NO BREACH OF THE CODE

CASES AUTH/3456/1/21 and AUTH/3457/1/21

COMPLAINANT v BOEHRINGER INGELHEIM AND ELI LILLY

Alleged promotion of Jardiance

An anonymous contactable complainant who described him/herself as a concerned UK health professional, complained about the promotion of Jardiance (empagliflozin) by the Boehringer Ingelheim Limited and Eli Lilly and Company Alliance.

The complainant provided a link to a website and a screenshot of an on-demand promotional webcast which included videos and slides. The webcast was entitled 'Improving cardiovascular outcomes in type 2 diabetes with SGLT2 inhibitors – What is the role of the cardiologist?' The complainant noted that if a reader accessed the website, the following statement, referenced to the summary of product characteristics (SPC), appeared at the bottom of the webpage:

> **'Jardiance is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise.**
>
> - **As monotherapy when metformin is considered inappropriate due to intolerance**
> - **In addition to other medicinal products for the treatment of diabetes**
>
> **Both improvement of glycaemic control and reduction of cardiovascular morbidity and mortality are an integral part of the treatment of type 2 diabetes'.**

The complainant noted, however, that Section 4.1 of the SPC stated 'For study results with respect to combinations, effects on glycaemic control and cardiovascular events, and the populations studied, see sections 4.4, 4.5 and 5.1' and not 'Both improvement of glycaemic control and reduction of cardiovascular morbidity and mortality are an integral part of the treatment of type 2 diabetes' as was stated on the webpage. The complainant alleged that at best this failed to reference the claim, and at worst the claim wilfully misled clinicians as to the indication in the Jardiance SPC - especially cardiologists who had less familiarity with that class of medicines as they did not treat diabetes.

The complainant referred to two slide sets and alleged that both promoted SGLT2 inhibitors as assisting in cardiovascular outcomes. The complainant provided screenshots from the first slide set and referred to slide 9 which was headed 'We now have evidence that some SGLT2 inhibitors and GLP-1 receptor agonists have cardiovascular benefits*'. A footnote to the graphic on that slide was a statement that [Jardiance] was not licensed for any cardiovascular benefits. That approach appeared to be the case throughout the slide deck showing data on improved cardiovascular

outcomes with a small footnote to state it was not licensed, with the only clarifications on the licence being that stated above.

The complainant alleged that the conclusion slide on page 48 was another example of the same. The slide stated that in the EMPA-REG OUTCOME empagliflozin compared with placebo showed: 3P-MACE ARR 1.8%; CV death ARR 2.2%; HHF ARR 1.4%; and all-cause mortality ARR 2.6%. The conclusion stated, 'Cardiologists are uniquely positioned to take the lead and become more involved in the treatment of patients with type 2 diabetes and cardiovascular disease'.

The complainant noted that the second slide deck had the same indication for Jardiance as stated above. As above, the statement was not in the SPC, although again that was the sole reference given. As the same wording was given in all cases, it appeared that the companies were using their 'interpretation' of their licence in a wide variety of cases, and not just these materials with no substantiation.

Cardiologists did not treat diabetes, but the slide set was aimed at clinicians who, under the current licence, did not treat these patients with Jardiance.

The complainant alleged that both slide sets would clearly encourage off-licence use of Jardiance, as it was well established that a footnote did not make the body of the slide acceptable. The complainant alleged that this failed to maintain high standards and brought the profession into disrepute.

The complainant alleged that prescribing information on the website was out of date. The complainant further alleged that the material was easily available to the public and appeared to demonstrate poor oversight of the third parties that the pharmaceutical companies worked with.

The detailed response from Boehringer Ingelheim and Lilly Alliance is given below.

The Panel noted the Alliance's submission that the two slide decks were updated in October 2020, due to a prescribing information update, and recertified as a single deck of 50 slides.

The Panel noted that Section 4.1, Therapeutic Indications, of the Jardiance SPC referred the reader to other sections of the SPC (including Section 5.1) for, amongst other things, study results with respect to the effects of Jardiance on cardiovascular events. In that regard, Section 5.1 under a heading of 'Clinical efficacy and safety', included that 'Both improvement of glycaemic control and reduction of cardiovascular morbidity and mortality are an integral part of the treatment of type 2 diabetes'. The Panel thus considered that the first statement highlighted by the complainant (which appeared on the webcast homepage and slide three of the combined slide set)

> **'Jardiance is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise.**
>
> - **As monotherapy when metformin is considered inappropriate due to intolerance**
> - **In addition to other medicinal products for the treatment of diabetes**

Both improvement of glycaemic control and reduction of cardiovascular morbidity and mortality are an integral part of the treatment of type 2 diabetes'

was substantiated by the reference cited (the SPC) and was not misleading as to the licensed indication for Jardiance; the primary reason for prescription was made clear at the outset ie the treatment of adults with insufficiently controlled type 2 diabetes. The Panel ruled no breaches of the Code in relation to each of the webcast homepage and the combined slide set.

With regard to the complainant's allegation that the slides promoted SGLT2 inhibitors as assisting in cardiovascular outcomes and would encourage off-licence use of Jardiance, as it was well established that a footnote did not make the body of the slide acceptable, the Panel noted that whilst the complainant alleged that it appeared to be the case throughout the slides, he/she only referred specifically to slides 9 and 48 of the combined deck as examples.

The Panel noted the content of slides 9 and 48, including the footnotes reminding the reader that Jardiance was not indicated for reduction of cardiovascular risk or the treatment of heart failure. The Panel noted that whilst it might have been helpful to include on the summary slide (slide 48), when discussing the outcomes of the EMPA-REG trial that it was conducted in patients with type 2 diabetes, it was clear from previous slides which discussed the trial. The Panel further noted the title of the webcast, the individual presentations and the multiple references to type 2 diabetes throughout the presentations, including the text in the red highlighted box on the summary slide which referred to cardiologists being positioned to take the lead and become involved in the treatment of patients with type 2 diabetes and cardiovascular disease and considered that it was clear that the information presented was set within the context of treating type 2 diabetes. The Panel did not consider that the complainant had established that the slide set was misleading or promoted Jardiance in a manner that was inconsistent with the particulars listed in its SPC as alleged and no breaches of the Code were ruled.

The Panel noted the complainant's statement that the entire slide set was aimed at cardiologists who did not treat diabetes and under the current licence, did not treat these patients with Jardiance. The Panel, however, noted the Alliance's submission that type 2 diabetes and cardiovascular disease were intrinsically connected; over a third of patients with type 2 diabetes had concurrent cardiovascular disease which remained the leading cause of morbidity and mortality in those patients. Further the Panel noted the Alliance's submission regarding the content of clinical guidelines on the treatment of type 2 diabetes and the use of SGLT2 inhibitors to reduce cardiovascular risk and the outcome of a survey from the ESC aimed at NHS consultant cardiologists.

The Panel noted its comments and rulings above and considered that with regard to the webcast homepage and the combined slide set there was no evidence that high standards had not been maintained. No breaches of the Code were ruled including no breach of Clause 2.

It appeared to the Panel that the out of date prescribing information provided by the complainant could only be accessed from the server by using specific terms in an

internet search engine or the specific URL provided by the complainant; it could not be accessed from the live website as alleged. The Panel considered that, on the balance of probabilities, the complainant had not shown that the out of date prescribing information in question was accessible to health professionals through the website. The Panel considered that what was now out of date prescribing information on the server, which could not be accessed from the website, did not amount to a breach of the Code as alleged. No breach of the Code was ruled.

The Panel, noting its comments above with regard to how the out of date prescribing information could be accessed, did not consider that the outdated prescribing information was easily available to the general public as alleged. No breach of the Code was ruled.

In the Panel's view, this case illustrated that companies should exercise extreme caution and wherever possible ensure that pages which were not intended for viewing were either fully deleted or securely hidden and thus inaccessible including through an internet search. Companies were responsible for the acts and omissions of third parties acting on their behalf in this regard.

In the Panel's view, the complainant had not established that the Alliance had poor oversight over the third parties it worked with as alleged. Although the Panel was concerned that out of date prescribing information had been accessed, given its comments and rulings above, it considered that, in the specific circumstances of this case, the Alliance had not failed to maintain high standards as alleged. No breach of the Code was ruled. The Panel consequently ruled no breach of Clause 2.

An anonymous contactable complainant who described him/herself as a concerned UK health professional, complained about the promotion of Jardiance (empagliflozin) by the Boehringer Ingelheim Limited and Eli Lilly and Company Alliance.

Jardiance, a sodium-glucose co-transporter-2 (SGLT2) inhibitor, was indicated for the treatment of certain adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise.

COMPLAINT

The complainant provided a link to a website and a screenshot of an on-demand promotional webcast which included videos that could be watched and slides that could be downloaded. The webcast was entitled 'Improving cardiovascular outcomes in type 2 diabetes with SGLT2 inhibitors – What is the role of the cardiologist?' The complainant noted that if a reader accessed the website, the following statement, referenced to the summary of product characteristics (SPC), appeared at the bottom of the webpage:

> 'Jardiance is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise.
>
> - As monotherapy when metformin is considered inappropriate due to intolerance
> - In addition to other medicinal products for the treatment of diabetes

Both improvement of glycaemic control and reduction of cardiovascular morbidity and mortality are an integral part of the treatment of type 2 diabetes'.

The complainant noted, however, that the SPC stated:

'**4.1 Therapeutic indications**

Jardiance is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise

- as monotherapy when metformin is considered inappropriate due to intolerance

- in addition to other medicinal products for the treatment of diabetes

For study results with respect to combinations, effects on glycaemic control and cardiovascular events, and the populations studied, see sections 4.4, 4.5 and 5.1.'

The complainant alleged that at best this failed to reference the claim, and at worst the claim wilfully misled clinicians as to what the indication was in the Jardiance SPC - especially cardiologists who had less familiarity with that class of medicines as they did not treat diabetes.

The complainant referred to two slide sets, providing the same link to each, and alleged that both promoted SGLT2 inhibitors as assisting in cardiovascular outcomes. In addition, the complainant provided screenshots from the first slide set.

In that regard the complainant referred to slide 9 which was headed 'We now have evidence that some SGLT2 inhibitors and GLP-1 receptor agonists have cardiovascular benefits*'. The complainant noted that in a footnote to the graphic on that slide was a statement that [Jardiance] was not licensed for any cardiovascular benefits. That approach appeared to be the case throughout with the body of the slide deck showing data on improved cardiovascular outcomes with a small footnote to state it was not licensed, with the only clarifications on the licence being that stated above.

The complainant stated that it appeared that the companies themselves did not believe their own statements on their interpretation of their licensed indication, but that might well be lost on clinicians.

The complainant submitted that the conclusion slide on page 48 was another example of the same. The slide stated that in the EMPA-REG OUTCOME empagliflozin compared with placebo showed: 3P-MACE ARR 1.8%; CV death ARR 2.2%; HHF ARR 1.4%; and all-cause mortality ARR 2.6%. The conclusion stated, 'Cardiologists are uniquely positioned to take the lead and become more involved in the treatment of patients with type 2 diabetes and cardiovascular disease'.

The complainant when referring to the second slide deck (same link provided as above) noted that it had the same indication for Jardiance as stated above. As above, the statement was not in the SPC, although again that was the sole reference given. As the same wording was given in all cases, it appeared that the companies were using their 'interpretation' of their licence in a wide variety of cases, and not just these materials with no substantiation.

The complainant noted that cardiologists did not treat diabetes, but the entire slide set was aimed at clinicians who, under the current licence, did not treat these patients with Jardiance.

The complainant alleged that both slide sets would clearly encourage off-licence use of Jardiance, as it was well established that a footnote did not magically make the body of the slide acceptable. The complainant alleged that this failed to maintain high standards and brought the profession into disrepute.

The complainant also alleged that prescribing information on the website was out of date and provided a link to and a pdf of the prescribing information. The pdf included the prescribing information for Jardiance (empagliflozin) dated January 2018 as well as that for other Boehringer Ingelheim and Lilly products including Trajenta (linagliptin) dated April 2017, Jentadueto (linagliptin and metformin hydrochloride) dated June 2017 and Abasaglar (human insulin analogue) cartridge and kwikpen which was undated.

The complainant further alleged that the material was easily available to the general public and appeared to demonstrate poor oversight of the third parties that the pharmaceutical companies worked with.

When writing to Boehringer Ingelheim and Eli Lilly, the Authority asked them to consider the requirements of Clauses 7.2 and 7.4 with regard to the allegations regarding information being misleading as to the SPC, the requirements of Clauses 3.2, 7.2 and 7.4 with regard to the slides and the requirements of Clauses 9.1 and 2. The companies were also asked to consider the requirements of Clauses 4.1 with regard to the allegations about the prescribing information, and Clauses 26.1, 9.1 and 2 in relation to the allegation about availability to the public.

RESPONSE

Boehringer Ingelheim, as the marketing authorisation holder for Jardiance, responded on behalf of the Boehringer Ingelheim and Lilly Alliance. The Alliance took compliance with the Code very seriously and had steps in place to ensure that robust procedures continued to underpin all of its activities; the Alliance embraced a compliance culture that was fully embedded into the business with the support of its ethics and compliance departments.

General background and rationale for inclusion of cardiologists

The Alliance noted that type 2 diabetes and cardiovascular disease were intrinsically connected; over a third of type 2 diabetics had concurrent cardiovascular disease which remained the leading cause of morbidity and mortality in those patients.

Diabetes clinical management guidelines prioritised the importance of assessing underlying cardiovascular risk and the presence of cardiovascular disease as a key step in the management strategy. Cardiology guidelines also focused on cardiovascular risk reduction and emphasised the application of management strategies in type 2 diabetes.

- In 2017, the Scottish Intercollegiate Guidelines Network (SIGN) published a clinical guideline ‘SIGN 154: Pharmacological management of glycaemic control in people with type 2 diabetes’ which recommended the use of SGLT2 inhibitors with proven cardiovascular benefit, such as Jardiance, as an add on therapy to metformin in type 2 diabetics with established cardiovascular disease.

- In 2019, the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) updated their 2018 recommendation on the management of hyperglycaemia. The changes included the use of SGLT2 inhibitors to reduce major cardiovascular events and cardiovascular death '…independently of baseline HbA_{1c} or individualised HbA_{1c} target' in patients with type 2 diabetes and established cardiovascular disease.

- The 2019 European Society of Cardiology (ESC) guidelines in diabetes, pre-diabetes and cardiovascular disease were developed in collaboration with the EASD. It was stated in Table 5 'For the first time, we have evidence from several cardiovascular outcome trials that indicate cardiovascular benefits from the use of SGLT2 inhibitors and GLP1-RAs in patients with cardiovascular disease, or at very high/high cardiovascular risk.' Those guidelines recommended SGLT2 inhibitors in patients with type 2 diabetes and atherosclerotic cardiovascular disease or very high/cardiovascular risk either in drug naïve patients or as add on to metformin.

Furthermore, in 2019, the ESC conducted an online survey aimed at NHS consultant cardiologists to obtain their views on prescribing diabetes medications for the cardiovascular risk reduction in patients with acute coronary syndromes. The Alliance noted that the survey reported that:

- cardiologists should play a key role in identifying appropriate patients and initiating treatment

- optimum management of patients with type 2 diabetes and cardiovascular disease might be best served by collaborative working between cardiology, diabetes, and primary care teams.

The SPC wording for Jardiance was amended in light of the cardiovascular outcome trial data from the Empa-Reg-Outcome trial from 'improvement of glycaemic control' to '…for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise…' with further wording in Section 4.1 to direct the reader to Section 5.1 which stated that 'Both improvement of glycaemic control and reduction of cardiovascular morbidity and mortality are an integral part of the treatment of type 2 diabetes.'

The Alliance also noted the following extract from the Jardiance EPAR (page 61):

> 'In line with the Guideline on Summary of Product Characteristics with regard to wording of the indication(s), the CHMP was of the view that the population studied in the EMPA-REG ie type 2 diabetes patients with established cardiovascular disease, is a sub-population of the already approved type 2 diabetes population for Jardiance and that the demonstrated effect of reduction of cardiovascular mortality is covered by the general indication "treatment of type 2 diabetes"; similarly, achievement of glycaemic control is covered. Thus, the effect on cardiovascular mortality does not constitute a separate (prevention) indication. Therefore, CHMP did not grant a separate cardiovascular prevention indication but deleted the endpoint 'glycaemic control' from section 4.1 to clarify that the treatment goal for empagliflozin is not limited to glycaemic control. The results of the EMPA-REG are reflected in section 5.1 of the SPC'.

The Alliance noted that in Case AUTH/3033/4/18 (Boehringer Ingelheim and Lilly v Novo Nordisk), cardiovascular risk management was integral to the treatment of type 2 diabetes patients. In its ruling, the Panel:

- ruled no breaches with respect to the promotion of the cardiovascular benefit of Victoza by Novo Nordisk
- considered that the cardiovascular benefit was an inclusive part of Victoza's attribute
- was within the licensed indication of the treatment of insufficiently controlled type 2 diabetes
- and noted the licence statement in the SPC for Victoza had been changed in July 2017; 'improvement of glycaemic control' had been deleted and replaced with '…for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise…' as a result of the variation to include the results of the LEADER trial (a cardiovascular outcome trial).

The Panel's ruling stated:

> 'The European Medicines Agency (EMA) considered that both the improvement of glycaemic control and reduction of cardiovascular morbidity and mortality were integral to the treatment of type 2 diabetes, which could best be expressed in a single indication for Victoza. The changed wording in Section 4.1 of the Victoza SPC as well as the additional wording in Section 5.1, which further explained the role of glycaemia and [cardiovascular] risk in type 2 diabetes therapy, reflected the regulatory agency's view that a more holistic treatment approach was needed when treating type 2 diabetes.'

The Alliance noted that in the Victoza SPC the indication statement in Section 4.1 with additional wording in Section 5.1 'Both improvement of glycaemic control and reduction of cardiovascular morbidity and mortality are an integral part of the treatment of type 2 diabetes' was identical to that of Jardiance (except that Victoza was licensed additionally for 10-17 year olds as well as adults, whereas Jardiance was for adults only).

Details of the website and webcast

The Alliance explained that the webcast in question was first broadcast live in the form of pre-recorded videos of two leading named professors (a professor of metabolic medicine and a professor of cardiology) that were streamed on 10 August 2020. After that live event, the videos and slides were hosted on a third party website for on-demand use and downloading. The content of those presentations was co-created with the speakers and approved and certified by the Alliance.

The Alliance noted that although the complainant referred to two slide decks, they were in fact the same deck of 50 slides (the last two slides of which were the UK and Irish prescribing information) but were available to view as 2 videos reflecting that there were two speakers (the original speaker decks were certified separately, along with an accompanying housekeeping deck). The Alliance also noted that due to a prescribing information update, the slide deck was updated in October (the only change being the prescribing information) and recertified as a single deck.

Health professionals with an interest in the topic could register for the webcast in advance through the website, having confirmed they were health professionals. In response to a request from the Alliance to comment on the complaint, the third party stated that all website users were served a pop-up message on entering the website, in which they were told that the site was for UK health professionals only, and if they wanted to proceed they had to confirm that they were UK health professionals. The third party also noted that all event pages on the website included a header stating that the website was intended for health professionals.

Prescribing information on the website

The Alliance noted that Clause 4.1 stated that prescribing information must be provided in a clear and legible manner in all promotional material. The slide deck used in the webcast included the current prescribing information at the end of the presentation and slide 1 of the deck informed the viewer at the outset where the prescribing information could be found. The third party website also directed health professionals to the latest prescribing information by a prominent link on the hosting page for on-demand content, in accordance with Clause 4.1.

As noted above, during the campaign period, the prescribing information was changed and the slides were re-approved with the new prescribing information as displayed at the end of the slide deck. The link to the prescribing information from the hosting website remained unaffected as the link took health professionals directly to the prescribing information for Jardiance which was hosted on the Boehringer Ingelheim repository (when the prescribing information was changed the new version replaced the previous version on the Boehringer Ingelheim repository). Thus, Boehringer Ingelheim could categorically reassure the Panel that the appropriate prescribing information version for Jardiance was provided throughout the campaign, both on the slides and accessible electronically on the third party website. Boehringer Ingelheim submitted that that demonstrated its commitment to keeping its materials up to date with latest prescribing information.

Response to specific clauses

The Alliance noted that the complainant objected to the statement on the website that included the sentence 'Both improvement of glycaemic control and reduction of cardiovascular morbidity and mortality are an integral part of the treatment of type 2 diabetes'; the complainant incorrectly stated that although the statement was referenced to the SPC, the statement was not in the SPC. The Alliance explained that the statement did appear in the SPC in Section 5.1 as discussed previously and Section 4.1 clearly referred the reader to see Section 5.1. That position was also reviewed by the Panel in Case AUTH/3033/4/18 and in ruling no breach in that case, the Panel highlighted that the licensed indication for Victoza, as stated in the SPC, was the treatment of type 2 diabetes which included considerations of both glycaemic control and cardiovascular morbidity and mortality. The Alliance therefore submitted that the important educational intent, content and delivery was within the licensed indication of Jardiance and was therefore not in breach of Clauses 3.2, 7.2 and 7.4.

Furthermore, the Alliance did not believe it had failed to maintain high standards or brought discredit to the pharmaceutical industry. In helping to support high standard medical education content, the Alliance considered that it had shown the ongoing importance of a pharmaceutical company supporting dissemination of evidenced-based medicine. Therefore, the Alliance also strongly rejected that it had breached Clauses 9.1 and 2.

Finally, the Alliance submitted that the complainant's assertion that cardiologists did not treat diabetes seemed to be at complete odds with numerous guidelines and opinion of top UK experts such as the named professors in the webcast. The Alliance believed that no-one viewing the presentation could be left in any doubt as to the exclusive focus of the presentation on type 2 diabetics with cardiovascular disease. The opening slide framed the presentation very clearly around the treatment of type 2 diabetes and that context was provided prominently throughout. To quote the Panel's ruling in Case AUTH/3033/4/18, when referring to Victoza, that 'the presentation was set within the context of type 2 diabetes'. Likewise, the webcast, was no different in presentation.

The Alliance noted the allegation that the prescribing information on the website was outdated and that the complainant had provided a link with evidence of that in a downloaded pdf copy of the outdated prescribing information. The Alliance noted, however, that the outdated prescribing information provided by the complainant was not the prescribing information in the slide deck nor accessible from the third party website, and furthermore was not linked to any promotional material.

Upon receiving this complaint, the third party instigated an investigation and found that the prescribing information provided by the complainant was only discoverable by using very specific search terms and in an internet search engine. As such, the Alliance refuted that the outdated prescribing information was 'easily available to the general public.' The third party was unaware of the continued existence of the prescribing information and had confirmed that the outdated prescribing information was linked to an expired 2017 campaign and was still hosted in error on its server, contrary to the previous specific instructions from the Alliance to remove that campaign. The third party had since rectified its mistake and removed the prescribing information, therefore the Alliance strongly refuted breaches of Clauses 4.1, 26.1, 9.1 and 2.

In conclusion, the Alliance considered that the educational intent, delivery and content of the webcast to health professionals only, was conducted to the highest standards and in accordance with the licensed indication of Jardiance, the only Alliance product mentioned, and did not breach any clauses of the Code.

PANEL RULING

The Panel noted the Alliance's submission that the complainant referred to two slide decks, and whilst the original speaker decks were certified separately and were available to view as two videos, reflecting that there were two speakers, the slide deck was updated in October 2020, due to a prescribing information update, and recertified as a single deck of 50 slides. The Panel noted that the links provided by the complainant when referring to each slide set were the same and linked to the combined 50 slide deck.

The Panel noted that Clause 3.2 required that the promotion of a medicine must be in accordance with the terms of its marketing authorisation and must not be inconsistent with the particulars listed in its SPC.

The Panel noted that Section 4.1, Therapeutic Indications, of the Jardiance SPC stated that Jardiance was indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise. Details were provided regarding the use of the medicine as monotherapy or in addition to other medicines for the treatment of diabetes and then the reader was referred to other sections of the SPC (including Section 5.1) for, amongst

other things, study results with respect to the effects of Jardiance on cardiovascular events. In that regard, in Section 5.1 under a heading of 'Clinical efficacy and safety', it was stated that 'Both improvement of glycaemic control and reduction of cardiovascular morbidity and mortality are an integral part of the treatment of type 2 diabetes'. The Panel thus considered that the first statement highlighted by the complainant (which appeared on the webcast homepage and slide three of the combined slide set)

> 'Jardiance is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise.
>
> - As monotherapy when metformin is considered inappropriate due to intolerance
> - In addition to other medicinal products for the treatment of diabetes
>
> Both improvement of glycaemic control and reduction of cardiovascular morbidity and mortality are an integral part of the treatment of type 2 diabetes'

was substantiated by the reference cited (the SPC) and so no breach of Clause 7.4 was ruled in relation to each of the webcast homepage and the combined slide set.

The Panel further did not consider that the statement was misleading as to the licensed indication for Jardiance; the primary reason for prescription was made clear at the outset ie the treatment of adults with insufficiently controlled type 2 diabetes, and no breach of Clause 7.2 was ruled in relation to the webcast homepage and the combined slide set.

The combined slide set in question, entitled 'Improving cardiovascular outcomes in type 2 diabetes with SGLT2 inhibitors – What is the role of the cardiologist?', consisted of two presentations. The first presentation from a professor of metabolic medicine was entitled 'Type 2 diabetes, cardiovascular outcomes and the role of SGLT2 inhibitors' and the second presentation, 'Putting the evidence into practice: Does the cardiologist have an expanded role in the treatment of type 2 diabetes?' was from a professor of cardiology.

The Panel noted the complainant's allegation that the slides promoted SGLT2 inhibitors as assisting in cardiovascular outcomes and would encourage off-licence use of Jardiance, as it was well established that a footnote did not magically make the body of the slide acceptable.

The Panel noted that whilst the complainant alleged that it appeared to be the case throughout the slides, he/she only referred specifically to slides 9 and 48 of the combined deck as examples. Slide 9 included brief details of various SGLT2 inhibitors and GLP-1 receptor agonists cardiovascular outcome trials which had occurred between 2014 and 2020 including the study name, primary endpoint and n number and was headed 'We now have evidence that some SGLT2 inhibitors and GLP-1 receptor agonists have cardiovascular benefits*'. Below this in smaller font it was stated that 'Trials included patients either with cardiovascular disease or at cardiovascular risk who had type 2 diabetes'. The Panel noted that the slide included a tick next to some of the trials detailing that they had shown cardiovascular benefits vs placebo. A footnote at the bottom of the slide stated 'Empagliflozin is not indicated for the reduction of cardiovascular risk' rather than [Jardiance] was not licensed for any cardiovascular benefits as alleged by the complainant. Slide 48 was entitled 'Summary' and was the last slide before the prescribing information and appeared to be within a sub-section of 6 slides which started with the question 'What does a cardiologist need to consider when managing patients with diabetes?'. This summary slide included outcome results of empagliflozin compared with

placebo from the EMPA-REG outcome trial including 3P-MACE (three point major adverse cardiovascular events – composite of nonfatal stroke, nonfatal myocardial infarction and cardiovascular death), cardiovascular death, HHF (hospitalisation for heart failure), and all-cause mortality. A small footnote on the slide stated 'Empagliflozin is not indicated for the reduction of cardiovascular risk or the treatment of heart failure'. A red highlighted box on the slide stated 'Cardiologists are uniquely positioned to take the lead and become more involved in the treatment of patients with type 2 diabetes and cardiovascular disease'.

The Panel noted the content of the two slides above (slides 9 and 48), including the footnotes reminding the reader that Jardiance was not indicated for reduction of cardiovascular risk or the treatment of heart failure. The Panel noted that whilst it might have been helpful to include on the summary slide (slide 48), when discussing the outcomes of the EMPA-REG trial that it was conducted in patients with type 2 diabetes, it was clear from previous slides in the deck which discussed the trial. The Panel further noted the title of the webcast, the individual presentations and the multiple references to type 2 diabetes throughout the presentations, including the text in the red highlighted box on the summary slide which referred to cardiologists being positioned to take the lead and become involved in the treatment of patients with type 2 diabetes and cardiovascular disease and considered that it was clear that the information presented was set within the context of treating type 2 diabetes. The Panel did not consider that the complainant had established that the slide set was misleading or promoted Jardiance in a manner that was inconsistent with the particulars listed in its SPC as alleged and no breach of Clauses 7.2 and 3.2 were ruled.

The Panel noted the complainant's statement that the entire slide set was aimed at cardiologists who did not treat diabetes and under the current licence, did not treat these patients with Jardiance. The Panel, however, noted the Alliance's submission that type 2 diabetes and cardiovascular disease were intrinsically connected; over a third of patients with type 2 diabetes had concurrent cardiovascular disease which remained the leading cause of morbidity and mortality in those patients. Further the Panel noted the Alliance's submission that clinical guidelines on the treatment of type 2 diabetes recommended the use of SGLT2 inhibitors to reduce cardiovascular risk and that a survey from the ESC aimed at NHS consultant cardiologists reported that cardiologists should play a key role in identifying appropriate patients and initiating treatment and that optimum management of patients with type 2 diabetes and cardiovascular disease might be best served by collaborative working between cardiology, diabetes, and primary care teams.

The Panel noted its comments and rulings above and considered that with regard to the webcast homepage and the combined slide set there was no evidence that high standards had not been maintained. No breach of Clause 9.1 was ruled. The Panel consequently ruled no breach of Clause 2.

The Panel noted the complainant's allegation that prescribing information available on the third party website was out of date. The Panel noted that whilst the complainant had provided a URL link which included reference to the third party website, the Panel also noted the Alliance's submission that the outdated prescribing information provided by the complainant was not linked to any promotional material or accessible from that website. The third party confirmed that the out of date prescribing information in question could not be accessed through direct searches using the website nor via any links on the site. It thus appeared that although the URL provided by the complainant included the name of the website, the out of date prescribing information in question could not be accessed from that website. This suggested that the

complainant was not on the live website when he/she had accessed the out of date prescribing information. The Panel further noted the Alliance's submission that the slide deck above which was accessible from the website included the current UK Jardiance prescribing information dated October 2020 and that the third party website directed health professionals to the latest prescribing information which was hosted on the Boehringer Ingelheim repository by a prominent link on the hosting page for on-demand content.

The Panel further noted that the third party had confirmed to the Alliance that the out of date prescribing information provided by the complainant was linked to an expired 2017 campaign which was in error not completely deleted from its server, contrary to previous instructions from the Alliance to remove that campaign. The Panel noted that whilst the third party was unaware of the continued existence of the out of date prescribing information it appeared that it remained accessible if searched for via Google using very specific search terms. The Panel further noted that on being notified of the issue, a number of staff searched Google for the prescribing information document which appeared anywhere between the bottom of page one and page eight in the search results depending on the user's browser history. The Panel, however, did not know what search terms had been used in this regard. The third party had since fully deleted the out of date document from its server.

It appeared to the Panel that the out of date prescribing information provided by the complainant could only be accessed from the server by using specific terms in an internet search engine or the specific URL provided by the complainant; it could not be accessed from the live third party website as alleged. The Panel considered that, on the balance of probabilities, the complainant had not shown that the out of date prescribing information in question was accessible to health professionals through the website. The Panel considered that what was now out of date prescribing information on the server, which could not be accessed from the third party website, did not amount to a breach of the Code as alleged. No breach of Clause 4.1 was ruled.

The Panel, noting its comments above with regard to how the out of date prescribing information could be accessed, did not consider that the outdated prescribing information was easily available to the general public as alleged. No breach of Clause 26.1 was ruled.

In the Panel's view, this case illustrated that companies should exercise extreme caution and wherever possible ensure that pages which were not intended for viewing were either fully deleted or securely hidden and thus inaccessible including through an internet search. Companies were responsible for the acts and omissions of third parties acting on their behalf in this regard.

In the Panel's view, the complainant had not established that the Alliance had poor oversight over the third parties it worked with as alleged. Although the Panel was concerned that out of date prescribing information had been accessed, given its comments and rulings above, it considered that, in the specific circumstances of this case, the Alliance had not failed to maintain high standards as alleged. No breach of Clause 9.1 was ruled. The Panel consequently ruled no breach of Clause 2.

Complaint received **19 January 2021**

Case completed **19 July 2021**