CASE AUTH/3392/9/20

COMPLAINANT v STIEFEL

Prescribing information for Toctino

A complainant who described him/herself as a concerned UK health professional, complained about prescribing information for Toctino (alitretinoin) placed on the Guidelines in Practice website by Stiefel. Toctino was indicated for use in adults who had severe chronic hand eczema that was unresponsive to treatment with potent topical corticosteroids.

The complainant noted that the Toctino prescribing information (link provided) was created in 2016, which was also when the material was prepared. The complainant doubted that the prescribing information had been rechecked since then and there had been six updates to the summary of product characteristics (SPC) since 2016 which had included alterations to most sections – including special warnings. Further, there was no black triangle present, which was required for Toctino which was a patient safety issue.

The detailed response from GlaxoSmithKline is given below.

The Panel noted GlaxoSmithKline's submission that it had commissioned a GP e-learning module at the end of 2017 but that it decided not to proceed with the project, which was subsequently cancelled as confirmed by the publisher. The content was therefore never approved to go live by GlaxoSmithKline and the promotional material and associated prescribing information should not have been published on the third-party website. The publisher had, however, without GlaxoSmithKline's knowledge and against its express instructions, created standalone prescribing information and posted it on the Guidelines in Practice portal on 18 February 2018. It appeared from the material provided by GlaxoSmithKline that the hosting page was certified on 23 February 2018.

An email from the publisher stated that the project was cancelled at a face-to-face meeting with GlaxoSmithKline on 8 August 2018. The email stated that the e-learning project was to be ended and that the e-learning module needed to be removed from the publisher's website. The email further stated that someone from the publisher should confirm that this had been done. According to the email, the publisher emailed the GlaxoSmithKline employee to confirm that the e-learning module had been removed from the website.

The Panel noted that the material should not have been available after 8 August. It appeared that both parties agreed that the project was cancelled by 8 August 2018. No written confirmation from GlaxoSmithKline to the publisher regarding the company's decision not to proceed with the project was provided.

It appeared that the Toctino prescribing information was made live in error by the publisher before the project was cancelled and the publisher had not removed it following cancellation of the project in August 2018.

The Panel noted that the complainant had not provided details of which updates to the SPC, in his/her view, had warranted changes to the prescribing information at issue; GlaxoSmithKline had made no submission in this regard except to state that the requirement for the addition of a black triangle only became necessary in July 2018 following a regulatory update and that GlaxoSmithKline had updated the Toctino prescribing information in July 2018 to include a black triangle.

As GlaxoSmithKline was unaware of the existence of the prescribing information in question on the Guidelines in Practice website, this was not updated. The Panel noted that the prescribing information in question therefore did not include a black triangle when it became necessary in July 2018, which was prior to the project being cancelled, and up until the material was removed at the time of the complaint (September 2020) and was thus out-of-date. The Panel therefore ruled breaches of the Code.

The Panel noted the circumstances of this case and considered that GlaxoSmithKline had been badly let down by the third party working on its behalf. As a result of the publisher, the out-of-date prescribing information for Toctino, which should not have been published in the first place, was available for over two years. The Panel noted its comments and rulings above and considered that high standards had not been maintained. A breach of the Code was ruled.

The Panel noted its rulings and comments above and that GlaxoSmithKline had taken immediate steps to ensure removal of the material from the third party website as soon as it was discovered. The Panel did not consider that the particular circumstances warranted a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such use.

A complainant who described him/herself as a concerned UK health professional, complained about prescribing information for Toctino (alitretinoin) placed on the Guidelines in Practice website by Stiefel. Toctino was indicated for use in adults who had severe chronic hand eczema that was unresponsive to treatment with potent topical corticosteroids.

COMPLAINT

The complainant provided a link to the Toctino prescribing information on the Guidelines in Practice website and noted that it was created in 2016, which was also when the material was prepared. The complainant doubted that the prescribing information had been rechecked since then as was required (ie every 2 years), as there had been 6 updates to the summary of product characteristics (SPC) since 2016 which had included alterations to most sections – including special warnings.

The complainant was also concerned that there was no black triangle present, which was required for Toctino and stated that this was a patient safety issue.

When writing to Stiefel, the Authority asked it to consider the requirements of Clauses 2, 4.1, 4.10 and 9.1 of the Code.

RESPONSE

GlaxoSmithKline noted that the prescribing information in question (ref UK/ART/0010/13(5) (copy provided) was posted on the Guidelines in Practice website. GlaxoSmithKline noted that the anonymous complainant had great insight into the number of updates to the Toctino SPC.

GlaxoSmithKline had taken the complaint extremely seriously and had conducted a thorough internal review.

GlaxoSmithKline strongly asserted that while it was extremely unfortunate that the incident occurred and it was taking steps to try to ensure that a similar incident did not occur again in the future, it could not be held responsible for the issue and therefore denied any breach of the clauses quoted.

Background

GlaxoSmithKline stated that Toctino was a licensed product of Stiefel, a GlaxoSmithKline subsidiary. The product had not been actively marketed by GlaxoSmithKline since 2018.

Guidelines in Practice was a third-party online journal aimed at health professionals. GlaxoSmithKline had a legal agreement in place with the parent company/publisher of Guidelines in Practice.

GlaxoSmithKline stated that it had commissioned a GP e-learning module with the publisher at the end of 2017. This proposed module would have consisted of a presentation, hosting page and email traffic drivers. The agreed project plan involved the following steps:

1 Creation of an e-learning module, hosting page (with the embedded prescribing information) and emails to drive traffic to the module (driver emails). This would be in the form of pdfs created off-line by the publisher on behalf of GlaxoSmithKline.

2 Approval of content in pdf format on the GlaxoSmithKline copy approval system.

3 Hosting of the approved content on a staging site (separate from the live site) for certification and final form approval by GlaxoSmithKline.

4 GlaxoSmithKline to notify the publisher of the final form approval and permission for the material to go live on the Guidelines in Practice site.

5 Content to go live.

The experienced GlaxoSmithKline signatory raised issues with the proposed email traffic drivers which could not be resolved simply. GlaxoSmithKline decided not to proceed with the project, which was subsequently cancelled, as confirmed by the publisher (copy of email provided).

The content was therefore never approved to go live by GlaxoSmithKline, as confirmed by the publisher. Therefore, the promotional material and associated prescribing information did not go ahead and should not have been published on the website.

Following the complaint and subsequent GlaxoSmithKline investigation, it became apparent that the publisher had unfortunately gone against the agreed process and, without

GlaxoSmithKline's knowledge, created a standalone prescribing information and hosted it on the Guidelines in Practice portal. The publisher posted the prescribing information on 18 February 2018 without GlaxoSmithKline's knowledge and against its express instructions. This was despite, as stated above, GlaxoSmithKline cancelling the entire project before the pdf format was approved.

The publisher had admitted culpability for detaching the prescribing information from the original source material and hosting it on its site. This happened without GlaxoSmithKline's knowledge and despite the clear instruction from the company not to proceed with publishing the material.

When GlaxoSmithKline was notified about the complaint and investigated the issue, the prescribing information on Guidelines in Practice was accessible by someone searching for 'Toctino' or 'Toctino prescribing information' on a search engine such as Google, Yahoo or Bing and clicking on the relevant link. The prescribing information could not be accessed by typing in the specific search terms in the search function on Guidelines in Practice. There were no Toctino-related promotional materials on the website. As part of this investigation, GlaxoSmithKline had confirmed with the publisher that it had changed its processes to prevent this from happening again in the future and had received the publisher's confirmation of this.

The publisher immediately took the Toctino prescribing information down from the Guidelines in Practice website when the issue was highlighted.

The prescribing information, dated June 2016, was correct when the campaign was being planned, but as noted above, was published without the knowledge of and contrary to the express instructions from GlaxoSmithKline. Toctino did not require a black triangle at the time, and the requirement for the addition of a black triangle only became necessary in July 2018 following a regulatory update. In line with GlaxoSmithKline's policy on prescribing information updates (copy provided), the prescribing information was accordingly updated in July 2018 to include the black triangle but as GlaxoSmithKline was completely unaware of the existence of the prescribing information on the Guidelines in Practice website, this link was not updated.

Response to alleged breaches of the Code

GlaxoSmithKline was extremely disappointed that prescribing information for Toctino, was published without its knowledge or instruction in the online journal 'Guidelines in Practice'. GlaxoSmithKline took its responsibility in abiding strictly to the Code very seriously and strongly contended that, given that the publisher had acted contrary to the agreed process, it had not breached Clauses 4.1 and 4.10 of the Code.

Therefore, GlaxoSmithKline asserted that it had maintained high standards; it was very clear that the proposed material was not to go ahead, and the project was cancelled. The prescribing information was updated in a timely manner following updates to the SPC.

Therefore, GlaxoSmithKline denied being in breach of Clauses 9.1 and 2.

Further comments from GlaxoSmithKline

In response to a request from the Panel regarding the date of cancellation, GlaxoSmithKline stated that it had conducted an extensive internal search for this information. This had been made difficult by the complexities of the product being marketed at the time by Stiefel, a GlaxoSmithKline subsidiary. Unfortunately, the person responsible for the project at the time

left the organisation in late 2018. GlaxoSmithKline had a policy of retaining emails for a maximum of 15 months and the company could not therefore proceed with a forensic search of its internal systems for emails or other evidence from the time. GlaxoSmithKline had hence been unsuccessful in finding email communication from GlaxoSmithKline to Guidelines in Practice regarding cancellation of the project for this reason.

The publisher had also done an extensive investigation of their systems. The individual involved in the project at the time on their side left the organisation a while ago and the publisher had therefore been unable to find any further evidence either. However, the publisher re-confirmed that the project was cancelled at a face-to-face meeting with GlaxoSmithKline on the 8 August 2018. This was in addition to their previous acknowledgement of culpability as set out in GlaxoSmithKline's original response.

Regarding whether cancellation of projects was recorded in the certification system, GlaxoSmithKline submitted that its standard operating procedure (SOP) on the recall of promotional and non-promotional materials did not explicitly cover cancellation of projects as in this case. The materials were therefore withdrawn following approval when they came to the natural end of their 2-year expiry period on the system. GlaxoSmithKline would look to include such situations in the SOP.

GlaxoSmithKline hoped that the existing evidence, including the acknowledgement from the publisher that they were culpable in hosting the prescribing information wrongly on the website for Guidelines in Practice despite the project not going ahead, would suffice in exonerating GlaxoSmithKline from the alleged breaches of the Code.

PANEL RULING

The Panel noted GlaxoSmithKline's submission that it had commissioned a GP e-learning module at the end of 2017 but that it decided not to proceed with the project, which was subsequently cancelled as confirmed by the publisher. The content was therefore never approved to go live by GlaxoSmithKline and the promotional material and associated prescribing information should not have been published on the third-party website. According to GlaxoSmithKline, under the agreed project plan the company was to notify the publisher of the final form approval and permission for the material to go live on the Guidelines in Practice site.

The Panel noted GlaxoSmithKline's submission that the publisher had, however, without GlaxoSmithKline's knowledge and against its express instructions, created standalone prescribing information and posted it on the Guidelines in Practice portal on 18 February 2018. It appeared from the material provided by GlaxoSmithKline that the hosting page was certified on 23 February 2018.

The Panel noted that it was a well-established principle under the Code that pharmaceutical companies were responsible for the acts or omissions of third parties working on their behalf, even if those acts and omissions were inconsistent with instructions given by the companies.

In response to a request for further information, GlaxoSmithKline provided a copy of an email from the publisher which stated that the project was cancelled at a face-to-face meeting with GlaxoSmithKline on 8 August 2018. The email stated that the GlaxoSmithKline employee said that the e-learning project was to be ended and that the e-learning module needed to be removed from the publisher's website. The email further stated that someone from the publisher should confirm that this had been done. According to the email, the publisher emailed

the GlaxoSmithKline employee to confirm that the e-learning module had been removed from the website.

The Panel noted that the material should not have been available after 8 August. It appeared that both parties agreed that the project was cancelled by 8 August 2018. No written confirmation from GlaxoSmithKline to the publisher regarding the company's decision not to proceed with the project was provided.

It appeared that the Toctino prescribing information was made live in error by the publisher before the project was cancelled and the publisher had not removed it following cancellation of the project in August 2018.

The Panel noted that the complainant referred to six updates to the summary of product characteristics (SPC) since 2016 which he/she stated had included alterations to most sections, including special warnings. The complainant had not provided details of which updates to the SPC, in his/her view, had warranted changes to the prescribing information at issue; GlaxoSmithKline had made no submission in this regard except to state that the requirement for the addition of a black triangle only became necessary in July 2018 following a regulatory update and that GlaxoSmithKline had updated the Toctino prescribing information in July 2018 to include a black triangle.

As GlaxoSmithKline was unaware of the existence of the prescribing information in question on the Guidelines in Practice website, this was not updated. The Panel noted that the prescribing information in question therefore did not include a black triangle when it became necessary in July 2018, which was prior to the project being cancelled, and up until the material was removed at the time of the complaint (September 2020) and was thus out-of-date. The Panel therefore ruled a breach of Clauses 4.1 and 4.10.

The Panel noted the circumstances of this case and considered that GlaxoSmithKline had been badly let down by the third party working on its behalf. As a result of the publisher, the out-of-date prescribing information for Toctino, which should not have been published in the first place, was available for over two years. The Panel noted its comments and rulings above and considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel noted its rulings and comments above and that GlaxoSmithKline had taken immediate steps to ensure removal of the material from the third party website as soon as it was discovered. The Panel did not consider that the particular circumstances warranted a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such use. No breach of Clause 2 was ruled.

Complaint received **1 October 2020**

Case completed **11 March 2021**