CASE AUTH/2738/10/14

VOLUNTARY ADMISSION BY BOEHRINGER INGELHEIM

Corporate email about Giotrif

Boehringer Ingelheim voluntarily admitted that an email which had been sent from its corporate headquarters in Germany to LinkedIn members via LinkedIn InMail to a global (including UK) audience was in breach of the Code. The email headed, 'Read new data on treatment outcomes with Giotrif' detailed the results from an abstract presented at the American Society of Clinical Oncology (ASCO) meeting, 2014 (Yang *et al* 2014) also included was an advertisement for Giotrif (afatinib) and a link to a press release.

The advertisement referred to overall survival benefit data for certain patients. The press release headed 'New data show Giotrif (afatinib) provided more than one year additional survival for lung cancer patients with the most common type of EGFR [epidermal growth factor receptor] mutation (del19) compared to chemotherapy', gave more detail including that Giotrif was the first treatment to demonstrate an overall survival benefit for certain patients. The press release was marked 'For Ex-US and Ex-UK Media Only'.

In accordance with Paragraph 5.6 of the Constitution and Procedure the Director treated the matter as a complaint.

Giotrif was indicated for the treatment of epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI)–naïve adults with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating EGFR mutation(s).

Boehringer Ingelheim stated it only knew about these activities when another UK pharmaceutical company brought them to its attention. Inter-company dialogue concluded with Boehringer Ingelheim confirming that it would report the activity to the PMCPA.

Boehringer Ingelheim stated that the intended audience was lung cancer health professionals based on the filter of medical, oncology and those who had not opted out of receiving promotional mailings. It was now clear that these filters were not restrictive enough as UK non health professionals were not excluded. The material did not contain the obligatory UK information and was not UK approved or certified.

The Giotrif advertisement was not intended for a UK audience and was not used by the UK company; Boehringer Ingelheim Corporate approved and distributed the advertisement. The content, claims and absence of tolerability information might be considered inconsistent with the Code.

In order to prevent future issues, the corporate organisation had been reminded not to send by any medium, materials or communications that were not UK certified to any UK recipients.

The detailed response from Boehringer Ingelheim is given below.

The Panel noted that the email had been created and distributed by Boehringer Ingelheim Corporate in Germany but insomuch as it was sent to UK recipients, that aspect came within the scope of the Code. UK companies were responsible for the activities of overseas affiliates where those activities came within the scope of the Code. Boehringer Ingelheim in the UK was thus responsible for the UK use of the email. As the email had not been certified the Panel ruled a breach of the Code.

The absence of prescribing information was also ruled in breach. The Panel ruled no breach of the Code with regard to the need to indicate where the prescribing information could be found. No breach was also ruled as the Panel considered the material satisfied the requirement for providing the date it was drawn up or last revised. The email did not include a prominent statement regarding the mechanism for reporting adverse events or an inverted black triangle. Breaches were ruled. As it was clear which company had sent the email the Panel ruled no breach.

The Panel noted that material should only be sent or distributed to those people whose need for, or interest in it could be reasonably assumed. Boehringer Ingelheim had implied that this might not have been so given that the filters defining who the email was sent to were not restrictive enough. The Panel considered that on the balance of probabilities, at least some health professionals with no interest in Giotrif had received the email. A breach was ruled.

A member of the public in Australia had received the email. No evidence had been provided to show that a particular member of the UK public had received the email but given the submission that the filters were inadequate, the Panel considered that on the balance of probabilities a member of the UK public had received the promotional email. A prescription only medicine had been promoted to the public and the advertisement would encourage a member of the public to ask their health professional to prescribe Giotrif. Breaches were ruled. The Panel noted Boehringer Ingelheim's submission that as the data did not come from the whole of the Yang *et al* study group it was not balanced and fair. A breach was ruled. The Panel also ruled breaches on

the basis that the artwork was misleading and that the material did not encourage the rational use of Giotrif.

The Panel ruled that high standards had not been maintained.

The Panel considered that Boehringer Ingelheim had been badly let down by its corporate colleagues who appeared to have failed to recognise, the need for the email to be approved for use in the UK. Nonetheless, the Panel did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 which was seen as a sign of particular censure and reserved for such. No breach of the Code was ruled.

Boehringer Ingelheim Limited voluntarily admitted that an email which had been sent from its corporate headquarters in Germany was in breach of the Code. The email, which was sent to some UK recipients, contained an advertisement for Giotrif (afatinib) and a link to a non-UK Giotrif related press release.

The email was headed 'Read new data on treatment outcomes with Giotrif' and detailed the results from an abstract which had been presented at the American Society of Clinical Oncology (ASCO) meeting, May/June 2014 (Yang *et al* 2014). Within the text was a link to a press release and on the right hand side of the text was an advertisement for Giotrif. The press release was entitled 'New data show Giotrif (afatinib) provided more than one year additional survival for lung cancer patients with the most common type of EGFR [epidermal growth factor receptor] mutation (del19) compared to chemotherapy'. The press release was marked 'For Ex-US and Ex-UK Media Only'.

In accordance with Paragraph 5.6 of the Constitution and Procedure the Director treated the matter as a complaint which was taken up with Boehringer Ingelheim.

VOLUNTARY ADMISSION

Boehringer Ingelheim explained that the email was generated and sent in error on 13 August 2014 from its corporate headquarters in Germany to LinkedIn members via LinkedIn InMail to a global (including UK) audience according to the LinkedIn settings described below.

Giotrif was indicated for the treatment of epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI)–naïve adults with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating EGFR mutation(s).

The advertisement referred to overall survival (OS) benefit data for certain patients taken from Yang *et al*. The email included a link to a press release which gave more detail including that Giotrif was the first treatment to demonstrate an overall survival benefit for patients with specific types of EGFR mutation positive NSCLC.

Boehringer Ingelheim stated it was not involved in these activities and did not know about them until another UK pharmaceutical company brought them to its attention on 17 September 2014. Inter-company dialogue with that company concluded with Boehringer Ingelheim confirming that it would report the activity to the PMCPA.

The intended audience for the LinkedIn InMail was lung cancer health professionals based on the filter of medical, oncology and those who had not opted out of receiving promotional mailings through their individual LinkedIn settings. Boehringer Ingelheim stated that it was now clear that these filters were not restrictive enough as UK non health professionals were not excluded. This would not have occurred if Boehringer Ingelheim in the UK had been notified of this activity which might be in breach of Clauses 9.10, 11.1, 23.1 and 23.2 of the Code.

The promotional email, advertisement and press release did not contain the obligatory UK information as the materials were generated and approved by Boehringer Ingelheim Corporate and were not sent for UK approval and certification. As such, this might be considered to be a breach of Clauses 4.1, 4.6, 4.9, 4.10, 4.11, and 25.1.

The Giotrif advertisement was not intended for a UK audience and was not used in the UK by the UK company; Boehringer Ingelheim Corporate had approved and distributed the advertisement. The content, claims and absence of tolerability information might be considered inconsistent with Clauses 7.2, 7.8 and 7.10 of the Code.

The Giotrif related press release, accessible via the link in the email, was also never intended for a UK audience and was never used in the UK by the UK company; again it had been approved and distributed by Boehringer Ingelheim Corporate. The communication was no longer in circulation and had been withdrawn from all UK LinkedIn members. In order to prevent future issues, the corporate organisation had been reminded that under no circumstances should it send by any medium, materials or communications that were not UK certified to any UK recipients.

Boehringer Ingelheim submitted that all corporate communications which fell within the scope of the Code and were directed at a global audience but which had not gone through full UK approval and certification, would be expressly defined as 'for non-UK recipients' and would comply with the digital communications and social media requirements and guidelines as set out by the Code and where relevant with the regulatory frameworks of the other pertinent jurisdictions.

Boehringer Ingelheim stated that it had acted immediately to withdraw the email and put measures in place, in collaboration with corporate colleagues, to ensure greater control on Boehringer Ingelheim Corporate activities in the UK. Boehringer

Ingelheim stated that it took its responsibilities under the Code very seriously.

When writing to the company the Authority asked it to respond to Clauses 9.1 and 2 in addition to the clauses raised by Boehringer Ingelheim. The company was also asked to provide further details including why it considered there might be breaches of Clauses 7.2, 7.8 and 7.10.

RESPONSE

Boehringer Ingelheim stated that the intended audience for the email in question was lung cancer health professionals globally, based on the filter of medical, oncology and those who had not opted out of receiving promotional mailings through their LinkedIn settings. It was now clear that these filters were not restrictive enough and did not exclude UK recipients. The email was sent to a global audience with the same filters and the mailing was also received by a member of the public in Australia. As the same filtering criteria were used for all countries it was likely that other members of the public would have received the email outside of the UK. The USA was excluded from these mailings.

Boehringer Ingelheim submitted that the content, claims and absence of tolerability information as written in the email and advertisement were not consistent with Clauses 7.2, 7.8 and 7.10. The information was not balanced and fair as it did not include the data for the whole EGFR mutation positive patient population in the study and provided overall survival data for the del19 mutational sub group (albeit one that represented 50% of the trial population). The graphic image of the pillar in the advertisement was labelled "EFFICACY – PFS [progression free survival] +OS", which implied that afatinib gained its licence based on OS benefit in addition to PFS benefit, rather than on the basis of PFS benefit alone.

Boehringer Ingelheim stated that the material did not mention the tolerability profile which might convey an unbalanced benefit/risk message and raised potential concerns for patient safety if prescribing was based on or influenced by the material. When taken collectively the materials might not encourage the rational use of Giotrif.

With regard to Clauses 9.1 and 2, Boehringer Ingelheim stated it had self-reported the potential breaches instigated by the corporate organisation. It accepted that this activity was not consistent with maintaining high standards. However, as soon as the company knew about this activity it ensured recall and termination of the communications as a matter of urgency. By self- reporting these breaches the company submitted it had demonstrated its strong commitment to maintaining high standards and had introduced robust measures, working collaboratively with corporate colleagues to ensure greater control of all Boehringer Ingelheim Corporate activities in the UK. The materials were not intended for a UK audience and were not used by the UK company. Patient safety and public health had not been compromised with respect to this activity and therefore Boehringer Ingelheim submitted that this was not a breach of Clause 2.

PANEL RULING

The Panel noted that the email had been created and distributed by the Boehringer Ingelheim Corporate team in Germany. The supplementary information to Clause 1.9, Applicability of Codes, required that activities carried out and materials used by a pharmaceutical company located in a European country must comply with the national code of that European country as well as the national code of the country in which the activities took place or the materials were used. The email in question was issued from a company based in Germany but insomuch as it was sent to UK recipients, the Panel considered that that aspect of its use came within the scope of the Code. The Panel also noted that it was an established principle under the Code that UK companies were responsible for the activities of overseas affiliates where those activities came within the scope of the Code. Boehringer Ingelheim in the UK was thus responsible for the UK use of the email. The Panel noted that the email was promotional and had not been certified for use in the UK and so it ruled a breach of Clause 14.1.

The Panel noted that the email promoted Giotrif but that there was no prescribing information within it. In that regard the Panel ruled a breach of Clause 4.1. The Panel noted that Clause 4.6 of the Code stated that in the case of material included on the Internet, there must be a clear, prominent statement as to where the prescribing information could be found. The Panel noted that although the material at issue was sent electronically, it was not material included on the Internet *per se*; it was an electronic mailing. In that regard the Panel noted its ruling of a breach of Clause 4.1 above. The Panel did not consider that Clause 4.6 applied to emails and so it ruled no breach of that clause. Boehringer Ingelheim had also voluntarily admitted a breach of Clause 4.9 which required that promotional materials, other than advertisements appearing in professional publications, must include a date upon which the material was drawn up or last revised. The Panel noted that the press release linked to the email was dated 1 September 2014 and that the email itself would bear the date upon which it was sent. In that regard the Panel considered that recipients would know when the material was sent and was thus current; no breach of Clause 4.9 was ruled. The email did not include a prominent statement regarding the mechanism for reporting adverse events; a breach of Clause 4.10 was ruled. The Panel noted from the Giotrif summary of product characteristics provided by Boehringer Ingelheim, that the medicine was one which was subject to additional monitoring and thus all promotional material was required to show the inverted black, equilateral triangle symbol. As the email in question did not include that symbol a breach of Clause 4.11 was ruled.

The Panel noted that Clause 9.10 required that all material relating, *inter alia*, to medicines and their uses, whether promotional or not, which was

sponsored by a pharmaceutical company must clearly state that it was sponsored by that company. The Panel noted that to the right of the text of the email was a Giotrif advertisement which clearly showed the Boehringer Ingelheim company logo and name. In addition, the linked press release was headed with the company logo. On balance, the Panel considered that it was clear that the email had been sent on behalf of Boehringer Ingelheim. No breach of Clause 9.10 was ruled.

The Panel noted that Clause 11.1 of the Code required that promotional material only be sent or distributed to those people whose need for, or interest in it could be reasonably assumed. Boehringer Ingelheim had implied that this might not have been so given that the filters defining who the email was sent to were not restrictive enough. The Panel considered that on the balance of probabilities, at least some health professionals with no interest in Giotrif had received the email. A breach of Clause 11.1 was ruled.

Clause 23.1 required that prescription only medicines must not be advertised to the public. Boehringer Ingelheim had submitted that it was possible that some of those who had received the email in the UK were not health professionals and that a member of the public in Australia had received the email. No evidence had been provided to show that a particular member of the UK public had received the email but given the submission that the filters in place did not preclude this from happening, the Panel considered that on the balance of probabilities a member of the UK public had received the promotional email. A breach of Clause 23.1 was ruled. Given its ruling of a breach of Clause 23.1, the Panel also ruled a breach of Clause 23.2 in that the advertisement would encourage a member of the public to ask their health professional to prescribe Giotrif.

The Panel noted Boehringer Ingelheim's submission about the balance of the data within the email. The data included did not come from the whole of the Yang *et al* study group and, according to Boehringer Ingelheim, was thus not balanced and fair. A breach of Clause 7.2 was ruled. The Panel also ruled a breach of Clause 7.8 on the basis that the artwork in the advertisement was misleading as to the basis of the Giotrif licence. A breach of Clause 7.10 was also ruled in that Boehringer Ingelheim had admitted that the material did not encourage the rational use of Giotrif.

The Panel noted its rulings above and considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel considered that Boehringer Ingelheim had been badly let down by its corporate colleagues who appeared to have failed to recognise that, if sent to UK recipients, the email needed to be approved for use in the UK. Nonetheless, the Panel did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 which was seen as a sign of particular censure and reserved for such. No breach of Clause 2 was ruled.

During its consideration of this case the Panel queried whether not opting out of receiving promotional material on LinkedIn settings was sufficient, given the very general nature of LinkedIn, to satisfy the requirement in Clause 9.9 of the Code which required recipients to consent to receive promotional material about medicines from pharmaceutical companies. The Panel considered that Boehringer Ingelheim would be well advised to consider how the arrangements for LinkedIn InMail fitted with the Code.

Complaint received **31 October 2014**

Case completed **9 January 2015**