non-UK based parent companies, such as Boehringer Ingelheim's, on its corporate website. However, the logistical arrangement exhibited in the website in question clearly demonstrated how UK based companies could 'safely' circumvent the regulations that prevented the promotion of products to consumers in the UK; the net effect of the Panel's ruling in this case was to facilitate this.

APPEAL BOARD RULING

The Appeal Board noted that the webpages for health professionals and those for patients/public were clearly separated and labelled such that the intended audience for each section was clear, in line with the supplementary information to Clause 24.1. The Appeal Board noted that the section of the website for patients and the public contained a short product overview for each indication and direct links to the Pradaxa PILs and SPCs via the eMC. Whilst there was no link to the PAR the EMA website address appeared at the end of the PIL from which readers would be able to access the Pradaxa PAR.

The Appeal Board noted that Clause 24.5 stated that 'Public assessment reports (European or UK), summaries of product characteristics, package leaflets and reference material for prescription only medicines *may* be included on the internet and be accessible by members of the public provided that they are not presented in such a way as to be promotional in nature.' (emphasis added). Thus although the Code advised that the PAR might be included it was not a requirement to do so.

In the Appeal Board's view the amount of information provided on the patient/public part of the website was not unreasonable. The Pradaxa SPCs and PILs were detailed. The PILs provided information designed specifically for the audience. The Appeal Board did not consider that either the amount or quality of the information provided was such that readers needed to look on the health professionals' section of the website for more information.

The Appeal Board did not consider that the open access nature of the material for health professionals and the amount of information provided to patients/public meant that a prescription only medicine had been advertised to the public as alleged and it upheld the Panel's rulings of no breach of Clause 22.1. It noted that the complaint was about the arrangements for accessing the site. The Appeal

Board upheld the Panel's ruling of no breach of Clause 22.2. The appeal was unsuccessful.

As the Appeal Board had ruled no breach Clauses 22.1 and 22.2 it did not need to consider the Panel's ruling of no breach of Clause 24.1.

2 Dose of Pradaxa

COMPLAINT

The complainant noted that the first reference to the indication of stroke prevention in atrial fibrillation did not specify that this only referred to 150/110mg doses of Pradaxa and did not include the 75mg dose. The same was the case for the hyperlinked content. This omission was misleading and clinically relevant.

RESPONSE

Boehringer Ingelheim noted that the complainant was concerned about the omission of the 75mg SPC. The company did not understand the basis for this complaint. Pradaxa was indicated for stroke prevention in SPAF (110mg and 150mg doses) and for prevention of venous thromboembolism after elective hip and knee replacement surgery (110mg and 75mg doses). On the SPAF section of the site there were hyperlinks to the relevant 150mg and 110mg doses. On the venous thromboembolism section of the site there were hyperlinks to the 110mg and 75mg dose. The company did not see how this could be any more clear or appropriate.

PANEL RULING

The Panel noted that the screen layout had nine tabs on the left hand side including 'Dose' and 'Educational pack'. As well as the heading that the page was intended for healthcare professionals the page was headed and subheaded with details of the stroke indication. The link to the SPC and the prescribing information appeared at the foot of the page.

The Panel noted that the recommended dose of Pradaxa for the prevention of stroke and systemic embolism in certain patients was 150mg twice daily. For patients aged 80 years or above this dose was decreased to 110mg twice daily. These dose recommendations could be accessed by clicking on the 'Dose' tab. The Panel did not consider that the failure to include a reference to the 75mg dose in the section clearly marked 'Stroke prevention in atrial fibrillation' was misleading as alleged. No breach of Clause 7.2 was ruled.

3 Location of prescribing information

COMPLAINT

The complainant noted that the location of where the prescribing information could be found was only clarified after prominent claims for Pradaxa had already appeared. This did not allow the reader to appreciate the promotional claims in relationship to the important information contained in the prescribing information.

RESPONSE

Boehringer Ingelheim submitted that the prescribing information was at the bottom of every page of the health professionals' part of the website (Clause 4.6).

As the complainant was critical of the availability of the prescribing information, Boehringer Ingelheim submitted that it had made the prescribing information even more prominent and added it additionally to the left hand tabs (white on dark blue) on the left hand side of each web page (for SPAF). The company considered that because the prescribing information had always been easy to find as a link at the bottom of each web page it had not contravened the Code but accepted that there was room for improvement and hoped that health professionals would find the change helpful.

On the first page of the site following confirmation of the identity of the reader as a UK health professional, there was a choice of the two indications, SPAF and the prevention of venous thromboembolism. There was no prescribing information on this page, although there were links to the three SPCs but this was because no product claims were made, there was only a statement of the licence for each indication. The company did not know if the complainant was stating that the prescribing information should be available on this page but that did not seem appropriate as it could cause confusion as to what doses were licensed for the two indications.

Boehringer Ingelheim submitted that the Pradaxa website was more visually attractive than some other companies' sites which supplied product information. However, the company had been careful not to make product claims. The information given related to the indication, dose, mode of action, initiation of Pradaxa, managing the anticoagulation effect, managing anticoagulation, clinical evidence, and access to the educational pack. The clinical evidence section was non-promotional and was a text document in black and white which gave a balanced account of the data from the RE-LY study which was relevant to the prescribers' understanding of the medicine. There were no marketing statements or claims. Boehringer Ingelheim considered that its report of the RE-LY study complied with Clause 7.2.

The company was very concerned to maintain high standards and welcomed any constructive criticism. It was inclined to attribute the negative remarks as having arisen from first impressions of the website. It was visually attractive; more so than some of its competitors' sites, but a pleasant visual aesthetic did not in itself constitute a breach of the Code.

As Pradaxa was an anticoagulant there was the potential for excess bleeding events, made more likely if it was not prescribed within the licence and

patients were not followed up appropriately. It was therefore imperative that the company provided health professionals with adequate, easily accessible information. The Pradaxa website helped the company to do that and allowed easy access to the educational pack, which was part of the agreed communication plan with the MHRA.

Boehringer Ingelheim emphasised that it took any allegation of a breach of the Code very seriously and although it considered that the Pradaxa website was not in breach it was concerned that the complainant had objected to some parts of it and therefore it had taken immediate action to improve clarity and quality by making the prescribing information links more prominent.

PANEL RULING

The Panel noted that Clause 4.6 required that promotional material on the Internet must contain a clear prominent statement as to where the prescribing information could be found.

The Panel noted that the first page of the site following confirmation of the identity of the reader as a UK health professional referred to the licensed indications for Pradaxa but did not indicate where the prescribing information could be found. The reader had to click on the relevant indication before reaching the page of the website that contained a link to the prescribing information. In the Panel's view, the prescribing information should have appeared on the page that referred to the licensed indications for Pradaxa which followed confirmation of the reader as a health professional. This part of the site was promotional. The Panel did not agree with Boehringer Ingelheim's submission that no product claims were made. Details of a product's indication was, in effect, a product claim. Nor did the Panel agree with Boehringer Ingelheim's submission that the provision of prescribing information on the first page would have caused confusion; a link to the relevant prescribing information could have been placed below each indication. A breach of Clause 4.6 was ruled in relation to the absence of a direct link to the prescribing information on the page in question.

Complaint received **19 October 2011**

Case completed **19 January 2012**