COMPLAINANT v BRISTOL-MYERS SQUIBB AND PFIZER

Eliquis website

A complainant who described him/herself as a 'concerned UK health professional' complained about the Eliquis (apixaban) website. Eliquis, co-marketed by Bristol-Myers Squibb and Pfizer, was an antithrombotic.

The complainant noted that pages of the Eliquis website which detailed special warnings and precautions for use, stated that care was to be taken if patients were treated concomitantly with non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin. That statement, however, differed significantly with the latest version of the summary of product characteristics (SPC) which stated that care was to be taken if patients were treated concomitantly with selective serotonin re-uptake inhibitors (SSRIs) or serotonin norepinephrine re-uptake inhibitors (SNRIs), or NSAIDs, including acetylsalicylic acid (aspirin). The complainant submitted that this could potentially be a patient safety issue.

The detailed response from Bristol-Myers Squibb and Pfizer is given below.

The Panel noted that the website in question was for health professionals and was headed 'Practical Information To assist your daily practice'. The section giving guidance on special warnings and precautions for use referred to a number of factors to consider; including 'interaction with other medicinal products affecting haemostasis'. The information in this part of the website included the need to take care if patients were treated concomitantly with NSAIDs including aspirin and concluded that 'Further information on interactions with other medicinal products is available in the Eliquis SmPC'. The template for the website included links to the prescribing information, the adverse event reporting information, the SPC and to the patient information leaflet. At the end of the list of factors to consider was a reference to 'see Eliquis SmPC for full prescribing information'.

The Panel noted the Alliance's submission that the links provided were to the amended SPC and prescribing information which had the information that care was to be taken if patients were treated concomitantly with SSRIs or SNRIs or NSAIDs including acetylsalicylic acid (Section 4.4) and that Eliquis should be used with caution when coadministered with SSRIs, SNRIs or NSAIDs (including acetylsalicylic acid) because these products typically increased the bleeding risk (Section 4.5).

The Panel considered that only referring to the cautions for coadministering NSAIDs and not referring to similar cautions with SSRIs or SNRIs on a detailed page about special warnings and precautions for use was misleading. The Panel ruled a breach of the Code. The Panel considered that although misleading, the omission did not necessarily mean that the material was inconsistent with the SPC and therefore ruled no breach of the Code.

The Panel ruled that the companies had failed to maintain high standards in breach of the Code.

The Panel noted its comments above and that neither SSRIs nor SNRIs were contra- indicated with Eliquis and health professionals would be cautious when initiating any therapy. The Panel considered that in the particular circumstances of this case the omission of information about the need for care if SSRIs or SNRIs were coadministered with Eliquis did not warrant a ruling of a breach of Clause 2 which was reserved as a sign of particular censure.

A complainant who described him/herself as a 'concerned UK health professional' complained about the Eliquis (apixaban) website. Eliquis, co-marketed by Bristol-Myers Squibb and Pfizer, was an antithrombotic.

COMPLAINT

The complainant noted that pages of the Eliquis website which detailed special warnings and precautions for use, stated that care was to be taken if patients were treated concomitantly with non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin. That statement, however, differed significantly with the latest version of the summary of product characteristics (SPC) which stated that care was to be taken if patients were treated concomitantly with selective serotonin re-uptake inhibitors (SSRIs) or serotonin norepinephrine re-uptake inhibitors (SNRIs), or NSAIDs, including acetylsalicylic acid (aspirin). The complainant submitted that this could potentially be a patient safety issue.

When writing to advise Bristol-Myers Squibb and Pfizer of the complaint, the Authority asked both companies to consider the requirements of Clauses 2, 3.2, 7.2 and 9.1 of the 2016 Code.

RESPONSE

Bristol-Myers Squibb responded on behalf of both companies (the Alliance) and stated that the special warnings and precautions for use section of the Eliquis website was approved and went live in May 2018 (webpage job number 432UK1800403-06).

The Alliance explained that the Eliquis SPC received a positive Committee for Medicinal Products for Human Use (CHMP) opinion on 18 June 2018 (date

of revised SPC) to include additional information regarding SSRIs and SNRIs in Sections 4.4 and 4.5. On receipt of the European Commission Decision on 3 August 2018, the final SPC of Eliquis was made available for UK health professionals as was the prescribing information and revised Eliquis materials.

In accordance with the relevant company standard operating procedures (SOPs) both companies prepared a list of all valid Eliquis promotional materials in use including the Eliquis website to ensure the review and re-approval in light of the SPC update. The majority of the materials only required the inclusion of updated prescribing information and/or SPC and no content revision was needed.

The Eliquis webpage in question was reviewed, and the links to the updated SPC/prescribing information were included. The content on the webpage included interactions with other medicines which affected haemostasis. A clear statement in the section stated, 'Further information on interactions with other medicinal products is available in the Eliquis SPC' and the latest SPC/prescribing information were directly linked on this page. However, in hindsight, the content in this particular webpage would have benefitted from being revised to additionally include the information related to SSRIs and SNRIs. The Alliance appreciated that this might have caused confusion and ambiguity to the readers and therefore it was being updated.

With regard to Clause 7.2, the Alliance submitted that all the information provided was accurate and fair in its entirety, considering the easy availability and accessibility of the most updated SPC/prescribing information through a clear and prominent direct single click link and a very clear sign posting which stated, 'Further information on interactions with other medicinal products is available in the Eliquis SPC'.

Although the Alliance submitted that it did not consider there was a breach of Clause 7.2 because of the prominent availability of prescribing information and sign posting to consult this information for all interactions, it had, nevertheless, decided to add this interaction to the webpage for additional clarity.

The Alliance submitted that the webpage in question met the requirements of Clause 3.2. The promotional content was in line with the marketing authorization and was not inconsistent with the particulars listed in the SPC/prescribing information. No promotional material suggested that Eliquis could be safely used in conjunction with SSRIs/SNRIs. There was a short summary of the haemorrhage risks, and a final paragraph, which stated 'Further information on interactions with other medicinal products is available in the Eliquis SPC'. In addition, on scrolling down to the bottom of the page a link to the Eliquis SPC and prescribing information was provided.

The Alliance submitted that it had followed the requirements of Clause 4.4 of the Code, which stated that in the case of digital material the prescribing information must be provided either: by inclusion in the digital materials itself, or by way of a clear and prominent direct single click link. Based upon the above information, the Alliance denied a breach of Clause 3.2 as all requirements of that clause had been met.

The Alliance stated that patient safety was at the core of its culture and it took it as its ethical responsibility to adhere to best practices when it came to patient safety. In this particular example it had met all the internal standard operating procedures (SOPs) and Code requirements with a sense of urgency and responsibility. The Alliance stated that it followed strict internal SOPs for promotional material reviews, and approvals. The Alliance further submitted that it ensured that all of its signatories were properly trained; skills and knowledge were maintained via internal training and refresher sessions. Since the SPC update, the promotional materials were reviewed and re-approved as per the SOP to contain the most updated SPC and prescribing information. During this process, the content of a number of promotional materials was also updated to include interactions with SSRIs/SNRIs as noted above.

The webpage at issue always contained the most up-to-date SPC/prescribing information with a simple 'one click' easy access and a clear direction to the readers to review the full information regarding any warnings and precautions of use related to Eliquis.

Following the regulatory additions of SSRI and SNRI in Sections 4.4 and 4.5 of the SPC, the Alliance immediately updated the link to all materials to include this new information.

The Alliance submitted that it had a strong process in place for the review and approval of materials and the update of promotional materials following the above update to the SPC followed the robust SOP. The Alliance thus considered that high standards at all times were met and that there was no breach of Clause 9.1.

The Alliance denied any breach of Clause 2. The companies had taken all the steps according to their SOPs and requirements of the Code to ensure that they did not reduce the confidence in the industry.

PANEL RULING

The Panel noted that the website in question was for health professionals and was headed 'Practical Information To assist your daily practice'. The section giving guidance on special warnings and precautions for use referred to a number of factors to consider; the second factor listed was 'interaction with other medicinal products affecting haemostasis'. The information in this part of the website included the need to take care if patients were treated concomitantly with NSAIDs including aspirin and concluded that 'Further information on interactions with other medicinal products is available in the Eliquis SmPC'. The template for the website included links to the prescribing information, the adverse event reporting information, the SPC and to the patient information leaflet. At the end of the list of factors to consider was a reference to 'see Eliquis

SmPC for full prescribing information'.
The Panel noted the Alliance's submission that the links provided were to the amended SPC and prescribing information which had the information that care was to be taken if patients were treated concomitantly with SSRIs or SNRIs or NSAIDs including acetylsalicylic acid (Section 4.4) and that Eliquis should be used with caution when coadministered with SSRIs, SNRIs or NSAIDs (including acetylsalicylic acid) because these products typically increased the bleeding risk (Section 4.5).

The Panel considered that only referring to the cautions for coadministering NSAIDs and not referring to similar cautions with SSRIs or SNRIs on a detailed page about special warnings and precautions for use was misleading. There was an implication that all relevant interactions with other medicinal products affecting haemostasis were included and this was not so. The section at issue mentioned that further information on interactions with other medicinal products was available in the Eliquis SPC but this did not specifically refer to medicines which affected haemostasis. The Panel ruled a breach of Clause 7.2 of the Code. The Panel considered that although misleading, the omission did not necessarily mean that the material was inconsistent with the SPC and therefore ruled no breach of Clause 3.2 of the Code.

The Panel considered that the companies had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted its comments above and that neither SSRIs nor SNRIs were contra indicated with Eliquis and health professionals would be cautious when initiating any therapy. The Panel considered that in the particular circumstances of this case the omission of information about the need for care if SSRIs or SNRIs were coadministered with Eliquis did not warrant a ruling of a breach of Clause 2 which was reserved as a sign of particular censure. The Panel therefore ruled no breach of Clause 2 of the Code.

Complaint received **5 February 2019**

Case completed **2 May 2019**