GENERAL PRACTITIONER v BOEHRINGER INGELHEIM and LILLY

Sponsored article on linagliptin

A general practitioner complained that an article on linagliptin published in Future Prescriber represented the exaggerated, misleading and disguised promotion of linagliptin before a UK marketing authorization had been granted.

The article 'Linagliptin: new class of DPP-4 [dipeptidyl peptidase-4] inhibitor in the treatment of T2DM [type 2 diabetes mellitus]' was written by two diabetes and endocrinology physicians. A declaration of the authors' interests was given in the final paragraph which stated 'Placement of this article has been funded by Boehringer Ingelheim and Lilly. The content has been independently commissioned by Future Prescriber and has been checked by Boehringer Ingelheim and Lilly for factual accuracy only. Editorial control of this article remains with Future Prescriber'.

The complainant stated that the authors had previously received support from the companies which suggested that their opinions were likely to be known by both the companies which were likely to have been involved in their selection and briefing.

The complainant noted that the article stated that linagliptin was now approved and due to launch in the UK; this was not so. Linagliptin had only received a positive opinion from the European Medicines Agency (EMA).

The complainant alleged that the title of the article was misleading and exaggerated. He knew of no recognised or accepted sub-class of DPP-4 inhibitors. The title suggested an unqualified and unsubstantiated superiority over currently licenced DPP-4 inhibitors, comparisons with which were made throughout the article.

The complainant asked if it was accurate to compare the maximal efficacy and potency of linagliptin with other DPP-4 inhibitors or claim that, in relation to use with concomitant medicines, linagliptin was safer than saxagliptin (Onglyza); especially given that there were no head-to-head data with other DPP-4 inhibitors to substantiate this.

The complainant alleged that the claim that linagliptin might have a positive and long enduring effect on beta-cell function and therefore glycaemic control was misleading and inaccurate; this was not a fact nor could it be substantiated. The complainant stated that an unbalanced and distorted promotional message was also elaborated with regard to renal acceptability. Saxagliptin was currently the only DPP-4 inhibitor with a UK licence for use in moderate/severe renal impairment. The complainant further alleged that the discussion of the possible cost of linagliptin compared with other DPP-4 inhibitors was not factual and potentially misled about cost-efficacy.

The complainant alleged that the decision to fund the development of this article and the evident lack of proper scrutiny of the facts suggested that the companies were keen to promote linagliptin prior to licence.

The detailed responses from Boehringer Ingelheim and Lilly are given below.

The Panel noted that it was acceptable for companies to sponsor material. It had previously been decided that the content would be subject to the Code if it was promotional in nature or if the company had used the material for a promotional purpose. Even if neither of these applied, the company would be liable if it had been able to influence the content of the material in a manner favourable to its own interests. It was possible for a company to sponsor material which mentioned its own products and not be liable under the Code for its contents, but only if it had been a strictly arm's length arrangement with no input by the company and no use by the company of the material for promotional purposes.

The Panel noted that the publishers of Future Prescriber has proposed *inter alia*, two complementary articles (one of which was the article in question) as part of the 'managed entry programme' for linagliptin 'to support the product' and 'prepare the market'. It was proposed that the article in question would examine current and future treatment options with particular focus on the DPP-4 class and forthcoming products. The proposal also stated that the article would be independently commissioned, peer reviewed and published within the main pages of the journal. There would be no input from the company other than for medical accuracy. Reprints would be made available following publication. Minutes of a meeting between Boehringer Ingelheim the publishers and Lilly once the complaint had been received stated, *inter alia*, that the agreement with the publisher was that it would take all responsibility for generation of the article, choosing of authors (although it could request

input from Boehringer Ingelheim, as it had done in relation to the article in question, but the publishers had made the final choice), managing the writing and review process and publication of the final article.

The Panel considered that it was clear from the proposal that the article would support linagliptin, and that Boehringer Ingelheim would have known this at the outset.

It appeared that although Boehringer Ingelheim did not pay for the article *per se*, it in effect commissioned it through an agreement to pay for 2,000 reprints. The Panel considered that Boehringer Ingelheim was inextricably linked to the production of the article and the company was responsible under the Code for the content.

Turning to the article itself, the Panel noted that the only mention of Boehringer Ingelheim was at the end of the article, after citation of all the references. The Panel considered that the article did not clearly indicate the involvement of the company, and ruled a breach of the Code. As the content was promotional, the Panel considered that it was disguised in that regard and ruled a breach of the Code.

The Panel noted that the article stated that linagliptin was approved in the UK. When the article was published, the product had not received a marketing authorization. The statement in relation to its licence was therefore inaccurate, and a breach of the Code was ruled. In addition, the article promoted a medicine prior to the grant of a marketing authorization and the Panel ruled a breach of the Code. As linagliptin did not have a marketing authorization, and therefore did not have a summary of product characteristics (SPC) at the time of publication, the Panel did not consider that the article promoted the medicine outwith the terms of its marketing authorization or inconsistently with its SPC, and ruled no breach of the Code.

On the evidence before it, the Panel did not consider that linagliptin represented a new class of DPP-4 inhibitors. The title of the article implied that the medicine had some special merit, which could not be substantiated, and the Panel ruled breaches of the Code.

The article made it clear that there were currently no head-to-head trials of linagliptin with other DPP-4 inhibitors. The Panel did not consider that the article made misleading comparisons of the efficacy of linagliptin and other DPP-4 inhibitors as alleged and ruled no breach of the Code.

The Panel noted that the article stated that as linagliptin did not interfere with CYP450 it was 'safer to use' concomitantly with certain medications than saxagliptin. Given that there was no head-to-head trial of linagliptin and saxagliptin, the Panel considered that this claim did not reflect available evidence and was not capable of substantiation by clinical experience, and ruled a breach of the Code.

The Panel noted the complainant's comments in relation to the effect on beta-cell function of linagliptin and renal acceptability of the medicine. The Panel did not know whether any of these claims were correct. The Panel noted that the complainant bore the burden of proof. The Panel also noted its comment above that the company was responsible for the article. The Panel considered that as the product did not have a marketing authorization at the time the article was published, its ruling above of a breach of the Code covered these allegations.

With regard to the allegation that the information about possible cost of linagliptin compared with other DPP-4 inhibitors was not factual and potentially misled in relation to the cost-efficacy of the medicine, the Panel noted that the complainant had not explained why the claim at issue was inaccurate. There was no actual or implied cost-efficacy claim. No breach of the Code was ruled. This ruling was unsuccessfully appealed by the complainant.

The Panel considered that Boehringer Ingelheim would have been aware at the outset of the promotional content of the article. For the company to consider it anything other than a promotional item demonstrated a serious lack of understanding of the Code. High standards had not been maintained and ruled a breach of the Code. The Panel considered that Boehringer Ingelheim's involvement with the publication brought discredit upon and reduced confidence in the pharmaceutical industry, and ruled a breach of Clause 2.

In relation to Lilly's involvement with, and responsibility for, the article, the Panel noted that at the time the content of the article was agreed, Lilly and Boehringer Ingelheim had not formed a co-marketing alliance. The proposal for the article in question was sent only to Boehringer Ingelheim and only Boehringer Ingelheim was mentioned in the title of the proposal. Lilly was not aware of the article until it was contacted by Boehringer Ingelheim. Given the exceptional circumstances the Panel did not consider that Lilly was responsible for the article at issue, and ruled no breach of the Code.

A general practitioner complained about an article on linagliptin published in Future Prescriber.

The article 'Linagliptin: new class of DPP-4 [dipeptidyl peptidase-4] inhibitor in the treatment of T2DM [type 2 diabetes mellitus]' was written by two diabetes and endocrinology physicians. A declaration of the authors' interests was given at the end of the article. The final paragraph, which followed the list of references, stated 'Placement of this article has been funded by Boehringer

Ingelheim and Lilly. The content has been independently commissioned by Future Prescriber and has been checked by Boehringer Ingelheim and Lilly for factual accuracy only. Editorial control of this article remains with Future Prescriber'.

COMPLAINT

The complainant stated that the article represented the exaggerated, misleading and disguised promotion of linagliptin before a UK marketing authorization for the product had been granted. The companies were directly responsible for this given that firstly they had funded development of this article, secondly they had reviewed the article for factual accuracy (which evidently was less than rigorous) and finally the authors (both from the same hospital department) had previously received support from the companies which strongly suggested that their views and opinions were likely to be known by both the companies and that they were likely to have been involved in their selection as authors and briefing.

It was stated that these companies had no editorial control but the complainant submitted that they had had an opportunity and responsibility to correct the following misleading, unsubstantiated and factually incorrect information in an article sponsored by them; which they failed to do.

The complainant noted that the article stated that linagliptin was now approved and due to launch in the UK. Most clinicians would reasonably infer that this meant that the medicine had obtained a marketing authorization from the European Commission (EC) before the article was published; this was not so. To date linagliptin had only received a positive opinion from the European Medicines Agency (EMA) which did not equate to the approval of linagliptin in the European Union as stated in the article. These statements were not only factually inaccurate but promoted the availability of linagliptin in the UK prior to full and final regulatory approval.

The complainant alleged that the title of the article 'Linagliptin: new class of DPP-4 inhibitor in the treatment of T2DM', was misleading and exaggerated. DPP-4 inhibitors belonged to a class of incretin-based therapies and the complainant knew of no other widely recognised or accepted sub-class within this that was clinically relevant. Linagliptin did not represent a new class of treatment for type 2 diabetes. To do so suggested an unqualified and unsubstantiated superiority over currently licenced DPP-4 inhibitors, comparisons with which were made throughout the article. If this were truly a new class of treatment then the complainant wondered why the authors cited the National Institute for Health and Clinical Excellence (NICE) guidelines which did not differentiate between different DPP-4 inhibitors based on sub-class. The complainant alleged that this was clearly a contrived marketing message used to promote linagliptin and noted that even the authors struggled to find any real basis to differentiate linagliptin on the basis of class given that, throughout, they referred to linagliptin as a DPP-4 inhibitor. Indeed, in the conclusions the authors explicitly stated that linagliptin had potential advantages over others in the same class. The only fact that was accurate was that linagliptin was a new DPP-4.

The complainant was surprised that, following the factual accuracy check undertaken by the sponsors, the article was permitted to misleadingly elaborate various comparisons of the safety and efficacy of linagliptin with some of the other DPP-4s mentioned. The complainant asked if it was acceptable or factually accurate to compare the maximal efficacy and potency of linagliptin with other DPP-4 inhibitors or claim that, in relation to use with concomitant medicines, linagliptin was safer than saxagliptin; especially given that there were no head-to-head data with other DPP-4 inhibitors to substantiate this.

The complainant alleged that the article was also misleading and inaccurate when it claimed that linagliptin, unlike other unspecified oral antidiabetic medicines, might have a positive and long enduring effect on beta-cell function and therefore glycaemic control; this was not a fact nor could it be substantiated. The claim that linagliptin had the potential to modify and delay the progression of type 2 diabetes was simply fiction as opposed to fact. Editorial control or not, it was clear that the sponsors had not exercised the necessary diligence in their review of the article.

The complainant stated that an unbalanced and distorted promotional message was also elaborated with regard to the important issue of renal acceptability. As no summary of product characteristics (SPC) or specific licence for use of linagliptin in patients with renal impairment was currently available, it was remarkable that the companies considered it was accurate to promote the renal profile of linagliptin by comparing it to the licensed renal indication for saxagliptin and suggesting that the need to reduce the dosage of saxagliptin in moderate to severe renal disease somehow rendered it inferior to linagliptin. Saxagliptin was currently the only DPP-4 inhibitor with a UK licence for use in moderate/severe renal impairment.

The complainant alleged that in the absence of specific details, it was incredible that the companies permitted the discussion of the possible cost of linagliptin compared with other DPP-4 inhibitors. This was not factual information and potentially misled about the cost-efficacy of this medicine.

The complainant alleged that the decision to fund the development of this article and the evident lack of proper scrutiny of the facts and accuracy of the contents suggested that these companies were keen to promote linagliptin prior to licence and inappropriately steal a competitive advantage over medicines such as saxagliptin.

When writing to Boehringer Ingelheim and Lilly, the Authority asked each to respond in relation to Clauses 2, 3.1, 3.2, 7.2, 7.4, 7.9, 7.10, 9.1, 9.10 and 12.1 of the Code.

RESPONSE

Case AUTH/2424/8/11

Boehringer Ingelheim submitted that in November 2010, the publisher of the article made a proposal to the company for the purchase of a quantity of reprints of four articles to be published in future editions of Future Prescriber. The publisher was to independently commission the articles, determine the outline for their content, select and pay the authors and then publish the article. A copy of the proposal from the publisher was provided.

Boehringer Ingelheim submitted that the primary purpose of the proposal document was to allow it to determine, in advance of the articles being written, whether it would like to pre-pay for the advance purchase of a number of reprints of the four articles. Boehringer Ingelheim provided details of the estimated and actual cost of 2000 reprints of the article in question. The company paid for the reprints before the article was written. No formal, written agreement was entered into for this transaction beyond an invoice from the publisher and a purchase order (from Boehringer Ingelheim), copies of which were provided.

Out of courtesy, the articles, including the one in question, were to be sent to Boehringer Ingelheim for a check of factual accuracy only, and as this was an independently authored piece, commissioned by the publisher, the decision to incorporate any feedback from Boehringer Ingelheim regarding changes to the article was at the discretion of the authors and the publisher.

On 5 July, the article in question was sent to Boehringer Ingelheim for a check of factual accuracy. By this time Boehringer Ingelheim and Lilly had formed an alliance in the diabetes arena. Lilly had no knowledge of, or part in, either the commissioning of the article, its review or of the arrangements with Boehringer Ingelheim for advance purchase of the reprints; these arrangements pre-dated the alliance.

On 15 July, Boehringer Ingelheim identified that the article, for which a factual accuracy check was requested, was not fit for purpose in that it contained multiple factual inaccuracies and breaches of the Code, and inaccurately described Lilly's involvement. Furthermore, Boehringer Ingelheim submitted that the article did not match the description contained in the proposal for which 2,000 reprints had been pre-purchased. For all these reasons Boehringer Ingelheim informed the publisher on 15 July that it did not want the article published (Boehringer Ingelheim understood that this was in advance of the date on which the issue of the journal containing the article went to press). Contrary to Boehringer Ingelheim's wishes, and in the full knowledge of Boehringer Ingelheim's concerns, the publisher sent the article to press and consequently it appeared in the print edition of Future Prescriber. At this point, Boehringer Ingelheim told Lilly about the article and its concerns. On the 18 July, and in response to the concerns raised on 15 July, the publisher wrote to Boehringer Ingelheim and restated its position that the article was independently commissioned by the editors of Future Prescriber, they had independently determined the outline and authorship of the article and that the responsibility for incorporation of any changes requested by Boehringer Ingelheim lay with the publisher.

On 4 August, Boehringer Ingelheim and Lilly informed the publisher about this complaint. Whilst it was not possible to recall the print edition of the journal, the companies asked the publisher to remove the article from the online version of Future Prescriber, which had not yet been published. Boehringer Ingelheim and Lilly had since been reassured by the publisher that the article would not appear in the online version of the journal.

Boehringer Ingelheim stated that linagliptin had not yet received a marketing authorization, although it had received positive opinion from the Committee of Medicinal Products for Human Use (CHMP) of the EMA. A decision from the EC was expected in early September.

In summary, Boehringer Ingelheim submitted that whilst the article failed to comply with the Code, it reassured the Authority that it took appropriate (if ultimately unsuccessful) steps to stop the article being published and, once published, against its wishes, had taken active steps to limit its circulation. Boehringer Ingelheim's only role was to pre-pay for a quantity of reprints of an article that when independently commissioned and written, and on publication did not match the description that Boehringer Ingelheim was given and on which it based its purchasing decision. Boehringer Ingelheim therefore maintained that it had not breached the Code.

In response to a request for further information regarding the substantive issues raised by the complainant and the clauses cited by the Authority, Boehringer Ingelheim strongly denied any breach of the Code as a result of any act or omission on its part. Boehringer Ingelheim submitted that it was clear that the article had been published against its wishes. At that stage the article had not been certified by Boehringer Ingelheim as numerous changes were required for it to comply with the Code. Boehringer Ingelheim submitted it was extremely disappointed that this situation had arisen and had addressed the issue with the publisher. Boehringer Ingelheim believed strongly in its internal approval processes and was committed to maintaining high standards and abiding by the Code at all times. Boehringer Ingelheim referred to this paragraph in response to

the Authority's request for it to consider the requirements of Clauses 3.1, 3.2, 7.2, 7.4, 7.9, 7.10 and 12.1.

Boehringer Ingelheim refuted the allegation of a breach of Clause 9.10. On page 5 of the article it was stated: 'Placement of this article has been funded by Boehringer Ingelheim and Lilly. The content has been independently commissioned by Future Prescriber and has been checked by Boehringer Ingelheim and Lilly for factual accuracy only…'. Boehringer Ingelheim submitted that this statement was incorrect. It did not place this article, it had only pre-paid for reprints of an article that was 'sold' to the company as a disease awareness piece, which when seen clearly was not, and this was why Boehringer Ingelheim tried to stop it being published.

Boehringer Ingelheim strongly refuted the allegation of a breach of Clause 9.1. The company submitted that it had clearly outlined above the sequence of events that led to the article being published. The company also submitted that it was clear that it had informed the publisher that the article was not approved for publication since numerous changes were required. It therefore knew that the article did not comply with the Code and at this stage it had not been certified by Boehringer Ingelheim. However, despite this the article was still published by the publisher against Boehringer Ingelheim's explicit wishes. The company submitted that once it knew that the article had been circulated it took significant steps to stop the publication and significant steps to limit its circulation. The company therefore believed that it had maintained high standards at all times and was not in breach Clause 9.1.

For the reasons stated above, Boehringer Ingelheim also strongly refuted the allegation of breach of Clause 2.

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Lilly noted that in January 2011 it entered into a worldwide alliance with Boehringer Ingelheim for the development and marketing of diabetes medicines. Lilly understood that the article in question was commissioned by Boehringer Ingelheim before the date of the alliance. Lilly had no involvement in the article and was unaware of either it or the arrangements for its publication until it was published in Future Prescriber.

Lilly submitted that the statement at the end of the article regarding its involvement in funding and checking the article for factual accuracy was incorrect and had been included without its approval and/or consent. Lilly stated that it would take the publisher to task over its unauthorised reference to its involvement. Lilly denied a breach of the Code.

Following a request for further information, Lilly submitted that it had not been involved in either commissioning the original article (which occurred in November 2010 prior to the formation of the alliance with Boehringer Ingelheim) nor the review or approval of it. Boehringer Ingelheim paid for the article with no contribution or knowledge of Lilly. Consequently, Lilly did not consider that it was in breach of the Code.

Lilly submitted that it agreed with Boehringer Ingelheim's response. In particular, Lilly noted that the reference to it having had no knowledge of, or part in, either the commissioning of the article, its review, nor the arrangements between Future Prescriber and Boehringer Ingelheim for the advanced purchase of reprints (arrangements which predated Lilly's alliance with Boehringer Ingelheim) was correct and provided evidence that the activity proceeded with no involvement from Lilly.

Lilly submitted that an arrangement for joint approval of alliance materials had been in place since February 2011. The core teams involved in approval for both Boehringer Ingelheim and Lilly were trained in May 2011. The standard operating procedure was formally approved by both companys' senior management and became effective in August 2011.

Lilly noted that the publisher had accepted responsibility for publication of the article in its letter dated 18 July, submitted to the Authority by Boehringer Ingelheim. Boehringer Ingelheim clearly stated that the article was sent to it for a factual accuracy check; no mention was made that Lilly was included and indeed Lilly was not aware of any communication between Boehringer Ingelheim and the publisher concerning the article. As the declaration statement on the article incorrectly referred to Lilly, the publisher had subsequently agreed to publish a correction statement in the next issue of the journal to state that Lilly had no involvement of any sort in the article.

PANEL RULING

Case AUTH/2424/8/11

The Panel noted that it was acceptable for companies to sponsor material. It had previously been decided that the content would be subject to the Code if it was promotional in nature or if the company had used the material for a promotional purpose. Even if neither of these applied, the company would be liable if it had been able to influence the content of the material in a manner favourable to its own interests. It was possible for a company to sponsor material which mentioned its own products and not be liable under the Code for its contents, but only if it had been a strictly arm's length arrangement with no input by the company and no use by the company of the material for promotional purposes.

The Panel noted that the proposal submitted to Boehringer Ingelheim by the publisher was entitled 'Proposal for Boehringer Ingelheim in support of

[Trajenta]. It stated that 'As part of the managed entry programme, appropriate messages must be communicated to healthcare payers in order to prepare the market for the launch of [Trajenta]', and that 'prescribers and payers…..will need to be informed about the unique advantages of [Trajenta]'. It proposed the development of a pair of complementary articles in Future Prescriber to 'support the product'. These would then be followed at launch with a pair of supplements in different journals aimed at payers and prescribers.

The proposal for the article in question was to 'look at the current and future treatment options with particular focus on the DPP4 class and forthcoming products. As the launch of [Trajenta] is likely to be approaching at this point we can include more data on [Trajenta] in this article as it will soon be a licensed option'. The proposal also stated that the article would be independently commissioned, peer reviewed and published within the main pages of the journal. There would be no input from the company other than for medical accuracy. Reprints (2000) would be made available following publication. The Panel noted that minutes submitted by Boehringer Ingelheim for a meeting it had with the publishers of the article and Lilly once the complaint had been received stated that the article format had been agreed as appropriate between the publishers and Boehringer Ingelheim within the timelines of the anticipated launch of Trajenta. The minutes also stated that the agreement with the publisher was that it would take all responsibility for generation of the article, choosing of authors (although it could request input from Boehringer Ingelheim, as it had done in relation to the article in question, but the publishers had made the final choice), managing the writing and review process and publication of the final article.

The Panel disagreed with Boehringer Ingelheim's statement that the article did not match the description given in the proposal on which Boehringer Ingelheim based its decision to purchase reprints, nor did it agree that the article was 'sold' to the company as a disease awareness piece. The Panel considered that it was clear from the proposal that the article would support Trajenta, and that Boehringer Ingelheim would have known this at the outset.

It appeared that although Boehringer Ingelheim did not pay for the article *per se*, it in effect commissioned it through an agreement to pay for 2,000 reprints. The article was a result of a business proposal between the publishers and Boehringer Ingelheim; it would not have been written without the company's agreement to purchase reprints in advance. The Panel considered that Boehringer Ingelheim was inextricably linked to the production of the article, there was no strictly arms length arrangement and in that regard the company was responsible under the Code for the content.

Turning to the article itself, the Panel noted that on the first page, under the heading, appeared the names and affiliations of the authors. The only mention of Boehringer Ingelheim was at the end of the article, after citation of all the references. The Panel considered that the article did not clearly indicate the involvement of the company, and ruled a breach of Clause 9.10. As the content was promotional, the Panel considered that it was disguised in that regard and ruled a breach of Clause 12.1.

The Panel noted that the article stated that linagliptin was approved in the UK and was 'due to launch here soon'. When the article was published, the product had not received a marketing authorization. The statement in relation to its licence was therefore inaccurate, and a breach of Clause 7.2 was ruled. In addition, the article promoted a medicine prior to the grant of a marketing authorization that permitted its sale or supply, and the Panel ruled a breach of Clause 3.1. As linagliptin did not have a marketing authorization, and therefore did not have an SPC at the time of publication, the Panel did not consider that the article promoted the medicine outwith the terms of its marketing authorization or inconsistently with its SPC, and ruled no breach of Clause 3.2.

The Panel noted that the article title was 'Linagliptin: new class of DPP-4 inhibitor in the treatment of T2DM' and the content referred to the medicine belonging to a 'new chemical class of xanthine-based DPP-4 inhibitors'. On the evidence before it, the Panel did not consider that linagliptin represented a new class of DPP-4 inhibitors. The statement implied that the medicine had some special merit, which could not be substantiated, and the Panel ruled a breach of Clauses 7.10 and 7.4.

The article detailed a number of placebo-controlled trials using linagliptin monotherapy or combination therapy with other oral antidiabetic agents. It made it clear that there were currently no head-to-head trials of linagliptin with other DPP-4 inhibitors. The Panel did not consider that the article made misleading comparisons of efficacy of linagliptin and other DPP-4 inhibitors as alleged and ruled no breach of Clause 7.2 in that regard.

The Panel noted that the article stated linagliptin did not interfere with CYP450 and so was 'unlikely to affect the pharmacokinetics of agents that are metabolized by this system'. It then went on to say that as a result of this, linagliptin was 'safer to use' concomitantly with medications such as rifampicin, ketoconazole or diltiazem than saxagliptin. Given that there was no head-to-head trial of linagliptin and saxagliptin, the Panel considered that this claim about the medicines comparative safety did not reflect available evidence and was not capable of substantiation by clinical experience, and ruled a breach of Clause 7.9.

The Panel noted the complainant's comments in relation to reference in the article to the effect on beta-cell function of linagliptin and renal acceptability of the medicine. The article stated that adequate DPP-4 inhibition by linagliptin offered increased availability of GLP-1 endogenously, which in turn stimulated the proliferation and differentiation of beta-cells and hence improved markers of beta-cell function. It also stated that, unlike treatment with other oral hypoglycaemic therapies, which progressively lost glycaemic control over time, linagliptin might have the desired effect of glycaemic durability, as its DPP-4 inhibitory action was glucose dependent. In relation to renal impairment, the article stated that in a phase 3 study, 50% of patients receiving linagliptin had moderate to severe renal function, yet the trough linagliptin concentration in the treatment group was similar to those with normal renal function. The article noted that this implied dose adjustment might not be required in renally impaired patients. The Panel did not know whether any of these claims were correct. The Panel noted that the complainant bore the burden of proof. The Panel also noted its comment above that the company was responsible for the article. The Panel considered that as the product did not have a marketing authorisation at the time the article was published, its ruling of a breach of Clause 3.1 above covered these allegations.

The Panel noted the complainant's allegation that the information about possible cost of linagliptin compared with other DPP-4 inhibitors was not factual and potentially misled in relation to the cost-efficacy of the medicine. The article stated that the cost of linagliptin was anticipated to be similar to the other already marketed DPP-4 inhibitors ie around £32 per month. The Panel noted that the complainant bore the burden of proof. The Panel noted that the complainant had not explained why the claim at issue was inaccurate. There was no actual or implied cost-efficacy claim. No breach of Clause 7.2 was ruled. This ruling was appealed by the complainant.

Taking all the circumstances in to account, the Panel considered that Boehringer Ingelheim would have been aware at the outset of the promotional content of the article. For the company to consider it anything other than a promotional item demonstrated a serious lack of understanding of the Code. The Panel considered that high standards had not been maintained and ruled a breach of Clause 9.1 in that regard. The Panel was concerned that the company had entered into the agreement with the publisher given that the proposal described promotional articles prior to the grant of the product's marketing authorization. The Panel noted that such activity was one of the examples given in the Code as likely to lead to a breach of Clause 2. The Panel noted that Boehringer Ingelheim's submission that it had tried to prevent publication, but considered that Boehringer Ingelheim's involvement with the publication brought discredit upon and reduced confidence in the pharmaceutical industry, and ruled a breach of Clause 2.

APPEAL BY THE COMPLAINANT

The complainant stated that the article extensively promoted the efficacy and other benefits of linagliptin in direct comparison to other DPP-4 inhibitors and then referred to the (unconfirmed) cost for linagliptin. In this context the statement that the anticipated cost of linagliptin was likely to be similar to the other already marketed DPP-4 inhibitors was a direct claim of the similar or comparable cost (and cost-efficacy) of linagliptin to other DPP-4 inhibitors. The complainant appealed the Panel's ruling of no breach of Clause 7.2.

COMMENTS FROM BOEHRINGER INGELHEIM

Boehringer Ingelheim did not comment upon the reasons for the appeal and had nothing further to add to its response to the Panel.

FINAL COMMENTS FROM THE COMPLAINANT

The complainant had no comment on Boehringer Ingelheim's response.

APPEAL BOARD RULING

The Appeal Board noted that the article had been published against Boehringer Ingelheim's wishes. The company had not provided any information for inclusion in the article. Boehringer Ingelheim submitted at the appeal hearing that the price range for linagliptin was not in the public domain when the article was published. It was not known what information the authors had relied upon when drafting the claim at issue. In the event it had turned out that the cost quoted in the article was similar to the actual cost of the medicine once launched and similar to the other DPP-4 inhibitors already marketed.

On the narrow grounds of the complaint the Appeal Board considered that when the claim at issue, 'The cost of linagliptin is anticipated to be similar to the other already marketed DPP-4 inhibitors (ie around £32 per month)', was made it was not in itself misleading as alleged. Further, the actual cost of the product did not, in the circumstances, render the claim misleading. The Appeal Board upheld the Panel's ruling of no breach of Clause 7.2. The appeal on this point was thus unsuccessful.

Case AUTH/2425/8/11

The Panel noted that at the time the content of the article was agreed, Lilly and Boehringer Ingelheim had not formed an alliance for the promotion of Trajenta. The proposal for the article in question was sent only to Boehringer Ingelheim and only Boehringer Ingelheim was mentioned in the title of the proposal. The Panel noted the submission from both companies that Lilly was not aware of the

article until it was contacted by Boehringer Ingelheim in July. Lilly had not contributed to the payment made to the publishers and the article was not sent to Lilly for it to check the factual accuracy of the content. The Panel noted that an arrangement for joint approval of materials had been in place since February 2011. The approval workflow referred to pre-launch materials. However, given the exceptional circumstances and irrespective of the fact that Lilly's name appeared on the material, the Panel did not consider that Lilly was responsible for the article at issue, and ruled no breach of Clauses 2, 3.1, 3.2, 7.2, 7.4, 7.9, 9.1, 9.10 and 12.1 of the Code.

Complaint received **3 August 2011**

Case AUTH/2424/8/11 completed **16 November 2011**

Case AUTH/2425/8/11 completed **4 October 2011**