CASE AUTH/3257/10/19

VOLUNTARY ADMISSION BY GLAXOSMITHKLINE

Use of outdated prescribing information

GlaxoSmithKline admitted that an email sent in September 2019, which had been certified as promotional, contained out-of-date prescribing information. The error was identified the following day by a GlaxoSmithKline medical signatory.

According to GlaxoSmithKline, as it was not possible to recall the original email, a corrective email was sent a week later to the same recipients. However, 10 days later GlaxoSmithKline found out that its agency, had only sent the corrective email to those GPs who had opened the original email. GlaxoSmithKline then asked the agency, as per its original request, to ensure that the second corrective email was sent to all GPs to whom the original email was sent.

GlaxoSmithKline gave details of the differences between the current prescribing information (dated November 2018) and the out-of-date prescribing information (dated November 2017). GlaxoSmithKline maintained that it had appropriate processes in place to ensure the update of prescribing information and the review and certification of promotional material; this was a case of human error.

The detailed response from GlaxoSmithKline is given below.

The Panel noted that the prescribing information in the email in question was dated November 2017. According to GlaxoSmithKline, the current SPC at the time the promotional email in question was distributed in September 2019 was dated November 2018. The Panel noted Glaxo SmithKline's submission about the changes to the November 2018 SPC: the extension of the indication to include patients who were not adequately treated by a combination of long-acting B_2-agonist and a long-acting muscarinic antagonist; the addition of new adverse events (bronchitis, sinusitis, urinary tract infection, dysphonia, constipation and dry mouth); and the increased frequency of candidiasis of the mouth and oropharyngeal pain which moved from uncommon to common.

The Panel noted that the prescribing information included in the email in question sent in September 2019 was out-of-date such that it did not include those new and common side effects which had been added to the SPC in November 2018. The Panel ruled a breach of the Code.

The Panel noted that the body of the email in question referred to the new indication. It was unclear to the Panel how an apparently withdrawn item could be repurposed as described by GlaxoSmithKline and subsequently certified. In the Panel's view, a robust compliance framework should minimize the risk of human error and the checks and balances such as the approval process including certification should identify where such an error had occurred. The Panel noted that the error had been quickly identified after

the email in question had been sent and corrective action taken. All recipients of the email received the subsequent corrective email on 3 October, 17 days after the original email was sent, and certain individuals had been retrained. The Panel considered that prescribing information was an important contributor to patient safety. In the Panel's view, the use of out-of-date prescribing information meant that high standards had not been maintained and a breach of the Code was ruled.

GlaxoSmithKline UK Limited voluntarily admitted that a sponsored promotional email (ref PM-GB-FVU-EML-190028) for Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol) had contained out-of-date prescribing information embedded within the email. Trelegy Ellipta was used in the maintenance treatment of certain adults with chronic obstructive pulmonary disease (COPD).

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with GlaxoSmithKline.

VOLUNTARY ADMISSION

GlaxoSmithKline explained that the email in question was sent on 16 September 2019 by GP Notebook. The email had been certified as promotional in compliance with Clause 14 of the Code. The out-of-date prescribing information was identified on 17 September by a GlaxoSmithKline medical signatory. A corrective email (ref PM-GB-FVU-EML-190043) containing the correct prescribing information was sent to the same audience on 23 September. GlaxoSmithKline submitted that on 18 September an internal investigation established that the email was sent to GPs via GP Notebook. The email was opened by 1,487 GPs and 35 clicked through to further information. It was established that no other emails had been sent with out-of-date prescribing information.

The error with the first email was caused because it had been modified from an old, approved, email; the prescribing information (now out-of-date) included at the end of that email was not updated. As it was not possible to recall that email a corrective email was sent a week later on 23 September to the original recipients via GP Notebook. However, on 3 October, GlaxoSmithKline found out that its agency had only sent the corrective email to those GPs who had opened the original email. GlaxoSmithKline then asked the agency, as per its original request, to ensure that the second email was sent to all GPs to whom the original email was sent. The agency understood this to be only those who had opened the incorrect email. GlaxoSmithKline provided a copy of the correspondence between it and the agency.

GlaxoSmithKline noted that the current prescribing information (dated November 2018) differed from the out-of-date prescribing information (dated November 2017) as follows:

1 New prescribing information had a broader indication. Previously Trelegy Ellipta was indicated as a maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who were not adequately treated by a combination of an inhaled corticosteroid and a long-acting β2-agonist. Trelegy Ellipta was now indicated as a maintenance treatment in adult patients with moderate to severe COPD who were not adequately treated by a combination of an inhaled corticosteroid and a long-acting β2-agonist *or a combination of a long-acting β2-agonist and a long-acting muscarinic antagonist* (emphasis added).

2 Following an update to the summary of product characteristics (SPC), bronchitis, sinusitis, candidiasis of the mouth, urinary tract infection, oropharyngeal pain and constipation had been added to the prescribing information as additional common side effects.

GlaxoSmithKline maintained that it had appropriate processes in place to ensure the update of prescribing information and the review and certification of promotional material; this was a case of human error. The individuals involved, and their manager had been informed and reminded of the processes and requirements under the Code in respect to provision of prescribing information.

GlaxoSmithKline acknowledged a breach of Clause 4.2.

When writing to GlaxoSmithKline, the Authority asked it to consider the requirements of Clauses 4.1, 4.2 and 9.1 of the Code.

RESPONSE

GlaxoSmithKline submitted that the SPC was approved and updated in November 2018 from which the updated prescribing information was drawn. Additional adverse events had been added to the November 2018 SPC (bronchitis, sinusitis, urinary tract infection, dysphonia, constipation and dry mouth) and the frequency of candidiasis of mouth and oropharyngeal pain moved from uncommon to common.

The company had the following processes in place to update prescribing information following an SPC change:

- The regulatory team notified the medical team of a change in SPC with the timelines for approval from the regulatory authority.
- When the SPC had been approved, the medical team certified new prescribing information if required.
- At that point all materials containing the out-of-date prescribing information were withdrawn.
- New materials were certified for use with the current updated prescribing information.

In this case an old version of a previously approved email was repurposed, and human error led to the out-of-date prescribing information not being replaced with the current prescribing information. The individuals involved, and their manager had been informed and action had been taken to remind staff of the processes and requirements under the Code in respect to provision of prescribing information.

GlaxoSmithKline acknowledged breaches of Clauses 4.1 and 4.2 due to the use of out-of-date prescribing information. The prescribing information was clear and legible however the supplementary information stated that it must be consistent with the SPC for the medicine. In this case, the prescribing information was not consistent with the SPC.

GlaxoSmithKline noted that Clause 9.1 required high standards to be maintained at all times. The company submitted that it took its obligations to the Code seriously and worked to high standards; it had processes in place to ensure prescribing information and other obligatory information were provided and up-to-date. GlaxoSmithKline submitted that this had been an

unfortunate isolated incident and the issue was identified quickly and the company acted to correct the matter. Therefore, GlaxoSmithKline considered that it had maintained high standards and denied a breach of Clause 9.1.

PANEL RULING

The Panel noted that prescribing information, the components of which were listed in Clause 4.2, must be up-to-date and satisfy the requirements of Clause 4.2 which included providing a succinct statement of, *inter alia*, common adverse reactions likely to be encountered in clinical practice, serious adverse reactions and precautions and contra-indications relevant to the indications in the advertisement, and giving in an abbreviated form the substance of the relevant information in the SPC. The relevant supplementary information to Clause 4.1 stated that prescribing information must be consistent with the SPC for the medicine. Failure to provide the required information in the prescribing information would be a breach of Clause 4.1. The Panel noted that a company could chose to provide the SPC as part of the prescribing information; in such circumstances the SPC provided must be the most current one. The Panel noted that the prescribing information was embedded within the email in question.

The Panel noted that the prescribing information in the email in question was dated November 2017. According to GlaxoSmithKline, the current summary of product characteristics at the time the promotional email was distributed in September 2019 was dated November 2018. The Panel noted Glaxo SmithKline's submission about the changes to the November 2018 SPC: the extension of the indication to include patients who are not adequately treated by a combination of long-acting B_2-agonist and a long-acting muscarinic antagonist; the addition of new adverse events (bronchitis, sinusitis, urinary tract infection, dysphonia, constipation and dry mouth); and the increased frequency of candidiasis of the mouth and oropharyngeal pain which moved from uncommon to common.

The Panel noted that the prescribing information included in the email in question sent in September 2019 was out-of-date such that it did not include those new and common side effects which had been added to the SPC in November 2018. Given that the prescribing information thus did not contain 'a succinct statement of common adverse reactions likely to be encountered in clinical practice' from the current SPC, the prescribing information listed in Clause 4.2 had not been provided as required by Clause 4.1. The Panel thus ruled a breach of Clause 4.1. The Panel noted that GlaxoSmithKline had acknowledged a breach of Clause 4.2 but noted, as set out above, that the failure to provide the prescribing information listed in Clause 4.2 was a breach of Clause 4.1. No ruling was made with regard to Clause 4.2.

The Panel noted GlaxoSmithKline's submission that it had processes in place to update prescribing information following an SPC change which included certifying a new prescribing information and withdrawing all materials containing the out-of-date prescribing information. The Panel did not have a copy of the relevant standard operating procedure or evidence that relevant materials had been withdrawn in accordance with it. According to GlaxoSmithKline human error had allowed a previous email to be modified without anyone noticing that the prescribing information was out-of-date. The Panel noted that the body of the email in question referred to the new indication. It was unclear to the Panel how an apparently withdrawn item could be repurposed as described and subsequently certified. In the Panel's view, a robust compliance framework should minimize the risk of human error and the checks and balances such as the approval process including certification should identify where such an error had occurred. The Panel noted that the error had been quickly identified after the email in question

had been sent and corrective action taken. All recipients of the email received the subsequent corrective email on 3 October, 17 days after the original email was sent, and certain individuals had been retrained. The Panel considered that prescribing information was an important contributor to patient safety. In the Panel's view, the use of out-of-date prescribing information meant that high standards had not been maintained and a breach of Clause 9.1 was ruled.

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[*Post-hoc* note: 'After the completion of this case, GlaxoSmithKline clarified that the email in question was based on a new localised ABPI approved version of a centrally created model email rather than one 'apparently withdrawn' as stated by the Code of Practice Panel. When editing this centrally created model email, out-of-date prescribing information was embedded in the localised version.'.]

Complaint received **9 October 2019**

Case completed **17 December 2019**