CASE AUTH/3612/2/22

COMPLAINANT v DAIICHI SANKYO

Promotion of Nilemdo and Nustendi at a symposium

CASE SUMMARY

This case was in relation to a live and on-demand promotional symposium for Nilemdo (bempedoic acid) and Nustendi (bempedoic acid and ezetimibe) which allegedly did not mention that both medicines were contraindicated with simvastatin >40mg on the indications slide and this was allegedly inconsistent with each medicine's marketing authorisation. The complainant further alleged that the prescribing information was displayed for an insufficient amount of time and that the recording of the presentation was accessible on an open access platform.

The Panel ruled a breach of the following Clause(s) of the 2021 Code for failing to make the contraindication with simvastatin >40mg immediately apparent when presenting Nilemdo and Nustendi's indications which referred to their therapeutic use in combination with a statin; and for failing to display prescribing information for adequate time for each medicine during the live symposium:

Breach of Clause 5.1	**Failure to maintain high standards**
Breach of Clause 2	**Bringing discredit upon, and reducing confidence in, the pharmaceutical industry**
Breach of Clause 12.5	**Failing to display prescribing information for sufficient duration so that it is easily readable**

The Panel ruled no breach of the following Clause(s) of the 2021 Code based on the complainant not having established that:

A lack of reference to Section 4.3 of the SPC meant that Nilemdo and Nustendi had been promoted inconsistently with their SPCs as alleged; nor that the prescribing information for each medicine, which could be paused by the viewer in the on-demand recording, was displayed for insufficient time; nor that the on-demand recording, which was hosted privately, and accessible from the on-demand section of the society's website where members had to self-certify that they were health professionals, constituted promotion of a prescription only medicine to the public; nor that information had been made available to the public:

No Breach of Clause 11.2	**The requirement for promotion to not be inconsistent with the SPC**
No Breach of Clause 12.5	**Requirement to display prescribing information for sufficient duration so that it is easily readable**
No Breach of Clause 26.1	**Requirement not to advertise prescription only medicines to the public**

No Breach of Clause 5.1	**Requirement to maintain high standards**
No Breach of Clause 2	**Requirement that activities or material must not bring discredit upon, or reduce confidence in, the pharmaceutica industry**

This summary is not intended to be read in isolation.
For full details, please see the full case report below.

FULL CASE REPORT

A contactable complainant who described him/herself as a health professional complained about the promotion of Nilemdo (bempedoic acid) and Nustendi (bempedoic acid and ezetimibe) at a symposium organised by Daiichi Sankyo.

COMPLAINT

The complainant referred to a promotional symposium organised by Daiichi Sankyo titled 'Do we know our ABC's: interpreting cardiovascular guidelines into everyday practice' and presented by a named doctor. (Ref CVD/21/0293, date of preparation November 2021).

The complainant stated that at the very start of the presentation (roughly 25 seconds in), indications for Nilemdo and Nustendi were provided but these were not consistent with the marketing authorisation. There was no mention on this slide with the presentation that both products were contraindicated with simvastatin >40mg. The summary of product characteristics (SPC) indication for both products specifically referred for the need to refer to Section 4.3, where this information on the contraindication was contained, but on the slide, the information about Section 4.3 was not shown yet the slide mentioned Nilemdo and Nustendi being able to be used in combination with a statin without any context provided. This was alleged to be a patient safety breach. The complainant alleged a breach of Clauses 11.2, 5.1 and 2 as a result of this slide not presenting the licence accurately and explaining the importance of not using both Nilemdo and Nustendi with simvastatin >40mg.

The complainant stated that prescribing information at the end of the presentation was not shown for an adequate amount of time for Nilemdo, Nustendi or Lixiana (edoxaban). Each prescribing information was very long and required at least three minutes of reading time for each of the three products, but the prescribing information was only shown for around ten seconds for each product. This was alleged to be a breach of Clause 12.5 as the duration was not long enough. The recording of the presentation was also available on Vimeo, an open access platform, which was allegedly promotional to patients breaching Clauses 26.1, 26.2, 5.1 and 2. The complainant provided a link to the recording and was dismayed that these compliance errors had occurred.

When writing to Daiichi Sankyo, the Authority asked it to consider the requirements of Clauses 2, 5.1, 11.2, 12.5, 26.1 and 26.2 of the Code.

RESPONSE

Daiichi Sankyo stated that it took its obligations under the Code seriously, strove to maintain high standards and behaved responsibly and ethically at all times.

Daiichi Sankyo stated that the complainant appeared to be the same complainant as in Case AUTH/3611/2/22.

Daiichi Sankyo denied all alleged breaches.

Daiichi-Sankyo confirmed that the promotional symposium to which the complainant referred was a recording of the Daiichi-Sankyo UK sponsored symposium session 'Do we know our ABC's: interpreting cardiovascular guidelines into everyday practice' at a learned society one-day virtual conference. The original promotional symposium was broadcast live on the date of the meeting in September 2021 using a broadcast platform.

The recording of the symposium was approved and certified as a video by Daiichi Sankyo. It lasted sixteen minutes thirty-four seconds and was hosted post-congress on the on-demand section of the society's website in December 2021.

Daiichi-Sankyo stated that it had no influence on the attendees to the symposium and there was no active recruitment by Daiichi Sankyo. Attendees were either contracted speakers for sessions on the society's agenda or were fully signed up members of the society. All promotion of the conference was conducted by the society.

The named speaker was selected because he/she was a consultant cardiologist who worked with primary care in this area. In advance of the learned society's annual conference, Daiichi Sankyo provided an outline of its symposium and speaker for the society's committee to approve. The committee reviewed the plans for all the symposium in terms of title and speaker and were happy to proceed. This approval was important as it indicated that the society deemed the speaker relevant to the educational topic and the audience attending the conference.

Allegation 1 – No mention that both products were contraindicated with simvastatin >40mg

Daiichi-Sankyo confirmed that the indications for Nilemdo and Nustendi were provided on slide 5 of the presentation within the recording, and this slide was first shown at 24 seconds into the video. Daiichi-Sankyo provided a screen shot:

The information in Section 4.3 of the SPC to which the complainant referred, was referencing where readers could find additional information available within the SPC for both Nilemdo and Nustendi. For the purpose of this response, section 4.3 of the SPC for Nilemdo and Nustendi listed 'Contraindications'.

Daiichi-Sankyo submitted that the Code did not stipulate a requirement to include the entire SPC within promotional materials, instead Daiichi Sankyo was required to include the pertinent sections including 'Contraindications' as a summary in the prescribing information. The information within Section 4.3 of the SPC ie, contraindications, had been provided as part of the prescribing information for both Nilemdo and Nustendi and included a clear statement on concomitant use with simvastatin >40mg daily. In addition, there was a clear statement in bold font which stated 'Prescribing information will be shown at the end of this meeting' allowing the audience to know that they could view the full prescribing information for further information if they required. The prescribing information was approved as part of the video and included the information required as stipulated by the Code, including the full list of contraindications.

Daiichi Sankyo therefore completely disagreed with the complainant's allegation of a breach of Clause 11.2 that the indications for Nilemdo and Nustendi 'were not consistent with the marketing authorisation'. Clause 11.2 stated, '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 summary of product characteristics'. The company submitted that the indications presented on slide 5 of the presentation within the recording and the information outlined in the prescribing information were all in line and consistent with the SPC for both products. There was no evidence to suggest that Daiichi-Sankyo had promoted inconsistently with the particulars listed in the SPC and Daiichi-Sankyo denied a breach of Clause 11.2.

Daiichi-Sankyo provided further information which the complainant had not included which it submitted demonstrated its commitment to ensure that the importance of not using both Nilemdo and Nustendi with simvastatin >40mg daily was both presented and communicated clearly in the recording. During the symposia, the speaker, who was a health professional, communicated the safety information on Nilemdo and Nustendi which included adverse events, safety precautions for use, as well as contraindications.

At minute 13:15, the speaker specifically took the opportunity to verbally communicate the contraindication on use with simvastatin >40mg, and directed the audience to look at the information on the slide on the simvastatin >40mg contraindication by saying 'if you look down here, concomitant use of simvastatin of more than 40mg once a day is also not recommended' with a sufficient pause after making this statement to allow the audience to absorb and take note of this contraindication. There was also a clear statement in large prominent font on the slide which stated 'For full prescribing information, please refer to the summary of product characteristics'.

Daiichi Sankyo submitted that the importance of not using both Nilemdo and Nustendi with simvastatin>40mg was communicated and presented clearly in this recording, both in writing and verbally by the presenter as well as being listed in the prescribing information at the end of the presentation. Overall, the company submitted that there was no evidence that it had failed to maintain high standards or prejudiced patient safety and thus it denied a breach of Clauses 5.1 and 2.

Allegation 2 - 'Prescribing information was not shown for an adequate amount of time for Nilemdo, Nustendi or Lixiana.

Daiichi Sankyo stated that Clause 12.5 outlined the requirement of the provision of the prescribing information in audio-visual material and in interactive data systems. It did not specify any length of time for which the prescribing information should be displayed and therefore did not apply to this allegation.

Daiichi Sankyo submitted that the recording which was classified as a promotional item, contained the required prescribing information for Nilemdo, Nustendi and Lixiana: this could be viewed on slides 41 and 42 of the presentation. There was clear sign posting of where the prescribing information could be found on the introduction slide, as well as on slides where the respective product indications were shown stating 'Prescribing information and adverse reporting details will be available at the end of this meeting'. Daiichi Sankyo submitted that as the relevant prescribing information had been included within the body of the slide deck, along

with clear instructions on where this could be viewed, the requirements of Clause 12.5 had been met.

With regard to the complainant's opinion that that the 'Prescribing information at the end of the presentation was not shown for an adequate amount of time', Daiichi Sankyo provided further information to demonstrate the considerations applied during the approval of this recording which respected and allowed health professionals to exercise their own autonomy to access prescribing information for an extended period if they so wished.

Prescribing information for Nilemdo and Nustendi was shown on slide 41 for a full 10 seconds, and similarly for Lixiana, on slide 42 for a further 10 seconds. As this was a recording, viewers had the option to pause and playback any section as they wished. Daiichi-Sankyo believed that the allocated 10 seconds was an acceptable amount of time allocated to display the respective prescribing information, providing health professionals the option to pause the recording and read in detail if they should choose to.

Allegation 3 - the 'recording of the presentation was also available on vimeo, a open access platform which was promotional to patients'.

Owing to the nature of the allegations, upon receipt of the complaint, the society were contacted by Daiichi Sankyo to request the removal of the symposium recording from the on-demand health professional members website. The removal of the video was confirmed by the society on 3 March 2022 at 09:53. The society were asked to comment on whether members of the general public could access the on demand hosted content of Daiichi Sankyo's 2021 symposium. The society replied at 14:12 on the 3 March and stated:

> 'The videos are hosted on Vimeo but with a private setting so that they are hidden from public view, they are therefore accessible only via the [society] website where users would have to confirm they are an HCP before proceeding to view any content. The only way a member of the public could access this video is by directly accessing the URL'.

Daiichi Sankyo stated in addition to the initial clarification received from the society, Daiichi Sankyo further investigated to demonstrate the steps and mitigation that was put in place by the society to ensure that this information was only intended for and accessible by health professionals who had self-certified as same, via their website.

Daiichi Sankyo provided the visitor route map to accessing the website and the actual page upon which the sponsored symposium was accessed. Currently the symposium was still listed as part of the agenda, but viewers could no longer access the recording.

In order to gain access to the webpage, there was a clear disclaimer upfront to state that 'This site is for healthcare professionals only. By entering the site, you confirm that you are a healthcare professional' and the visitor was given a further option to either self-certify as a health professional 'YES, I AM A HEALTHCARE PROFESSIONAL AND WISH TO ENTER THE SITE' or to select, 'NO, I AM NOT A HEALTHCARE PROFESSIONAL".

Once confirmation was made that the site visitor was a health professional, the main society site opened and on demand content could be found under the annual conference drop down menu.

When 2021 annual conference was selected a button to select the agenda was given. This page showed the sponsors of the meetings and gave the visitor options to become a member or log in to the members portal.

Upon clicking the agenda button, a new page opened listing the full days programme for the conference held virtually in September 2021. Within the agenda, hyperlinks were available to access the on-demand content on Vimeo.

Once an on-demand video was selected it could then be viewed. When the viewer clicked to view, they were brought to the private Vimeo landing page which housed the recording. The URL could be seen which could be copied and shared.

Daiichi Sankyo stated that the society had confirmed that the video content could not be searched for directly. If a session was searched for, it would bring up the society conference menu or the society website main page. If a video was accessed on demand by a site visitor who had self-certified themselves as a health professional and the URL was copied and shared, the video could then be accessed directly. The complainant, who had declared themselves as a health professional, would therefore have had full eligibility to access this self-certified platform upon entry to the website. Consequently, this health professional had access to the site, the content of the site and could copy the URL if they desired. There was no evidence to suggest that this information could be accessible to anyone but those site visitors who had self-certified that that they were indeed health professionals.

As the recording of the symposium video was housed on Vimeo, on a private setting and was accessible only via the society website with a clear requirement for site visitors to self-certify their health professional status prior to entering the site, there was no evidence to suggest that this was in any way promoting to the public (no breach of Clause 26.1), or to patients as the complainant alleged, and consequently, Clause 26.2 did not apply. Therefore, taking into consideration the above information that Daiichi Sankyo and the society had provided, there was no evidence to suggest that Daiichi Sankyo had failed to maintain high standards, therefore no breach of Clause 5.1. Additionally, there was no evidence to show that this in anyway had prejudiced patient safety (Clause 2) consequently there was no breach of Clause 2.

Daiichi-Sankyo provided further supporting information which it submitted demonstrated that it took all steps necessary to ensure that content intended for health professionals, was viewed only by them. This was of particular importance in the current digital environment. The first slide in this meeting alerted the viewer that the content would contain information on Daiichi-Sankyo prescription only medicines and that the meeting was intended for a UK health professional audience only.

Conclusion

Based on the evidence provided above, Daiichi Sankyo UK submitted that it had acted in line with the requirements of the Code, maintained high standards, and had not brought discredit upon, or reduced confidence in, the industry.

PANEL RULING

The Panel noted that the complainant referred to a promotional symposium session sponsored by Daiichi Sankyo UK titled ‘Do we know our ABCs: interpreting cardiovascular guidelines into

everyday practice'. The Panel noted that the symposium took place at a learned society one-day virtual conference.

The Panel noted Daiichi Sankyo's submission that the promotional symposium was broadcast live in September 2021 and the recording of the symposium was certified as a video and hosted post-congress on the society's website in December 2021.

The Panel noted that the complainant provided the video recording but did not narrow his/her allegations to just the recording and thus the Panel considered the complaint in relation to both the live session and on-demand recording.

The Panel noted the complainant's allegation that at the start of the presentation, the indications for Nilemdo and Nustendi were provided, but these were not consistent with the marketing authorisation which specifically referred the reader to Section 4.3 of the SPC 'Contraindications'; there was no mention on this slide that both products were contraindicated with simvastatin >40mg and therefore the information in relation to therapeutic use in combination with a statin was not put in context.

The Panel noted that Section 4.1, Therapeutic indications, of the Nilemdo and Nustendi SPCs each referred the reader to Sections 4.2 (posology and method of administration), 4.3 (contraindications) and 4.4 (special warnings and precautions for use) when referring to the use of each medicine in combination with a statin (emphasis added by the Panel below):

> 'Nilemdo is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
> - **in combination with a statin** or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin **(see sections 4.2, 4.3, and 4.4)** or,
> - alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.'
>
> 'Nustendi is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
> - **in combination with a statin** in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin in addition to ezetimibe **(see sections 4.2, 4.3, and 4.4)**,
> - alone in patients who are either statin-intolerant or for whom a statin is contraindicated, and are unable to reach LDL-C goals with ezetimibe alone,
> - in patients already being treated with the combination of bempedoic acid and ezetimibe as separate tablets with or without statin.'

The Panel considered that Section 4.3 of the SPC gave important safety information in relation to concomitant use with simvastatin including that both Nilemdo and Nustendi were contraindicated in patients taking simvastatin >40mg daily.

In the Panel's view, given that simvastatin was a commonly prescribed lipid lowering treatment, and the indications on the slide referred to therapeutic use of Nilemdo or Nustendi in combination with a statin, the contraindication regarding concomitant use with simvastatin >40mg daily needed to be immediately apparent to health professionals in promotional material.

Whilst the Panel considered that it was misleading not to refer to the contraindication with simvastatin >40mg on the indications slide, which specifically referred to therapeutic use in combination with a statin, the Panel, nonetheless, did not consider that the complainant had established that a lack of reference to Section 4.3 of the SPC, or to the contraindication with simvastatin >40mg daily, on the indications slide in question (slide 5), meant that Nilemdo and Nustendi had been promoted in a manner that was inconsistent with their respective SPCs and no breach of Clause 11.2 was ruled in that regard.

The Panel noted that no reference had been made on the indications slide for viewers to consult Section 4.3 of the SPC, Contraindications, nor had it been explained that this important safety information would be provided later on in the presentation. The Panel considered that reference to the contraindication 26 slides later was not sufficient in this regard and did not negate the misleading immediate impression given that Nilemdo and Nustendi could be used in combination with any dose of any statin which was not so.

The Panel noted Slide 31 was shown for 20 seconds and contained information for consideration in special populations including in the elderly, renal impairment, hepatic impairment, paediatrics and a list of contraindications. The row titled contraindications included 'concomitant use with simvastatin >40mg daily' amongst others. Whilst the Panel noted Daiichi Sankyo's submission that the speaker specifically communicated this contraindication at 13 minutes 15 seconds, along with verbalising considerations in the elderly and renal impairment, the Panel noted the speaker did not refer to concomitant use with simvastatin >40mg as being a contraindication but rather 'not recommended'. In the Panel's view, the reference to the contraindication was insufficiently clear in this regard. The presentation of the contraindication towards the end of the video, after 13 minutes into the 16 minute 34 second video, meant it was not immediately apparent to health professionals given that the therapeutic use of Nilemdo or Nustendi in combination with a statin was first referred to just 24 seconds into the video.

The Panel, noting the above, considered that Daiichi-Sankyo had failed to maintain high standards in this regard and a breach of Clause 5.1 was ruled.

The supplementary information to Clause 2 listed prejudicing patient safety as an activity likely to lead to a breach of this clause. Given that simvastatin was a commonly prescribed statin, the Panel was concerned that in referring to therapeutic use in combination with a statin on slide 5, but not referring to the contraindication with simvastatin>40mg until 26 slides later, meant that important context was not immediately apparent to health professionals. Furthermore, when the contraindication was stated on slide 31, the speaker incorrectly referred to such use as 'not recommended' rather than contraindicated. Taking everything into consideration, the Panel considered that there was a risk that some patients on simvastatin >40mg daily might be inappropriately treated with Nilemdo or Nustendi. Patient safety was of the utmost importance and the Panel considered that the material might prejudice patient safety and was such as to reduce confidence in, and bring discredit upon, the pharmaceutical industry. A breach of Clause 2 was ruled.

In relation to the allegation that prescribing information was shown for inadequate time, the Panel noted that Clause 12.5 stated, *inter alia*, that in audiovisual material, prescribing information may be provided by way of a document made available to all persons to whom the material is shown and/or by inclusion in the material itself. The supplementary information to Clause 12.5 (Prescribing Information on Audiovisual Material) stated that where prescribing

information is shown on audiovisual material, it must be of sufficient clarity and duration so that it is easily readable.

The Panel noted Daiichi Sankyo's submission that the prescribing information for Nilemdo, Nustendi and Lixiana were each shown for 10 seconds, which, according to Daiichi Sankyo, was acceptable as this was a recording and viewers had the option to pause and playback. The Panel, noting that viewers of the on-demand video were able to press pause, ruled no breach of Clause 12.5 in relation to each medicine with regard to the on-demand recording of the symposium.

The Panel noted, however, that that the original virtual symposium was broadcast live and stated on the opening slide that prescribing information would be available at the end of the meeting. The agenda and invite made no reference to prescribing information and it therefore appeared that prescribing information was only available to attendees of the live virtual symposium via the slides at the end of the meeting. The Panel considered that the length of time the prescribing information was displayed, 10 seconds for each product, was insufficient to allow attendees of the live symposium to read it. A breach of Clause 12.5 was ruled in relation to each medicine with regard to the live symposium.

The Panel noted that, contrary to the complainant's allegation, Daiichi Sankyo submitted the videos were hosted on Vimeo privately so that they were hidden from public view and accessible only via the society's website where users would have had to have confirmed they were a health professional before proceeding to view any content; the only way a member of the public could access this video was by having direct access to the specific URL which would only happen if a society site visitor, after confirming that they were a health professional, copied and shared the URL.

The Panel did not consider that the complainant had established that the video, hosted on Vimeo privately and accessible from the on-demand section of the society's website where members had to self-certify that they were health professionals, constituted promotion of a prescription only medicine to the public and no breach of Clause 26.1 was ruled. Nor did the Panel consider that the arrangements meant that information had been made available to the public and no breach of Clause 26.2 was ruled. Accordingly, the Panel ruled no breaches of Clauses 5.1 and 2 in this regard.

Complaint received **19 February 2022**

Case completed **23 February 2023**