CASE AUTH/3632/4/22 ***NO BREACH OF THE CODE***

COMPLAINANT v DAIICHI SANKYO

Allegations about a Lixiana webinar

CASE SUMMARY

This case was in relation to a promotional video on how to initiate Lixiana (edoxaban) on a learned society's website.

The Panel ruled no breach of the following Clauses of the 2021 Code because on the evidence available before it the material had not been made available to health professionals and was draft content, on what appeared to be an unlisted staging site:

No Breach of Clause 2	**Requirement that activities or material must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**
No Breach of Clause 5.1	**Requirement to maintain high standards**
No Breach of Clause 6.1	**Requirement that information must be accurate, up-to-date and not misleading**
No Breach of Clause 6.2	**Requirement that claims/information/comparisons must be capable of substantiation**
No Breach of Clause 8.1	**Requirement to certify promotional material**

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

FULL CASE REPORT

A complainant who described him/herself as a cardiac expert complained about what he/she described as a webinar on how to initiate Lixiana (edoxaban), marketed by Daiichi Sankyo.

COMPLAINT

The complainant stated that a recent webinar on how to initiate Lixiana (edoxaban) had no information presented on the importance of hepatic function monitoring on initiation and the specific contra-indications related to hepatic function. The webinar only focused on renal function which the complainant stated was strange considering hepatic function was also a gold standard to check when initiating a new patient onto Lixiana and was mandatory as documented within the summary of product characteristics (SPC).

The complainant provided a link to a webpage and referred to the second video of three on the webpage titled: Transitioning patients from warfarin to a DOAC [direct oral anticoagulant] in NVAF [nonvalvular atrial fibrillation]– an edoxaban case study (ref EDX/22/0058) and stated that it seemed the video was put together for hosting on a learned society website in March 2022.

The complainant stated that around 2 minutes and 14 seconds into this second video, a slide was presented which discussed prescribing Lixiana in newly diagnosed patients with atrial fibrillation. At the bottom of this slide was renal function considerations. However, no hepatic function considerations were provided. The following information was from section 4.2 of the Edoxaban SPC:

> 'Edoxaban is contraindicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk (see section 4.3).
>
> In patients with severe hepatic impairment edoxaban is not recommended (see sections 4.4 and 5.2).
>
> In patients with mild to moderate hepatic impairment the recommended dose is 60 mg edoxaban once daily (see section 5.2). Edoxaban should be used with caution in patients with mild to moderate hepatic impairment (see section 4.4).
>
> Patients with elevated liver enzymes (alanine aminotransferase (ALT) or aspartate transaminase (AST) > 2 x upper limit of normal (ULN)) or total bilirubin ≥ 1.5 x ULN, were excluded in clinical studies. Therefore, edoxaban should be used with caution in this population (see sections 4.4 and 5.2). Prior to initiating edoxaban, liver function testing should be performed.'

The complainant alleged that missing out this information could cause major harm to patients considering elderly patients often had diminished/reduced hepatic capability. The case study that followed on in the video from the slide that mentioned how to start Lixiana also did not mention liver function testing.

It was also not clear if this video had been certified or just the slides had been certified (then the learned society added the video in the background) as on this same slide, the speaker mentioned 'needing to reduce the edoxaban dose to 30mg if on any drugs which were INDUCERS but this was only applicable to INHIBITORS'.

The complainant alleged breaches of Clauses 6.1, 6.2, 5.1 and 2. If the video had not been certified as part of the slides then a further breach of Clause 8.1 was also possible.

When writing to Daiichi Sankyo, the Authority asked it to consider the requirements of Clauses 2, 5.1, 6.1, 6.2 and 8.1 of the Code.

RESPONSE

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

Daiichi Sankyo denied breaches of Clauses 2, 5.1, 6.1, 6.2 and 8.1 of the Code.

Daiichi Sankyo stated that the item in question was not a webinar, but one of a series of videos intended to be placed on a learned society website designed for health professional education, in partnership with said learned society. This was to be part of a password protected educational section for registered health professionals. Daiichi Sankyo contracted committee members of the learned society who were experts in their field, to create and deliver educational

Talking Head videos for health professionals in England, which addressed common questions about edoxaban and the NHSE&I commissioning recommendations. No health professionals had seen this material as it had not been finalised, nor shared, nor were health professionals present since this was not presented to any health professionals as this was not a live webinar.

These videos were not shared nor advertised by Daiichi Sankyo as this webpage was not yet certified and not ready for distribution at the time of the complaint. The website provided by the complainant was an unlisted staging site provided and created by the learned society and used for testing and review purposes for Daiichi Sankyo, which was not shared with, nor advertised to, health professionals or anyone else beyond the development and review teams. There was no link to the staging site from the learned society main website as this was not intended to be a live site; Daiichi Sankyo and the learned society had validated this internally. It was unclear to Daiichi Sankyo how this was available to view externally and allegedly promoted as the complainant had not provided evidence of whether it was available externally, and the learned society had confirmed that there was no active live promotion of it. As these materials had not yet been certified and approved for use, Daiichi Sankyo requested that the alleged breaches were dismissed as these were not intended for use. Therefore, Daiichi Sankyo denied a breach of Clause 8.1.

In terms of the complaint regarding hepatic function monitoring, Daiichi Sankyo submitted that the materials were produced by a Cardiology GPwSI (a General Practitioner with special interest in Cardiology) specifically to address dosing with edoxaban and renal function considerations related to dose reduction, to ensure appropriate use of the 60mg or 30mg dose. According to the health professional contracted, up to 40% of patients in the UK were prescribed the incorrect dose of a DOAC and therefore, the focus on these videos was to educate clinicians regarding how to initiate and prescribe the appropriate dose for the patient and according to what criteria. In addition, a direct link was available within the site to the full prescribing information, and health professionals were also advised to refer to the SPC before prescribing edoxaban by the statement ‘See Lixiana Summary of Product Characteristics (SmPC) prior to prescribing’.

Daiichi Sankyo submitted that the inducer/inhibitor comment had already been picked up during Daiichi Sankyo’s review of the videos and corrected. This was admittedly an error by the speaker verbally (the correct term was used in the slide provided) and had already been addressed and rectified before receiving the complaint.

Daiichi Sankyo stated that as review of materials in stages was part of the certification process to ensure alignment with the Code, all amends through the review process were considered as part of the standard development and approval process of promotional materials. Additionally, the materials were developed in consultation with multidisciplinary cardiac healthcare professional experts and included information necessary for the prescribing of edoxaban. Any amends to items were actioned as part of the development and certification process before promotion to health professionals, and before going live, to ensure accurate, fair and balanced information. In this case, once these videos were certified and deemed accurate, then the videos would be uploaded onto the learned society live site and contained within their education page which was password protected. Only validated health professionals who were registered members of the learned society would be able access this area of the site.

Daiichi Sankyo confirmed that, as with all promotional materials, a prominent and direct single click link was provided as seen in the screenshot to the prescribing information with the

recommendation to refer to the SPC before prescribing and included all relevant special warnings and precautions for use, including information on hepatic considerations before initiating a patient on edoxaban.

Therefore, Daiichi Sankyo denied a breach of Clauses 6.1, 6.2, 8.1, 5.1 and 2.

In conclusion, Daiichi Sankyo stated 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 provided a link to a webpage hosting a video that allegedly had no information presented on the importance of hepatic function monitoring on initiation nor the specific contraindications related to hepatic function.

The webpage accessed by the case preparation manager, via the link provided by the complainant, included, amongst other things, three videos, a link to a leavepiece, a link to speaker profiles and a link to a downloadable certificate. Concerns about the leavepiece were raised by the same complainant and considered by the Panel in Case AUTH/3634/4/22.

The complainant had not provided any evidence to show how the webpage had been accessed from publicly available webpages. The Panel noted Daiichi Sankyo's submission that the website provided by the complainant was an unlisted staging site provided and created by the learned society, which was not shared with, nor advertised to, health professionals or anyone else beyond the development and review teams; it had been validated by Daiichi Sankyo and the learned society that there was no link to the staging site from the learned society's main website.

The Panel noted the complainant referred specifically to the second video titled 'Transitioning patients from warfarin to a DOAC in NVAF – an edoxaban case study' and cited EDX/22/0058. However, on receipt of the videos from Daiichi Sankyo, it appeared that EDX/22/0058 was the job bag number of the third video on the webpage titled 'The practicalities of initiating DOACs in line with NHS England and NHS Improvement's commissioning recommendations'. Both videos had the same speaker and presented the slide referred to by the complainant which included information on prescribing Lixiana and renal function dosing considerations.

In relation to the complainant highlighting that the speaker incorrectly stated the need to reduce the edoxaban dose with inducers as opposed to inhibitors, the Panel noted Daiichi Sankyo's submission that this error had already been identified during the material review process and corrected before the complaint was received. According to Daiichi Sankyo, no health professionals had seen the videos nor webpage as it had not been finalised nor shared nor was it presented to any health professionals as it was not a live webinar; Daiichi Sankyo submitted that these materials had not yet been certified and approved for use.

The Panel noted Daiichi Sankyo's submission that the materials included information necessary for the prescribing of edoxaban and that there was a prominent and direct single click link to the prescribing information which included information on hepatic considerations before initiating a patient on edoxaban.

The Panel considered that whether a contraindication or special warning or precaution needed to be highlighted within a particular section of promotional material, in addition to its requirement to be included within the prescribing information that was required on all promotional material, depended on a consideration of all of the circumstances including the nature of the contraindication/warning/precaution and the content, layout, audience and intended use of the material.

The Panel noted the hepatic considerations for edoxaban in its SPC including that it was not recommended in patients with severe hepatic impairment and that it should be used with caution in patients with mild to moderate hepatic impairment. The Panel further noted that the SPC stated that liver function testing should be performed prior to initiating edoxaban and that periodic hepatic monitoring was recommended beyond 1 year. Noting Daiichi Sankyo's submission that the materials included information necessary for the prescribing of edoxaban and referred to the practicalities of initiating treatment, the Panel queried the omission of information about the hepatic considerations of edoxaban in the body of the videos. In the Panel's view, it might be relevant to include such information in the body of material that was intended to advise health professionals on the practicalities of prescribing the medicine.

Nonetheless, the Panel noted its comments above that at the time of the complaint, on the balance of probabilities, the webpage in question appeared to be an unlisted staging site for internal review and had unlikely been accessed by health professionals external to those on the development and review team. Taking all the factors into account, and on the evidence available before it, that the material had not been made available to health professionals, **the Panel did not consider that the allegations regarding draft content, on what appeared to be an unlisted staging site, amounted to breaches of Clauses 2, 5.1, 6.1, 6.2 and 8.1 of the Code as alleged and ruled accordingly.**

Complaint received **11 April 2022**

Case completed **3 April 2023**