CASE AUTH/3381/9/20 *NO BREACH OF THE CODE*

COMPLAINANT v BOEHRINGER INGELHEIM

Online promotion of Trajenta

A complainant, who described him/herself as a concerned UK health professional, complained about a Trajenta (linagliptin) dynamic digital banner advertisement (ref PC-GB-101179) placed by Boehringer Ingelheim on the Guidelines in Practice website. Trajenta was indicated as an adjunct to diet and exercise to improve glycaemic control in certain adult patients with type 2 diabetes.

The complainant alleged that the headlines 'Simplicity' and 'Reinforced' and the claim 'for a broad range of adults with type 2 diabetes' was not a licenced indication for Trajenta. The indication for Trajenta as stated in the summary of product characteristics (SPC) was:

> **'Trajenta is indicated in adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control as:**
>
> **monotherapy**
>
> **• when metformin is inappropriate due to intolerance, or contraindicated due to renal impairment.**
>
> **combination therapy**
>
> **• in combination with other medicinal products for the treatment of diabetes, including insulin, when these do not provide adequate glycaemic control (see sections 4.4, 4.5 and 5.1 for available data on different combinations).'**

The complainant stated that on the website itself, the writing on the banner was so small and it cycled so rapidly that he/she was unable to read the writing on the right-hand side – which included where the prescribing could be found.

The complainant provided an image of another one of the frames and noted that it included the claim 'Unique convenience through always one dose, once daily'. The complainant submitted that Trajenta was not the only medicine that was one dose, once daily.

The detailed response from Boehringer Ingelheim is given below.

The Panel noted that the case preparation manager had raised Clause 4.1 which required that the prescribing information be provided in a clear and legible manner in all promotional material for a medicine except for abbreviated advertisements. In the Panel's view, there was no allegation that the prescribing information had not been provided; the allegation was that the link to the prescribing information was so small, and cycled so quickly, that it could not be easily read. The Panel thus did not consider that Clause 4.1 was relevant to the complaint and so it ruled no breach of the Code in that regard.

The Panel noted that Clause 4.6 stated that in the case of promotional material included on the Internet, there must be a clear, prominent statement as to where the prescribing information could be found. Although Clause 4.6 had not been raised by the case preparation manger, Clause 9.1 (high standards) had been raised and so the Panel considered the allegation about the legibility of the link to the prescribing information under that clause instead. The Panel noted that at the very least, there was a disparity between the size of the claims in the banner advertisement and that of the statement as to where the prescribing information could be found; the complainant referred to having to increase the font size to read the latter but it did not appear that he/she had had to do the same to read the promotional claims. Nonetheless, on the evidence before it, and bearing in mind the difficulty of knowing exactly how the banner advertisement appeared on the complainant's screen, on balance, the Panel did not consider that the link to the prescribing information was too small or cycled too rapidly to be read as alleged and no breach was ruled.

The Panel noted that the complainant provided an image of one frame of the banner advertisement which stated 'for a broad range of adults with type 2 diabetes' but had provided no reasons to support his/her allegation that the phrase was not a licensed indication for Trajenta. It was not for the Panel to make out a complainant's case. The Panel noted Trajenta's indication and Boehringer Ingelheim's submission that according to Section 4.2 of its SPC, no dose adjustment or specific caution was needed for the elderly nor adults with renal or hepatic impairment. The Panel noted that the complainant bore the burden of proof. A judgement had to be made based on the available evidence. The Panel did not consider, based on the allegation, that the complainant had established that the claim 'for a broad range of adults with type 2 diabetes' was inconsistent with the particulars listed in the Trajenta SPC and no breach of the Code was ruled.

With regard to the claim 'Unique convenience through always one dose, once daily', the complainant stated that Trajenta was not the only medicine that was one dose, once daily and referred to an oral contraceptive pill, Cerazette (desogestrel) as an example. The Panel further noted Boehringer Ingelheim's submission that 'unique' had been used in the context of treatments for type 2 diabetes and that Trajenta 5mg dosing was referred to as 'unique' as only one dose, once daily was always needed in adults with type 2 diabetes, regardless of renal or liver function or age of the patient. The Panel further noted Boehringer Ingelheim's submission that Trajenta did not need a separate initiation dose, nor did it need dose adjustments according to patient needs and no other currently available treatments for type 2 type diabetes (oral or injectables) had those combined dosing qualities. Based on the evidence before it, the Panel did not consider that the complainant had shown that the claim 'Unique convenience through always one dose,

once daily' in relation to Trajenta for type 2 diabetes was misleading or incapable of substantiation and no breaches of the Code were ruled.

The Panel noted its comments and rulings above and did not consider that there was evidence to show that Boehringer Ingelheim had failed to maintain high standards and no breach of the Code was ruled.

A complainant, who described him/herself as a concerned UK health professional, complained about a Trajenta (linagliptin) dynamic digital banner advertisement (ref PC-GB-101179) placed by Boehringer Ingelheim on the Guidelines in Practice website. Trajenta was indicated as an adjunct to diet and exercise to improve glycaemic control in certain adult patients with type 2 diabetes.

COMPLAINT

The complainant provided an image of one of the frames making up the banner advertisement which included the headlines 'Simplicity' and 'Reinforced' and the claim 'for a broad range of adults with type 2 diabetes'. The complainant stated that unsurprisingly, that phrase was not a licenced indication for Trajenta. The indication for Trajenta as stated in the summary of product characteristics (SPC) was:

> 'Trajenta is indicated in adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control as:
>
> monotherapy
>
> • when metformin is inappropriate due to intolerance, or contraindicated due to renal impairment.
>
> combination therapy
>
> • in combination with other medicinal products for the treatment of diabetes, including insulin, when these do not provide adequate glycaemic control (see sections 4.4, 4.5 and 5.1 for available data on different combinations).'

The complainant stated that on the website itself, the writing on the banner was so small and it cycled so rapidly that he/she was unable to read the writing on the right-hand side – which was very important as it included where the prescribing could be found (he/she had to alter the text size on his/her monitor to do so).

The complainant provided an image of another one of the frames and noted that it included the claim 'Unique convenience through always one dose, once daily'. The complainant submitted that Trajenta was not the only medicine that was one dose, once daily, eg Cerazette [desogestrel, Organon Pharma] was also one dose, once daily.

When writing to Boehringer Ingelheim, the Authority asked it to consider the requirements of Clauses 3.2, 4.1, 7.2, 7.4 and 9.1 of the Code.

RESPONSE

Boehringer Ingelheim Limited stated that it took compliance with the Code very seriously. As per the requirements of the Code, Boehringer Ingelheim had a Standing Operating Procedure (SOP) in place for materials approval, which ensured that all materials were reviewed and certified for accuracy and compliance with the Code prior to being made available.

Boehringer Ingelheim stated that the Trajenta dynamic digital banner advertisement in question had been placed on the digital edition of Guidelines in Practice and was scheduled to appear on a fortnightly basis from March 2020 until the first week of December 2020. A pdf copy of the advertisement and associated approval certificate were provided.

Boehringer Ingelheim stated that Trajenta had been licensed for more than 9 years, therefore its brand name, active ingredients, and dosing regimen were generally well known amongst health professionals. The purpose of the advertisement was to remind health professionals of the benefits of Trajenta, including convenience of its dosing regimen.

Boehringer Ingelheim stated that the dynamic digital banner advertisement appeared at the bottom of appropriate webpages on the online edition of Guidelines in Practice (ie a 'crawler' banner). In order to access the contents on the digital edition of Guidelines in Practice, UK-based doctors, nurses and pharmacists could register for free, and other health professionals could access the contents by a low-cost subscription. Therefore, only registered users who were confirmed as UK health professionals could view Guidelines in Practice and thus the advertisement for Trajenta. The intended audience of the digital edition of Guidelines in Practice was made clear on each webpage which stated 'This site is intended for UK healthcare professionals'. The intended audience was also made clear on the dynamic digital banner advertisement itself as it stated it was for 'Healthcare professionals only'.

The dynamic digital banner advertisement was comprised of five rotating frames which appeared in sequential order. The advertisement always started with the first frame. Each frame was visible for approximately 3 seconds, making the whole advertisement approximately 15 seconds in duration. The prescribing information and adverse event reporting link could be found on the right-hand side of each frame and was static throughout the whole duration of the advertisement, ie appeared on each of the frames of the digital banner advertisement at all times.

The item was certified as a dynamic digital banner advertisement only, with the resolution of the digital advertisement (728 x 90 pixels) included in the description of the job bag. As per the company's Materials Approval SOP, the final form of the advertisement and the associated prescribing information were checked and found to be legible and in line with the requirements of Clause 4.1. Boehringer Ingelheim noted that in the description of the job bag in the meta-data, a test link was provided which showed the dynamic banner advertisement as it would appear in the digital edition of Guidelines in Practice.

Boehringer Ingelheim noted that the complainant referred to the claim '…for a broad range of adults with type 2 diabetes…'. Boehringer Ingelheim submitted that the licenced indication for Trajenta as per the SPC was:

> 'Trajenta is indicated in adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control as:
>
> <u>Monotherapy</u>

• when metformin is inappropriate due to intolerance, or contraindicated due to renal impairment.

Combination therapy

• in combination with other medicinal products for the treatment of diabetes, including insulin, when these do not provide adequate glycaemic control.'

Boehringer Ingelheim noted that, additionally, as per section 4.2 of the SPC, no dose adjustment or caution was needed for the elderly nor adults with renal or hepatic impairment. The safety and efficacy of Trajenta in children and adolescents had not yet been established and therefore they were excluded.

Boehringer Ingelheim noted that Clause 3.2 stated that 'The promotion of a medicine must be in accordance with the terms of its marketing authorization and must not be inconsistent with the particulars listed in its summary of product characteristics'. The Blue Guide from the Medicines and Healthcare products Regulatory Agency (MHRA) reinforced this and stated that 'An advertisement might include statements not included in the SPC provided these could be substantiated and are not inconsistent with the SPC information'.

Boehringer Ingelheim submitted that the claim 'broad range of adults with type 2 diabetes' was indicative of the extensive marketing authorisation for Trajenta as no adult categories were excluded, (such as patients with renal or hepatic impairment or the elderly population) and was not inconsistent with the SPC nor the clinical trial data found within the SPC.

The prescribing information (which was provided via a direct single click link on the digital banner advertisement throughout), provided the full indication for Trajenta which health professionals could refer to should they wish to at any point whilst viewing the digital banner advertisement.

Therefore, Boehringer Ingelheim stated that the claim 'broad range of adults with type 2 diabetes' was not inconsistent with the licensed indication for Trajenta and so met the requirements of Clause 3.2 of the Code and MHRA guidance as described above.

Boehringer Ingelheim noted that the complainant considered that the writing on the advertisement was small. He/she also stated that the digital banner advertisement cycled rapidly and so these two things together meant that he/she was unable to view the information on the right-hand side which included the prescribing information and adverse event reporting link.

Boehringer Ingelheim noted that the banner advertisement started with the first frame, continued in a sequential fashion until the end, and then looped back to the beginning to the first frame. The scroll time was approximately 3 seconds on each frame, and the total duration for the whole advertisement was approximately 15 seconds. Boehringer Ingelheim did not consider that the advertisement cycled too quickly; readers had enough time to read all the information in the context of type 2 diabetes.

The right-hand side of the digital banner, which contained the prescribing information and adverse event reporting link, was provided as part of the advertisement, and remained static and unchanged throughout the whole cycle duration of approximately 15 seconds, so that

readers could view the information via a single direct click at any point whilst looking at the advertisement.

The resolution of the advertisement was included in the description of the job bag (728 x 90 pixels). It was anticipated that the advertisement would be of sufficient resolution to be viewed on any device. The digital banner advertisement and all links visible on the advertisement (including the prescribing information and adverse event reporting link) were checked by the final signatory via a test link to ensure that the functionally, accuracy and legibility met the requirements of the Code and matched the certified item before the advertisement went live. This was documented by the signatory when he/she signed the second box on the approval certificate.

The advertisement was also checked by the originator once it had gone live on the digital edition of Guidelines in Practice to ensure that the functionality, accuracy and legibility met Code requirements.

Therefore, Boehringer Ingelheim believed that the banner advertisement, its cycling time, and associated prescribing information and adverse event reporting link appeared in a clear and legible manner as per the requirements of Clause 4.1. The link to the prescribing information and adverse event reporting link, positioned for ease of access for the viewer, was static and visibly associated with every cycling frame. Boehringer Ingelheim thus considered that the advertisement and associated prescribing information met all the requirements of Clause 4.1.

With regard to the claim 'Unique convenience, through always one dose, once daily', Boehringer Ingelheim submitted that 'unique' had been used in the context of treatments for type 2 diabetes. Trajenta 5mg dosing was referred to as 'unique' as only one dose, once daily was always needed in adults with type 2 diabetes, regardless of the level of renal or liver impairment or in the elderly population. Additionally, Trajenta did not need a separate initiation dose, nor did it need dose adjustments according to patient needs. No other currently available treatments for type 2 type diabetes (oral or injectables) had these combined dosing qualities. The claim was substantiated by the information in the Trajenta SPC. Careful consideration of the word 'unique' had been used, and an extensive review of all marketed products in the UK for type 2 diabetes had been completed to ensure Boehringer Ingelheim met the requirements of Clauses 7.2 and 7.4.

Boehringer Ingelheim stated that it would continue to review the range of available treatments for type 2 diabetes to ensure it continued to meet requirements of Clauses 7.2 and 7.4 and would update its materials accordingly.

Boehringer Ingelheim noted the complainant's allegation that the claim was not true, as other medicines on the market also had one dose, one daily; in that regard he/she explicitly referred to Cerazette. It was clear from the digital banner advertisement that the claim had been made in the context of treatments for type 2 diabetes and not as a comparison with all or any medicines available in the UK market, which made the comparison with Cerazette not applicable. Therefore, Boehringer Ingelheim considered that it had met the requirements of Clauses 7.2 and 7.4 respectively.

In conclusion, Boehringer Ingelheim considered that it had provided evidence, explanation and substantiation that it had ensured its digital banner advertisement met all requirements of the Code, specifically Clauses 3.2, 4.1, 7.2 and 7.4. Therefore, Boehringer Ingelheim did not

consider that it had failed to maintain high standards in the pharmaceutical industry; the company denied a breach of Clause 9.1.

PANEL RULING

With regard to the time that the prescribing information link was visible, the Panel noted Boehringer Ingelheim's submission that it was on the right-hand side of each of the five rotating frames and thus essentially remained static and unchanged throughout the advertisement's whole cycle duration of approximately 15 seconds; readers could view the information via a single direct click at any point whilst looking at the advertisement. With regard to how easy it was to read where the prescribing information could be found, the Panel noted that the link to the prescribing information on the right-hand side of the banners in the screenshots provided by the complainant was much less prominent than the claims within each banner. The Panel further noted that the overall readability of the second screenshot provided by the complainant appeared diminished compared with the first screenshot he/she provided. The Panel did not know what device the complainant had used and so it was difficult to know exactly how the advertisement appeared to him/her. The Panel noted, however, that the complainant had stated that he/she had altered the text size on his/her monitor in order to read the information on the right-hand side of the banner which included where the prescribing information could be found. The Panel noted Boehringer Ingelheim's submission about the resolution of the digital advertisement and that it anticipated that it would be of sufficient resolution to be viewed on any device. The Panel noted Boehringer Ingelheim's submission that the advertisement and all links including the prescribing information and adverse event reporting link were checked by the final signatory via a test link to ensure that the functionally, accuracy and legibility met the requirements of the Code. The Panel noted Boehringer Ingelheim's submission that the advertisement was also checked by the originator once it had gone live to ensure that the functionality, accuracy and legibility met Code requirements. It was not clear which device(s) the signatory and originator had used to perform their check; Boehringer Ingelheim made no submission in that regard.

The Panel noted that the case preparation manager had raised Clause 4.1 which required that the prescribing information listed in Clause 4.2 be provided in a clear and legible manner in all promotional material for a medicine except for abbreviated advertisements. In the Panel's view, there was no allegation that the prescribing information had not been provided; the allegation was that the link to the prescribing information was so small, and cycled so quickly, that it could not be easily read. The Panel thus did not consider that Clause 4.1 was relevant to the complaint and so it ruled no breach of Clause 4.1 in that regard.

The Panel noted that Clause 4.6 stated that in the case of promotional material included on the Internet, there must be a clear, prominent statement as to where the prescribing information could be found. Although Clause 4.6 had not been raised by the case preparation manger, Clause 9.1 (high standards) had been raised and so the Panel considered the allegation about the legibility of the link to the prescribing information under that clause instead. The Panel noted that at the very least, there was a disparity between the size of the claims in the banner advertisement and that of the statement as to where the prescribing information could be found; the complainant referred to having to increase the font size to read the latter but it did not appear that he/she had had to do the same to read the promotional claims. Nonetheless, on the evidence before it, and bearing in mind the difficulty of knowing exactly how the banner advertisement appeared on the complainant's screen, on balance, the Panel did not consider

that the link to the prescribing information was too small or cycled too rapidly to be read as alleged and no breach of Clause 9.1 was ruled.

The Panel noted that the complainant provided an image of one frame of the banner advertisement which stated 'for a broad range of adults with type 2 diabetes' but had provided no reasons to support his/her allegation that the phrase was not a licensed indication for Trajenta. It was not for the Panel to make out a complainant's case. The Panel noted Trajenta's indication and Boehringer Ingelheim's submission that according to Section 4.2 of its SPC, no dose adjustment or specific caution was needed for the elderly nor adults with renal or hepatic impairment. The Panel noted that the complainant bore the burden of proof. A judgement had to be made based on the available evidence. The Panel did not consider, based on the allegation, that the complainant had established that the claim 'for a broad range of adults with type 2 diabetes' was inconsistent with the particulars listed in the Trajenta SPC and no breach of Clause 3.2 was ruled.

With regard to the claim 'Unique convenience through always one dose, once daily', the complainant stated that Trajenta was not the only medicine that was one dose, once daily and referred to Cerazette [desogestrel] as an example. The Panel noted that Cerazette was an oral contraceptive pill. The Panel further noted Boehringer Ingelheim's submission that 'unique' had been used in the context of treatments for type 2 diabetes and that Trajenta 5mg dosing was referred to as 'unique' as only one dose, once daily was always needed in adults with type 2 diabetes, regardless of renal or liver function or age of the patient. The Panel further noted Boehringer Ingelheim's submission that Trajenta did not need a separate initiation dose, nor did it need dose adjustments according to patient needs and no other currently available treatments for type 2 type diabetes (oral or injectables) had those combined dosing qualities. Based on the evidence before it, the Panel did not consider that the complainant had shown that the claim 'Unique convenience through always one dose, once daily' in relation to Trajenta for type 2 diabetes was misleading or incapable of substantiation and no breach of Clauses 7.2 and 7.4 were ruled.

The Panel noted its comments and rulings above and did not consider that there was evidence to show that Boehringer Ingelheim had failed to maintain high standards and no breach of Clause 9.1 was ruled.

Complaint received **10 September 2020**

Case completed **22 March 2021**