CASE AUTH/3356/5/20

COMPLAINANT v ALEXION

Alleged disguised promotion of Soliris

A complainant, who described him/herself as a concerned UK health professional, complained that Alexion Pharma UK Ltd had disguised its promotion of Soliris (eculizumab). Soliris was indicated for, amongst other things, the treatment of paroxysmal nocturnal haemoglobinuria (PNH) in adults and children.

The complainant drew attention to a PNH guidance document (ref UK/SPNH/12/0022(3)a October 2014) on a named hospital website. The complainant stated that, on the face of it, it appeared to be a non-promotional, educational document; the disclaimer near the bottom of the first page ['This publication was supported by an unrestricted educational grant from Alexion. The content of these guidelines was not influenced by Alexion.'] clearly stated as much. Then in much smaller writing at the bottom of the first page there was reference to prescribing information for Soliris on the back of the document where there was further branding for Alexion.

The complainant alleged that as the document included prescribing information, it was clearly a promotional item, albeit one there had been an attempt to disguise. The complainant stated that when the document was created there were no other treatments for PNH, and so extreme care needed to be taken that items aimed at disease awareness were not indirectly promotional. In the complainant's view, such extreme care had not been taken.

The complainant noted that the first mention of Soliris (on the front of the document) did not include a generic name. The prescribing information included was extremely out of date. Since 2014 there had been numerous updates to the summary of product characteristics (SPC) including contraindications and special warnings. The complainant stated that as the item had potentially not been updated since 2014, but was still available online 6 years later, this demonstrated at best extremely lax internal processes.

The detailed response from Alexion is given below.

The Panel noted that the material at issue titled 'Guidance for flow cytometric testing for GPI-deficient populations and Paroxysmal Nocturnal Haemoglobinuria (PNH)', was dated October 2014 and included an Alexion job bag code and the Soliris prescribing information, dated June 2014 on the back page.

The Panel noted Alexion's submission that it had provided support for the development of the guidelines and whilst the focus was on screening and diagnosis of PNH, the company recognised, on balance, that inclusion of the Soliris prescribing information meant that the material was promotional.

The Panel noted that immediately below the title, the document stated 'This guidance has been developed by the [named hospital]' in bold type font. The disclaimer near the bottom of the first page stated:

> **'This publication was supported by an unrestricted educational grant from Alexion. The content of these guidelines was not influenced by Alexion'.**

The disclaimer was followed by the Alexion corporate logo. The Panel considered that the implication was that there was an arm's length arrangement between the parties, which was not so; evidence provided by Alexion indicated that the company had had significant input into the development of the material. The Panel noted Alexion's involvement and considered that although prescribing information was included, the disclaimer at the outset was such that the promotional nature of the material was disguised. A breach of the Code was ruled, as acknowledged by Alexion.

The Panel noted that the first (and the most prominent) mention of the brand name was not followed by the non-proprietary name and a breach of the Code was ruled as acknowledged by Alexion.

The Panel considered that the availability of the promotional guidelines on the publicly accessible hospital website might encourage a member of the public to ask their health professional to prescribe Soliris and a breach of the Code was ruled as acknowledged by Alexion.

The Panel noted the complainant's allegation that since 2014 there had been numerous updates to the SPC including contraindications and special warnings and that the prescribing information included in the material at issue was thus out of date. Whilst the Panel was concerned to note that it appeared that prescribing information dated September 2015 was included on the revised guidelines and a further update to the prescribing information was referred to by the representative in May 2018, it noted that the complainant bore the burden of proof In the Panel's view the complainant had not provided any details of which updates to the SPC had warranted changes to the prescribing information and if so that any such changes had not been made. The Panel therefore, on balance, ruled no breach of the Code.

The Panel noted Alexion's submission that it approached the hospital about removing the 2014 guidelines in May 2018 but despite a number of follow-up attempts over several months, the material remained on the hospital's website until early 2019 when there was some difficulty in removing the guidelines entirely from the internet, in that whilst they no longer appeared on the hospital's website, an image still seemed to appear in Google images until April 2019 when following a final Google search, it was confirmed that they no longer appeared as such. The Panel noted, however, that it appeared that the complainant was still able to view the guidelines in May 2020. The Panel was extremely concerned that the material was available on the hospital website in the knowledge of some Alexion staff and for such a long time. The Panel considered that Alexion had failed to maintain high standards in this regard and a breach of the Code was ruled as acknowledged by Alexion.

A complainant, who described him/herself as a concerned UK health professional, complained that Alexion Pharma UK Ltd had disguised its promotion of Soliris (eculizumab). Soliris was

indicated for, amongst other things, the treatment of paroxysmal nocturnal haemoglobinuria (PNH) in adults and children.

COMPLAINT

The complainant drew attention to a PNH guidance document (ref UK/SPNH/12/0022(3)a October 2014) (link provided) on a named hospital website. The complainant stated that, on the face of it, it appeared to be a non-promotional, educational document; the disclaimer near the bottom of the first page ['This publication was supported by an unrestricted educational grant from Alexion. The content of these guidelines was not influenced by Alexion.'] clearly stated as much. Then in much smaller writing at the bottom of the first page there was reference to prescribing information for Soliris on the back of the document where there was further branding for Alexion.

The complainant alleged that as the document included prescribing information, it was clearly a promotional item, albeit one there had been an attempt to disguise. The complainant stated that when the document was created there were no other treatments for PNH, and so extreme care needed to be taken that items aimed at disease awareness were not indirectly promotional. In the complainant's view, such extreme care had not been taken.

The complainant noted that the first mention of Soliris (on the front of the document) did not include a generic name. The prescribing information included was extremely out of date. Since 2014 there had been numerous updates to the summary of product characteristics (SPC) including contraindications and special warnings. The complainant stated that as the item had potentially not been updated since 2014, but was still available online 6 years later, this demonstrated at best extremely lax internal processes.

When writing to Alexion, the Authority asked it to consider the requirements of Clauses 4.1, 4.3, 9.1, 12.1 and 26.2 of the Code.

RESPONSE

Alexion noted that the complainant appeared to have accessed a Google image of withdrawn material that could only be viewed in this way ie it did not appear to be accessible through the named hospital.

To the extent possible, Alexion had investigated the sequence of events that led to the development of the 2014 PNH guidelines at issue and their appearance on the hospital website. Unfortunately, due to a lack of historical documentation and key staff having left Alexion, there were still some gaps in Alexion's knowledge, although its understanding of the company's involvement in the development of similar guidelines for a second named hospital provided a possible explanation as to the origin of the 2014 PNH guidelines at issue.

Initial development of guidelines on PNH

Alexion stated that it appeared that an ex-employee took up a role at one of the named hospitals in 2012. The representative who covered the area confirmed that the concept of the screening guidelines for PNH came from an informal conversation with the ex-employee working at the hospital and it was agreed that Alexion would provide support for the formatting, printing and dissemination of those guidelines. The objective of the guidelines was to raise the

profile of the hospital's screening services for PNH. Alexion provided a copy of that guideline which appeared to have been produced in 2013.

Alexion submitted that it was possible that these guidelines were somehow shared with the first named hospital and were then used to develop the 2014 guidelines now at issue. The representative who covered that hospital at the time was no longer with the company and so the company had no further evidence of the extent of its involvement in the 2014 guidelines. However, it appeared that Alexion had provided the prescribing information on the 2014 guidelines and there was an approval code on the item, indicating that it had gone through the company's approval system, although it had no record of this.

Further development of the guidelines

Alexion stated that a number of emails demonstrated that the company was subsequently involved in the revision of the guidelines in 2015-2016; they also provided some insight into the involvement of Alexion with this revision together with the initial development of the guidelines. Details were provided and email trails which Alexion submitted indicated that Alexion might have had significant input into the previous version of the guidelines.

Alexion stated that a further email from a representative in November 2015 indicated that he/she knew about the guidelines at issue in this case, that they were on the first named hospital's website and that they needed to be updated. The same email trail indicated that Alexion also had input into the covering letter to be sent with the revised guidelines to advertise the hospital's screening service. A copy of the email was provided which had attached what appeared to be the final version of the letter that was to accompany the distribution of the revised guidelines.

In February 2016, the representative emailed health professionals at the hospital indicating that the revised guidelines had been updated and approved by Alexion. The email trail also indicated that Alexion was involved in developing a distribution list for the revised guidelines and printing copies for distribution. A copy of the revised guidelines approved by Alexion was provided; they also contained prescribing information and they were approved as a promotional item as indicated by the meta data from the Alexion approval system. Alexion stated that from this the reviewers and signatories of the item had been informed that this was described as an item that would be provided to health professionals by field staff, and there was no indication that it would be placed on the hospital website although the representative had confirmed that a copy was placed on the hospital's intranet.

Alexion provided emails which it stated further showed that the company had input into the distribution list for the revised guidelines. Some of the emails could be taken to imply that Alexion was hoping that this entire activity would provide a return on investment in some way.

Copies of some of the emails indicated that Alexion was supporting other hospitals in a similar way, for example inputting into local screening guidelines and helping with distribution. Again, there was no indication that these guidelines appeared on the relevant health organisations' websites and they appeared to have been distributed by the sale force as a promotional item.

Recent Actions Taken to Address the Matter

Alexion stated that in May 2018, the representative knew that the prescribing information for Soliris had been updated and discussed the need to update the revised guidelines with a medical science liaison (MSL) colleague. At this point the representativeshowed the MSL the 2014 guidelines at issue on the named hospital's website andthe MSL raised a concern about having apparently promotional material on a publicly accessible website. The representative therefore notified a member of the Alexion medical staff who in turn was concerned that there was what appeared to be promotional material on the hospital website and that it should be removed. The medical employee contacted one of the health professionals involved in the development of the revised guidelines in May 2018, explained the potential compliance issues inherent in the guidelines being posted on the hospital's website and requested that the material be removed at the earliest opportunity. The health professional was surprised, as he/she did not appreciate the potential compliance issues with having the guidelines on the hospital's website but undertook to look into it and contact the hospital's IT department with a view to removing the material. However, despite a number of follow-up calls and follow-up visits by an MSL over several months, stressing the urgency of the situation for Alexion, the material remained on the hospital's website (an email summary of the attempts to speak with the hospital consultant was provided).

Alexion stated that in early 2019, it and the health professional agreed that Alexion would develop, as a medical and educational good/service, a non-promotional schematic of the guidelines and the health professional agreed to meet with Alexion. In parallel, correspondence continued between the hospital and Alexion in an attempt to remove the guidelines from the website. There was some difficulty in removing the guidelines entirely from the internet, in that whilst they no longer appeared on the website, an image still seemed to appear in Google images.

In April 2019 the revised guidance in schematic form was provided by Alexion to the hospital and following a final Google search, it was confirmed that the guidelines at issue no longer appeared as a Google image.

Response to relevant clauses

Alexion stated that it was confused as to how the complainant had accessed the 2014 guidelines given the efforts that were taken to ensure its removal from the hospital website and wider internet. However, it seemed that some Alexion staff knew that the version of the 2014 guidelines at issue, which the company had supported, was available on the publicly accessible hospital website for some time. Whilst the focus of the 2014 guidelines was very much screening and diagnosis Alexion recognised that, by including prescribing information for Soliris it thus referred to the medicine by name and its indication. For this reason and on balance, Alexion considered that the guidelines were promotional.

Given that the guidelines contained prescribing information Alexion considered that the requirements of Clause 4.1 had been met, and it denied a breach of Clause 4.1. However, the guidelines did not contain the non-proprietary name next to the most prominent display of the brand name and so the company acknowledged a breach of Clause 4.3.

As noted above, although the guidelines at issue were promotional, this might not have been clear to a reader of the hospital website, particularly as the declaration in relation to the involvement of Alexion implied an arm's length arrangement, which was not the case. Alexion

thus accepted that the promotional nature of the guidelines was disguised, in breach of Clause 12.1.

Alexion submitted that when considering the requirements of Clause 26.2, and in particular that statements should not be made that might encourage members of the public to ask their health professional to prescribe a specific prescription only medicine, it was important to note that Soliris was used to treat an ultra-rare condition and could only be prescribed by two nationally appointed PNH treatment centers. However, on balance, the appearance of the guidelines on the publicly accessible hospital website was contrary to the requirements of Clause 26.2 in that regard and Alexion acknowledged a breach of that clause.

Given the length of time that the guidelines were available on the hospital website, in the knowledge of a small number of Alexion staff, this also amounted to a failure to maintain high standards, in breach of Clause 9.1, for which the company sincerely apologised.

As a final point, Alexion noted that the sequence of events leading to the development and distribution of the guidelines were historical and pre-dated a number of senior employees joining the company, details were provided. Since these key staff had taken up their roles at Alexion there had been a significant strengthening of the compliance framework to support staff and details were provided
Whilst the issues highlighted in this case indicated a historical issue with the governance of certain materials, Alexion was confident that the steps taken to enhance its compliance programme had ensured that this was no longer a matter of concern.

PANEL RULING

The Panel noted that the material at issue titled 'Guidance for flow cytometric testing for GPI-deficient populations and Paroxysmal Nocturnal Haemoglobinuria (PNH)', was dated October 2014 and included an Alexion job bag code and the Soliris prescribing information, dated June 2014 on the back page.

The Panel noted Alexion's submission that it had provided support for the development of the guidelines and whilst the focus was on screening and diagnosis of PNH, the company recognised, on balance, that inclusion of the Soliris prescribing information meant that the material was promotional.

The Panel noted that immediately below the title, the document stated 'This guidance has been developed by the [named hospital' in bold type font. The disclaimer near the bottom of the first page stated:

> 'This publication was supported by an unrestricted educational grant from Alexion. The content of these guidelines was not influenced by Alexion'.

The disclaimer was followed by the Alexion corporate logo. The Panel considered that the implication was that there was an arm's length arrangement between the parties, which was not so; evidence provided by Alexion indicated that the company had had significant input into the development of the material. The Panel noted Alexion's involvement and considered that although prescribing information was included, the disclaimer at the outset was such that the promotional nature of the material was disguised. A breach of Clause 12.1 was ruled, as acknowledged by Alexion.

The Panel noted that the first mention (and the most prominent mention) of the brand name, Soliris, was on the foot of the first page which referred to the location of the prescribing information and this was not followed by the non-proprietary name as required by the Code. A breach of Clause 4.3 was ruled as acknowledged by Alexion.

The Panel considered that the availability of the promotional guidelines on the publicly accessible hospital website might encourage a member of the public to ask their health professional to prescribe Soliris and a breach of Clause 26.2 was ruled as acknowledged by Alexion.

The Panel noted that it appeared that a revised version of the 2014 guidelines was approved in February 2016 (ref UK/SOL-PNH/16/0005, January 2016) and contained prescribing information dated September 2015. The Panel did not know how the September 2015 prescribing information differed from the June 2014 prescribing information; Alexion made no submission in this regard. The Panel noted Alexion's submission that these revised guidelines were certified for field staff to provide to health professionals and there was no indication to the signatories that it would be placed on the hospital website. The Panel noted however that the representative who was aware that the 2014 guidelines were available on the website had emailed a copy of the revised guidelines to the hospital and confirmed that a copy was placed on the hospital's intranet. The Panel was unclear why the 2014 guidelines were not withdrawn from the hospital's publicly accessible website at this time. The Panel further noted that in May 2018, the representative knowing that the prescribing information for Soliris had been updated again, discussed the need to update the revised guidelines with a medical science liaison (MSL) colleague and at this point showed the MSL the 2014 guidelines on the hospital's website. The Panel was again unclear what update to the Soliris prescribing information had occurred.

The Panel noted the complainant's allegation that since 2014 there had been numerous updates to the SPC including contraindications and special warnings and that the prescribing information included in the material at issue was thus out of date. The Panel noted that the complainant had provided no details in support of this allegation. The Panel noted that the general principle was that prescribing information (defined by Clause 4.2) must be up-to-date, must comply with Clauses 4.1 and 4.2 and must not be inconsistent with the SPC. The Panel further noted that some changes to an SPC might not necessarily have to be reflected in the prescribing information. For example, information relevant only to an indication not being promoted might not need to be included in the prescribing information. Whilst the Panel was concerned to note that it appeared that prescribing information dated September 2015 was included on the revised guidelines and a further update to the prescribing information was referred to by the representative in May 2018, it noted that the complainant bore the burden of proof. In the Panel's view the complainant had not provided any details of which updates to the SPC had warranted changes to the prescribing information and if so that any such changes had not been made. The Panel therefore, on balance, ruled no breach of Clause 4.1.

The Panel noted Alexion's submission that it approached the hospital about removing the 2014 guidelines in May 2018 but despite a number of follow-up attempts over several months, the material remained on the hospital's website until early 2019 when there was some difficulty in removing the guidelines entirely from the internet, in that whilst they no longer appeared on the hospital's website, an image still seemed to appear in Google images until April 2019 when following a final Google search, it was confirmed that they no longer appeared as such. The Panel noted, however, that it appeared that the complainant was still able to view the guidelines in May 2020. The Panel was extremely concerned that the material was available on the

hospital website in the knowledge of some Alexion staff and for such a long time. The Panel considered that Alexion had failed to maintain high standards in this regard and a breach of Clause 9.1 was ruled as acknowledged by Alexion.

Complaint received **28 May 2020**

Case completed **12 February 2021**