ANONYMOUS, NON-CONTACTABLE v BOEHRINGER INGELHEIM

Symposia at a meeting

An anonymous, non-contactable complainant noted that medical symposia at a European congress held in London in 2015 included off-label discussions and discussions about grants for medical research while stating that prescribing information was available. The complainant thought that prescribing information was associated with promotion and provided a copy of a slide from a Boehringer Ingelheim symposium as an example. Boehringer Ingelheim marketed Pradaxa (dabigatran) which was a novel oral anticoagulant (NOAC).

The detailed response from Boehringer Ingelheim is given below.

The Panel noted that the slide was from a symposium entitled 'Your patients, your practice, your choice: NOACs in the clinic' which comprised four presentations focussing on the use of dabigatran. The complainant had not provided details of what he/she considered to be off-label. Conversely, Boehringer Ingelheim provided copies of all of the presentations and submitted that although two were about topics currently under debate with ongoing studies, both were in line with dabigatran's marketing authorization. Whilst Boehringer Ingelheim submitted that the fourth presentation referred to its reversal agent for dabigatran which did not have an EU licence the Panel noted it did not have a complaint in this regard and it was thus obliged to rule no breach of the Code. The complaint solely concerned off-label promotion which in the Panel's view meant that a product was licensed but its promotion was inconsistent with that licence. There was no evidence before the Panel that Boehringer Ingelheim had promoted Pradaxa outside the terms of its marketing authorization or in a manner inconsistent with the particulars listed in its summary of product characteristics and on this narrow ground no breach of the Code was ruled.

The Panel noted its rulings above and considered that Boehringer Ingelheim had not failed to maintain high standards and thus ruled no breach of the Code and consequently ruled no breach of Clause 2.

With regard to the complainant's comment about grants for medical research being discussed at medical symposia where prescribing information was available, the Panel considered that the complainant had not explained why such activity might be in breach of the Code. The complainant was non-contactable and so the Panel could not ask him/her for more information. A judgement had to be made on the evidence provided by the parties. The Panel noted Boehringer Ingelheim's submission that its corporate team had supported the congress organiser's Grants for Medical Research Innovation and information relating to the grant was only shown at the end of Boehringer Ingelheim sponsored sessions, where the main information about the scientific research grant programme had been shared by the congress organiser itself. The agreement was neither dabigatran specific nor was dabigatran mentioned anywhere on the related documents. The Panel considered that the complainant had not demonstrated that, in displaying information about a medical research grant, Boehringer Ingelheim had breached the Code and the Panel thus ruled no breaches of the Code.

During its consideration of this case, the Panel noted that the fourth symposium presentation included claims for a specific reversal agent for dabigatran. The Panel was concerned that the medicine had thus been promoted prior to the grant of a marketing authorization which permitted its sale or supply and requested that Boehringer Ingelheim be advised of its concerns in this regard.

An anonymous, non-contactable complainant, who described him/herself as a UK health professional, complained about medical symposia at the European Society of Cardiology (ESC) Congress held in London 29 August – 2 September 2015. Boehringer Ingelheim marketed Pradaxa (dabigatran) which was a novel oral anticoagulant (NOAC).

COMPLAINT

The complainant asked for clarification on medical symposia. He/she understood that promotional presentations always went hand-in-hand with abbreviated prescribing information. However, a couple the complainant had attended had included discussions that were off-label and discussions about grants for medical research etc but the prescribing information was available and stated on the slides. The complainant did not think that having prescribing information available at a meeting made it promotional but he/she was confused about how to perceive such a meeting.

The complainant provided a copy of a Boehringer Ingelheim slide entitled 'Panel discussion and Q&A' from a symposium moderated by a US health professional. The slide stated 'Prescribing information is available at this meeting'.

When writing to Boehringer Ingelheim the Authority asked it to respond in relation to Clauses 3.1, 3.2, 9.1 and 2 of the 2015 Code. Boehringer Ingelheim was subsequently asked to comment on Clause 19 after it referred to this clause in its initial response.

RESPONSE

Boehringer Ingelheim stated that the details of the exact issue seemed unclear as the complainant appeared to be seeking clarity on the interpretation of the Code without reference to a specific presentation apart from a final Q&A slide. This made it difficult for Boehringer Ingelheim to respond, but it endeavoured to address what it interpreted as the substance of the apparent complaint.

The complainant had provided a photograph from the Boehringer Ingelheim sponsored satellite symposium held on Sunday, 31 August at the ESC Congress; the complainant had not detailed what he/she considered to be off-label and Boehringer Ingelheim strongly rejected any suggestion that it might have engaged in off-licence promotion during the sponsored symposium. Boehringer Ingelheim submitted that it conformed with Clauses 3.1 and 3.2 and had maintained high standards (Clause 9) and not brought the industry into disrepute (Clause 2).

The complainant also mentioned grants for medical research but provided no evidence to support the detail of this. For the purposes of clarity Boehringer Ingelheim dealt with the two issues separately.

1 Sponsored satellite symposium: Your patients, your practice, your choice: NOACs in the clinic

This was an hour long symposium organized and sponsored by Boehringer Ingelheim as part of a series of industry satellite symposia during ESC, offering delegates the opportunity to learn and exchange on the latest scientific information and developments from industry. Boehringer Ingelheim's sponsorship was made clear on all relevant materials, hence the reasoning for prescribing information being available.

The symposium comprised of four talks by speakers globally recognized for their expertise in anticoagulation and atrial fibrillation (AF), followed by a moderated Q&A (the photograph of the slide sent by the complainant). All topics were of interest to cardiologists in this disease area. Attendees at the ESC came from around the world, although there was a larger proportion from Europe. A link to the distribution of delegates' countries of origin published by the ESC was provided.

The first speaker provided an overview of the four currently licensed non vitamin K oral anticoagulants (NOACs); he also mentioned data from post-marketing sources and introduced the format and speakers for the remainder of the symposium (5 minutes).

The second presentation was about the management of patients on anticoagulation for AF who required ablation, an interventional procedure to help control the symptoms of atrial fibrillation. This was a topic under debate currently with a number of phase IV studies underway and was in line with the marketing authorization for Pradaxa in the UK and Europe (15 minutes).

The third speaker discussed the current challenges and decisions required in the management of AF patients who required a coronary stent following an acute cardiac event. Again this was a widely debated topic given the challenges of both an interventional procedure and the requirement for additional antiplatelet therapy on top of anticoagulant therapy. Updated ESC guidelines on this topic were presented during another session at this meeting and the speaker sought permission to present this again in Boehringer Ingelheim's symposium. Again, a number of studies were running in this area, which like the second presentation was in line with the marketing authorization for Pradaxa in the UK and Europe (15 minutes).

The fourth and final speaker, relevant to the two previous talks, discussed the management of patients needing either elective or emergency surgery whilst receiving long-term anticoagulation. A patient case study was used to help communicate the current advice contained in the Pradaxa summary of product characteristics (SPC), as well as the risk management materials. Published data from sub-analyses of the RELY trial (phase III study for dabigatran in non-valvular atrial fibrillation) were also presented. The status of current developments in reversal agents was briefly discussed at the end of the session in order to provide fair, balanced and scientifically accurate content. All three reversal agents under current investigation, including Boehringer Ingelheim's specific reversal agent for dabigatran were presented and relevant slides contained a clear disclaimer that these were investigational compounds and not available for use in the EU in line with supplementary information to Clause 3. One slide was not used in the presentation as it had been prepared in case of FDA approval, so that the most up-to-date information could be provided should the situation change (15 minutes).

Boehringer Ingelheim submitted that the symposium focussed on the use of dabigatran in line with its marketing authorization and presented in a balanced, fair and accurate way. Boehringer Ingelheim believed that high standards had been maintained at all times.

2 Medical research grant

Boehringer Ingelheim submitted that the reference to the medical research grant was the support of an ESC research grant programme by Boehringer Ingelheim described below, although given the lack of specificity in the complaint it was difficult to be certain.

The corporate Boehringer Ingelheim cardiovascular team had financially supported a scientific programme developed by the ESC, entitled ESC Grants for Medical Research Innovation. The programme was covered by an agreement between Boehringer Ingelheim corporate and the ESC. A link to the programme outline on the ESC website was provided. It was neither dabigatran specific nor was dabigatran mentioned anywhere on the related documents. It was a specific condition of the programme that any applications seeking to investigate NOACs must include more than one NOAC.

Information relating to the grant was only shown at the end of Boehringer Ingelheim sponsored sessions at the ESC, where the main information

about the scientific research grant programme had been shared by the ESC itself. Boehringer Ingelheim submitted that the sponsorship of the research grant complied with the Code, in particular Clause 19.2 and took consideration of the supplementary information to Clause 19.1.

In conclusion, Boehringer Ingelheim submitted that the activities during the satellite symposium of 31 August 2015 and the research grant to the ESC were not in breach of Clauses 2, 3.1, 3.2, 9 or 19 of the Code.

Upon receipt of the response, the case preparation manager noted Boehringer Ingelheim referred to Clause 19 in its response. This was not raised initially but Boehringer Ingelheim was asked for any further comments.

Boehringer Ingelheim stated that the medical research grant was a global initiative between Boehringer Ingelheim (corporate) and the ESC. A copy of the contract with the financial details redacted for reasons of confidentiality was provided

The ESC was based in France and the research grant was governed by French law. The award of the grant therefore took place outside the UK. The eligibility for applying for the grant was global. This was not a grant made by or to a UK organisation and therefore potentially fell outside the scope of the Code.

Boehringer Ingelheim acknowledged, however, that the existence of the grant was advertised in the UK at the ESC meeting. The grant would in any case have complied with the requirements of Clause 19.2, if applicable, because it:

- was made to an association of health professionals and not to a health professional personally
- was made for the purpose of supporting research
- was documented and kept on record
- was not an inducement to prescribe, and
- would be publicly disclosed.

The recipient of the grant was the ESC, an association of health professionals with a stated mission to reduce the burden of cardiovascular disease in Europe. ESC's work included supporting research. The grant was not provided by Boehringer Ingelheim to any health professional personally. The purpose of the grant was to support four research projects in a number of cardiovascular areas. The research projects were selected by a scientific committee independently appointed by ESC. No research project in the UK was selected. The grant was documented and would be kept on record in accordance with Boehringer Ingelheim's normal records retention policy.

The provision of the financial support was very clearly non-promotional as indicated by section 1.1 of the contract:

> 'Any promotion for certain products or promotional language shall be avoided in the [Program]. Furthermore, the Grantee shall ensure that no product advertisements or promotional materials will be published on the same web page as the [Program] content.'

This was further reinforced by Section 3.1:

> 'Boehringer Ingelheim and the Grantee agree and confirm that this Agreement has not been concluded in order to influence current or future sales transactions. The sponsoring does not commit the Grantee or its employees to accept or prefer services or products from Boehringer Ingelheim. Boehringer Ingelheim does not expect any preference for its products (Principle of Separation).'

Schedule 1 also clearly stated:

> 'Study proposals evaluating Non Vitamin K Anticoagulants (NOACs) must include more than one NOAC.'

This caveat was to avoid any possible link to Pradaxa.

A communication plan was included in the schedule outlining the ESC's role in announcing the grant programme. This was prepared and announced by the ESC. Boehringer Ingelheim used this same communication to announce the programme at the end of the scientific symposia held at the ESC meeting in 2015. Boehringer Ingelheim's role in supporting the grant programme was clearly disclosed and reference was made to the ESC web page.

As required by the supplementary guidance to Clause 19.2, the details of this grant would be publicly disclosed by Boehringer Ingelheim corporate in accordance with the EFPIA Disclosure Code.

PANEL RULING

The complainant was anonymous and non-contactable and so the Panel could not ask him/her for more information. As stated in the introduction to the Constitution and Procedure, anonymous complaints were accepted and like all complaints, judged on the evidence provided by the parties. A complainant had the burden of proving his/her complaint on the balance of probabilities. The Panel noted that the complainant had alleged that presentations he/she had attended included off-label discussions and discussions about grants for medical research. The complainant provided a copy of a Boehringer Ingelheim slide entitled 'Panel discussion and Q&A' from a symposium moderated by a US health professional. The slide stated 'Prescribing information is available at this meeting'.

The Panel noted Boehringer Ingelheim's submission that the slide provided by the complainant was from a Boehringer Ingelheim sponsored satellite symposium entitled 'Your patients, your practice, your choice: NOACs in the clinic'. The symposium comprised four presentations; 'Beyond the trials: NOACs in practice'; 'Your patient requires AF ablation: what would you do?'; 'Your patient with NVAF requires a coronary stent: what would you do?'; and 'Your patient requires surgery: what

would you do?'. The Panel noted that the focus of all four presentations was on the use of dabigatran as submitted by Boehringer Ingelheim. The complainant had not provided details of what he/she considered to be off-label. Conversely, Boehringer Ingelheim provided copies of all of the presentations and submitted that the topics of two presentations were currently under debate and a number of studies were ongoing in the areas but both topics were in line with dabigatran's marketing authorization. Whilst Boehringer Ingelheim submitted that the fourth presentation referred to its reversal agent for dabigatran which did not have an EU licence the Panel noted it did not have a complaint in this regard. The complaint solely concerned off-label promotion which in the Panel's view meant that a product was licensed but its promotion was inconsistent with that licence. There was no evidence before the Panel that Boehringer Ingelheim had promoted Pradaxa outside the terms of its marketing authorization or in a manner inconsistent with the particulars listed in its SPC contrary to Clause 3.2 and on this narrow ground no breach of that Clause was ruled.

The Panel noted that Boehringer Ingelheim had been asked by the case preparation manager to respond in relation to the requirements of Clause 3.1 which required that a medicine must not be promoted prior to the grant of the marketing authorization which permitted its sale or supply. As in the Panel's view the complainant had not alleged that an unlicensed medicine had been promoted, the Panel was obliged to rule no breach of Clause 3.1.

The Panel noted its rulings above and considered that Boehringer Ingelheim had not failed to maintain high standards and thus ruled no breach of Clause 9.1 and consequently ruled no breach of Clause 2.

With regard to the complainant's comment about grants for medical research being discussed at medical symposia where prescribing information was available, the Panel considered that the complainant had not explained why such activity might be in breach of the Code. The complainant was anonymous and non-contactable and so the Panel could not ask him/her for more information. A judgement had to be made on the evidence provided by the parties. The Panel noted Boehringer Ingelheim's submission that its corporate team had supported the ESC Grants for Medical Research Innovation and information relating to the grant was only shown at the end of Boehringer Ingelheim sponsored sessions at the ESC, where the main information about the scientific research grant programme had been shared by the ESC itself. The agreement was neither dabigatran specific nor was dabigatran mentioned anywhere on the related documents. The Panel considered that the complainant had not demonstrated that in displaying information about a medical research grant Boehringer Ingelheim had breached the Code and the Panel thus ruled no breaches of Clauses 19.1, 9.1 and 2 accordingly.

During its consideration of this case, the Panel noted that the Boehringer Ingelheim satellite symposium was promotional and within that context the fourth presentation discussed the management of patients needing either elective or emergency surgery whilst receiving long-term anticoagulation and discussed the status of current developments in reversal agents. The Panel noted Boehringer Ingelheim's submission that all three reversal agents currently under investigation, including Boehringer Ingelheim's specific reversal agent for dabigatran, were presented and relevant slides contained a clear disclaimer that these were investigational compounds and not available for use in the EU in line with supplementary information to Clause 3 of the Code. The Panel assumed that the supplementary information referred to by Boehringer Ingelheim was that to do with the promotion of medicines at international meetings held in the UK when such medicines did not have a marketing authorization in the UK although they were authorized in another major industrialised country. It appeared that Boehringer Ingelheim's medicine was not licensed for use anywhere in the world and so it could not be promoted. The Panel noted that the final presentation in a promotional symposium had referred to the unlicensed medicine and included a slide which stated that it had a binding affinity ~ 350 times higher than dabigatran for thrombin, no procoagulant or anticoagulant effects expected, onset of action within 1 minute and a short half-life. The Panel noted that, as stated above, the complainant had not alleged that an unlicensed medicine had been promoted at the meeting. The Panel was concerned that the slide promoted the unlicensed medicine prior to the grant of a marketing authorization which permitted its sale or supply and requested that Boehringer Ingelheim be advised of its concerns in this regard.

Complaint received **21 December 2015**

Case completed **8 February 2016**