CASE AUTH/2592/4/13

VOLUNTARY ADMISSION BY GLAXOSMITHKLINE

Benlysta case studies

GlaxoSmithKline voluntarily admitted that two promotional case studies for Benlysta (belimumab), were emailed to health professionals without being certified. Benlysta was indicated as add-on therapy in adults with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity despite standard therapy.

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.

GlaxoSmithKline explained that some of the information provided in the case studies was inconsistent with the Benlysta summary of product characteristics (SPC) and the link to the prescribing information did not work. However, the prescribing information could be accessed through the link to the product website. The company immediately recalled the non-compliant emails and investigated the events surrounding this error.

The detailed response from GlaxoSmithKline is given below.

The Panel noted that two case studies which promoted the use of Benlysta were emailed as a 'Dear Doctor' letter to health professionals prior to certification. The Panel acknowledged that as soon as GlaxoSmithKline became aware of the problem, it emailed the recipients to recall the information and to alert them that some of the information (ie the case study in the lupus nephritis class IV patient) might have been inconsistent with the Benlysta SPC. The recall email stated that Benlysta had not been studied in, and was not recommended in, *inter alia*, severe active lupus nephritis. The relevant part of the SPC was reproduced. Recipients were asked to acknowledge receipt of the recall email. The Panel noted with concern that recipients were not asked to delete the original 'Dear Doctor' letters.

The Panel noted that the letters were promotional and had not been certified. A breach of the Code was ruled. The emailed letters did not include the Benlysta prescribing information and the prescribing information link was not active. Although recipients could access the prescribing information via a link to the product website, the Panel did not consider that this was acceptable; prescribing information should be provided as an integral part of promotional material and should not be separate from it. The emails were 'Dear Doctor' letters sent electronically. A breach of the Code was ruled.

The Panel noted that according to its SPC, Benlysta had not been studied in, and was not recommended in severe active lupus nephritis. One of the case studies was of a patient who had lupus nephritis class IV in renal biopsy. The Panel noted that the clinician who had submitted the case study confirmed that in his/her opinion this patient was classed as having severe active lupus nephritis. The Panel thus considered the case study promoted the use of Benlysta in a manner which was inconsistent with the particulars listed in its SPC and was misleading in that regard. Breaches of the Code were ruled.

GlaxoSmithKline UK Limited voluntarily admitted that two promotional case studies for Benlysta (belimumab), were emailed to health professionals without being certified. Benlysta was indicated as add-on therapy in adults with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity despite standard therapy.

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.

COMPLAINT

GlaxoSmithKline stated that the breaches related to two Benlysta case studies that were sent to health professionals in error before they had gone through the company's standard review process for promotional materials.

The case studies were from a health professional who used Benlysta and were submitted to head office by a commercial manager to go through the promotional material approval process. The case studies were in email format. The purpose of the case studies was, in the anticipation of the final National Institute for Health and Care Excellence (NICE) guideline, to inform other lupus specialists of an important although limited experience with the product. Health professionals were encouraged to share their experience with GlaxoSmithKline in the first instance, which would be shared with other health professionals in accordance with the requirements of the Code.

Another member of the business unit team was responsible for raising new case study items in Zinc (GlaxoSmithKline's electronic system for approval of promotional materials). The case studies were duly added to Zinc to start the approval process.

There was a lag of two weeks from the case studies being submitted to head office and the new items being raised in Zinc. An email was sent to the commercial manager to confirm that the items had been raised in Zinc; the email stated the reference codes for the items and confirmed that they were awaiting review. The commercial manager mistakenly thought that the items had been approved and, forwarded the two unapproved

case studies to 48 health professionals (who had previously agreed to receive promotional emails). Members of the GlaxoSmithKline commercial business unit and medical team were blind copied on the emails.

Three days later a medical advisor and ABPI signatory returned from leave and realised that the case study emails had not been reviewed and approved. Further that some of the information provided in the case studies was inconsistent with the Benlysta summary of product characteristics (SPC) and that the link to the prescribing information did not work. However, the prescribing information could be accessed through the link to the product website. The matter was reported to the medical director who instigated an immediate recall of the non-compliant emails and an investigation into the error.

A commercial manager subsequently issued an email to recall the unapproved patient case studies, explained the essence of the error and asked recipients to confirm receipt of the recall email. In addition, the recall email contained a corrective statement with regard to the approved label as per the SPC.

Of the 48 recipients, 3 were returned undelivered which left 45 to be followed up. Two days prior to the submission of the voluntary admission 44 out of 45 confirmations had been received. The non-responder was being followed up for documented evidence acknowledging the receipt of recall.

GlaxoSmithKline submitted that the following further corrective actions were in process;

1 Ensuring that the health professional who had not yet responded confirmed receipt of the recall message.
2 Re-training the commercial manager on the approval process.
3 Production of a case study for sharing with the broader organisation to ensure that lessons were learnt from this error.
4 Initiation of a specific audit to review release of materials following certification.

GlaxoSmithKline submitted that this was an administrative error which led to the circulation of unapproved promotional case studies. GlaxoSmithKline was confident that this was an isolated incident.

GlaxoSmithKline stated that it took its obligations to comply with the Code seriously and was committed to ensuring that all staff were appropriately trained and acted in compliance with the Code.

When writing to GlaxoSmithKline the Authority asked it to consider the requirements of Clauses 3.2, 4.1, 7.2 and 14.1.

RESPONSE

GlaxoSmithKline explained that Benlysta was indicated as add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (eg positive anti-dsDNA and low complement) despite standard therapy. Section 4.4 of the SPC, Special Warnings and Precautions for Use, stated that Benlysta had not been studied in a number of patient groups, and was not recommended, *inter alia*, in severe active lupus nephritis.

GlaxoSmithKline noted that one of the case studies was that of a 35 year old female. In the section entitled 'symptoms/disease activity' the description was 'Lupus nephritis class IV on renal biopsy'. With regard to Clause 3.2, the sender of the email had not appreciated that this might be interpreted as one of the conditions listed in Section 4.4 of the SPC. GlaxoSmithKline had contacted the treating clinician who had confirmed that in his/her opinion this patient was classed as having severe active lupus nephritis. The clinician and the team involved knew the limitations of the licence and had made a clinical decision to prescribe.

With regard to Clause 7.2, GlaxoSmithKline submitted that the information contained in the email was accurate, fair and balanced.

Details of the product website landing page at the time the emails were sent were provided.

GlaxoSmithKline reiterated that although a link to the Benlysta prescribing information was not active the email included an active link to the Benlysta website hosted on the health professional part of health.gsk.co.uk, a promotional website with current prescribing information, therefore recipients would have been able to access the prescribing information from the email. A screen shot of the home page the reader was directed to on confirmation that they were a health professional, and the prescribing information which was active when the email was sent, were provided.

PANEL RULING

The Panel noted that the two case studies which promoted the use of Benlysta were emailed as a 'Dear Doctor' letter to health professionals prior to certification. The Panel acknowledged that as soon as GlaxoSmithKline became aware of the problem, it emailed the recipients of the case studies to recall the information and to alert them that some of the information (ie the case study in the lupus nephritis class IV patient) might have been inconsistent with the Benlysta SPC. It was noted in the recall email that Benlysta had not been studied in, and was not recommended in, *inter alia*, severe active lupus nephritis. The relevant part of the SPC was reproduced. Recipients were asked to acknowledge receipt of the recall email. The Panel noted with concern that recipients had not been asked to delete the original 'Dear Doctor' letters.

The Panel noted that the letters were promotional and had not been certified. A breach of Clause 14.1 was ruled. The emailed letters did not include the Benlysta prescribing information. In addition, the Panel noted that the prescribing information link was not active. Although the Panel noted

GlaxoSmithKline's submission that recipients could access the prescribing information via a link to the product website, it did not consider that this was acceptable; prescribing information should be provided as an integral part of promotional material and should not be separate from it. The emails were 'Dear Doctor' letters sent electronically. A breach of Clause 4.1 was ruled.

The Panel noted that Section 4.4 of the Benlysta SPC stated that Benlysta had not been studied in, and was not recommended in, *inter alia*, severe active lupus nephritis. One of the case studies sent to health professionals was of a patient who had lupus nephritis class IV in renal biopsy. The Panel noted that the clinician who had submitted the case study confirmed that in his/her opinion this patient was classed as having severe active lupus nephritis. The Panel thus considered the case study promoted the use of Benlysta in a manner which was inconsistent with the particulars listed in its SPC and was misleading in that regard. Breaches of Clauses 3.2 and 7.2 were ruled.

Complaint received **11 April 2013**

Case completed **14 May 2013**