CASE AUTH/3521/6/21

EX-EMPLOYEE v ASTRAZENECA

Alleged promotion of Calquence at a webinar

An ex-employee complained about an acalabrutinib (Calquence) Early Access Programme (EAP) Clinical Practice Learns (CPL) Webinar held on 11 May 2021 by AstraZeneca UK Limited.

The complainant alleged that this promotional event for Calquence had been disguised as a non-promotional webinar explaining key learns from the early access programme. Furthermore, the slides were not certified and had only been examined. This type of disguised promotion had a big impact on the way that pharmaceutical companies were perceived by health professionals.

The detailed response from AstraZeneca is given below.

The Panel noted that the webinar needs assessment internal form stated that, prior to Calquence receiving its marketing authorisation on 5 November 2020, AstraZeneca had initiated an early access programme (EAP) on 1 April 2020 which had enrolled approximately 600 patients in over 100 UK hospital centres. The webinar objectives were to provide an invitation only (closed) non-promotional educational forum for a clinical practice learns webinar to EAP enrolled consultant haematologists only. An objective of this meeting was to allow discussion, debate and to share clinical learns for the adverse event management of chronic lymphocytic leukaemia (CLL) and in particular, those haematologists who had prescribed acalabrutinib through the EAP.

The Panel noted that the footer of the first webinar slide stated, 'This non-promotional webinar has been organised and funded by AstraZeneca UK'. The Panel noted that the second slide described the webinar as non-promotional and referred to AstraZeneca supporting an educational forum for consultant haematologists enrolled on the early access programme. The second bullet point stated that the agenda and content of the meeting had been developed in collaboration with the faculty. In relation to the faculty, the Panel noted AstraZeneca's submission that having decided to address certain matters by holding a meeting, it then established a steering committee and selected and contracted with three haematologists, all of whom were participating in the EAP to become steering committee members. An additional speaker, recommended by one of the steering committee members, who also participated in the EAP, also presented.

The Panel noted that during the webinar, five patient case studies were shared by the four haematologists including treatment outcomes and key takeaways. The slides highlighted when a treatment approach was potentially inconsistent with the acalabrutinib SPC.

The Panel noted that there was no reference to prescribing information on the slides, however, the second slide contained an adverse event reporting statement.

The Panel considered that all the case studies presented, although discussing the management of side-effects, were overall positive about the use of acalabrutinib. The case studies were detailed and referred to treatment effectiveness in addition to the management of side-effects.

In the Panel's view, AstraZeneca appeared to have classified the meeting in question as non-promotional in the same way that an investigator meeting for clinical trials might be classified; however, the Panel considered that there were fundamental differences between a meeting for investigators involved in a clinical trial and a meeting for health professionals who had previously been involved in an early access programme for a medicine which now had a marketing authorisation; one such difference being the current relationship between the company and the health professionals involved.

The Panel noted the broad definition of promotion in Clause 1.2 and considered that the proactive presentation of acalabrutinib data which, although mainly discussing the management of adverse events, shared overall positive experiences of acalabrutinib use, could not be anything other than the promotion of acalabrutinib. In the Panel's view, neither the role of the Steering Committee nor that the audience was restricted to consultant haematologists who had participated in the EAP meant that the webinar was non promotional as implied by AstraZeneca. In the Panel's view, the webinar slides were promotional material; the webinar slides had been examined and not certified and therefore a breach of the Code was ruled.

The Panel considered that in referring to the meeting as non-promotional in all of the associated materials, including the invitation to the meeting and the meeting slides, the promotion of Calquence had been disguised and the Panel ruled a further breach of the Code.

An ex-employee complained about an acalabrutinib (Calquence) Early Access Programme (EAP) Clinical Practice Learns (CPL) Webinar held on 11 May 2021 by AstraZeneca UK Limited.

COMPLAINT

The complainant provided several screenshots of the webinar and stated that, on the surface of it, it appeared that this was a non-promotional webinar explaining key learns from the early access programme. However, looking into the agenda and the webinar itself, especially with the number of case studies that were discussed and the discussion challenge for health professionals treating patients with Calquence, it was quite evident that this was actually a promotional event for Calquence which had been disguised. Furthermore, as a promotional event the slides were not certified and had only been examined. The complainant stated that this was a real worry as this type of disguised promotion really did have a big impact on the way that pharmaceutical companies were perceived by health professionals.

The complainant subsequently provided an image of a piece written about the webinar the day after it took place by a team member (who was involved in organising the meeting) on an internal AstraZeneca platform which according to the complainant clearly outlined the thought process behind the meeting and the clear promotional aspect of the meeting.

When writing to AstraZeneca, the Authority asked it to consider the requirements of Clauses 12.1 and 14.1 of the Code.

RESPONSE

AstraZeneca noted that the complainant's allegations could be broken down as follows:

1 the webinar constituted disguised promotion, 'especially with the number of case studies' presented;
2 the evidence submitted in relation to a post on an internal AstraZeneca platform showed 'the clear promotional aspect of the meeting'; and
3 the meeting slides were not appropriately certified and 'only examined'.

AstraZeneca strongly refuted all of these allegations and any suggestion that Clauses 12.1 and 14.1 had been breached. This was a non-promotional webinar and all of the activities conducted in relation to it were executed according to AstraZeneca's standard operating procedures (SOPs) and were entirely permissible within the Code.

AstraZeneca submitted that in its response to these allegations, it would establish that this was a legitimate, well-planned and well-executed non-promotional webinar and would provide further information on:

- the business needs for the webinar, including the planning process and engagement with the Steering Committee in the lead up to it;
- the selection and engagement of the Steering Committee and Faculty;
- the selection of the attendees;
- the agenda for the webinar and its execution; and
- the approval process for this webinar.

Finally, AstraZeneca addressed each of the complainant's allegations according to the relevant clause of the Code of.

Background to the webinar

Acalabrutinib (Calquence) received a marketing authorisation from the European Medicines Agency (EMA) for first line (1L) Chronic Lymphocytic Leukaemia (CLL) and relapsed/refractory (RR) CLL on 5 November 2020 following an assessment process that started in October 2019. Due to the lack of an alternative oral treatment option for 1L CLL patients at the time of marketing authorisation [sic], AstraZeneca initiated an Early Access Programme (EAP) to address this area of high unmet clinical need. AstraZeneca's EAP was extremely well received by the clinical community, in particular, because it provided an alternative option for patients to be treated away from the hospital. This was vitally important during the COVID-19 pandemic, as the CLL patient population were often elderly and frail, with multiple co-morbidities and so they were often required to shield from the outside world. AstraZeneca's actions were highly praised by the clinical community and NHS England during this time of crisis. The summary of product characteristics (SPC) for acalabrutinib was provided.

Through AstraZeneca's various interactions with the haematologists who prescribed acalabrutinib through the EAP ('EAP Haematologists'), it became evident that there was a diversity of opinion and experience amongst the EAP haematologists in relation to the clinical

management of CLL and BTK (Bruton Tyrosine Kinase) inhibitor (BTKi) related adverse events (AEs). AstraZeneca therefore felt that there was a real educational value in bringing together these EAP haematologists to discuss and share their learnings on the management of AEs and complications for their CLL patients receiving acalabrutinib through the EAP.

The Steering Committee

AstraZeneca selected a steering committee comprised of three haematologists, all of whom were participating in the EAP. The role of the Steering Committee was to direct the content of the webinar and select clinically-relevant topics for discussion. AstraZeneca therefore had no role in the selection of the cases or shaping of the final agenda.

AstraZeneca contracted and briefed each individual member of the Steering Committee on the non-promotional nature of this webinar. The Steering Committee met on two occasions in March 2021. It was decided by the Steering Committee that presenting the themes as case studies would be the ideal way in which to share clinical learnings and experiences of managing patients on the acalabrutinib EAP. The final webinar took the form of five distinct case studies, with each case presenting a unique perspective on the management of CLL patients with a BTKi.

The set-up of the webinar

As the Steering Committee members were all from large teaching hospitals across the UK, the members thought it beneficial to include an additional speaker to provide the perspective of a consultant haematologist working in a district general hospital setting. This allowed for the presentation of the differing challenges that exist in the management of CLL patients across secondary and tertiary centres. An EAP haematologist was recommended by one of the Steering Committee members for this purpose.

All materials associated with the webinar were non-promotional in nature and examined in accordance with AstraZeneca's SOP and the ABPI Code. A record of the slide deck, along with the meta-data and signatory approval flow details from Veeva was provided.

The webinar

The Steering Committee and additional EAP haematologist were selected by AstraZeneca to be the presenters at this webinar ('the Faculty'), which took place on 11 May 2021 via Zoom. All of AstraZeneca's Faculty were briefed and understood the non-promotional nature of the meeting. No efficacy or safety data from the clinical development programme for acalabrutinib was presented at the meeting, only specific aspects of individual patients' disease management was discussed. At no point was acalabrutinib presented or discussed in a promotional manner – AstraZeneca strongly denied all of the complainant's allegations in this regard.

The webinar attendees

Only EAP haematologists were invited to the webinar. To ensure that this meeting was directed at the appropriate target audience, AstraZeneca gave clear instructions to all invitees and added a clear disclaimer stating '*This invitation is limited to the named haematologist only. Please do not distribute'* to clarify that the invitation was not to be forwarded to any unintended individuals. Furthermore, to verify the eligibility of attendees, a cross-check was performed by the

AstraZeneca Medical team to ensure that each registering attendee was indeed an EAP haematologist.

Posting on the AstraZeneca internal social media platform (Workplace) post meeting

Workplace was an internal, online collaboration platform within AstraZeneca which could not be accessed externally. AstraZeneca encouraged its employees to actively share success stories, projects, outcomes and achievements in order to positively affirm the work that it did on behalf of its patients.

AstraZeneca had reviewed the post in question carefully and could not see how the complainant's allegations had arisen. The post demonstrated that the webinar was a legitimate and well-executed meeting. The complainant was deliberately misrepresenting AstraZeneca's intention. The complaint was clearly unfounded and inaccurate. AstraZeneca was extremely disappointed to receive such allegations set out by the complainant.

Response to alleged breach of Clauses 12.1 and 14.1 of the ABPI Code of Practice

AstraZeneca strongly refuted all of the allegations and denied any suggestion that Clauses 12.1 and 14.1 of the Code had been breached. AstraZeneca stated that the PMCPA would note that no element of the meeting or any of the supporting meeting materials could be deemed as being 'promotional'. Furthermore, great care was taken to follow the relevant AstraZeneca SOPs to ensure that the non-promotional nature of this webinar remained intact.

Summary of AstraZeneca's position

AstraZeneca submitted that it had established that the webinar was conducted compliantly and in line with both the Code and all of AstraZeneca's internal SOPs. The webinar was a closed meeting exclusively for haematologists that had participated in the EAP. The content was directed by an external Steering Committee and the webinar provided key clinical learnings for EAP haematologists in improving the management of their CLL patients.

AstraZeneca strongly refuted any allegations that this was a promotional meeting and any suggestion that Clauses 12.1 and 14.1 had been breached. Great care was taken to ensure the non-promotional intention and nature of the webinar. AstraZeneca deliberately restricted access to the webinar to ensure that only those EAP Haematologists were invited to participate. AstraZeneca was extremely disappointed to receive such a complaint regarding this meeting – the complainant's allegations were categorically false and, in its opinion, vexatious.

AstraZeneca was profoundly proud of its efforts, not only to have made acalabrutinib available to CLL patients via an EAP, which of itself was a significant commitment, but also to have enabled such an important meeting to take place so that UK clinical experts could share their learnings within the programme in order to improve the quality of care for their patients. These were difficult to treat patients with very limited treatment options – all that AstraZeneca had done was advance clinical practice in the UK for patients with CLL, and for that, it would remain unapologetic.

PANEL RULING

The Panel noted that the webinar in question was held on 11 May 2021. The webinar needs assessment internal form stated that, prior to Calquence receiving its marketing authorisation on

5 November 2020, in the UK, AstraZeneca had initiated an early access programme (EAP) on 1 April 2020 which had enrolled approximately 600 patients in over 100 UK hospital centres. The form further stated that outside of trials, the EAP was the first clinical experience that the majority of UK haematologists had had with acalabrutinib in first line CLL patients. The webinar objectives were to provide an invitation only (closed) non-promotional educational forum for a clinical practice learns webinar to EAP enrolled consultant haematologists only and that these consultant haematologists would be identified and invited by using the data in the AstraZeneca EAP applications; this was to ensure that only consultant haematologists who had been actively involved in the EAP were invited. The form further stated that an objective of this meeting was to allow discussion, debate and to share clinical learns for the adverse event management of CLL and in particular, those haematologists who had prescribed acalabrutinib through the EAP. The Panel noted that the meeting aims included, *inter alia*:

> 'to allow these consultant haematologists to share case studies, including both best practice and challenging examples for the routine clinical management of CLL patients being treated with acalabrutinib on the EAP. Specifically, related to routine clinical management of CLL and associated complications that may be out of the scope of the acalabrutinib SmPC advice.'

The Panel noted that the needs assessment form referred to the establishment of a steering committee and the steering committee's role in jointly helping to develop the agenda, content and guidance on clinical relevance of topics etc. The steering committee was contracted to work with AstraZeneca in formulating an agenda and content. The form stated that details of the specific content was decided by the steering committee and that the webinar was not intended to deliver or reinforce any efficacy messages or to promote acalabrutinib in any manner.

The Panel noted AstraZeneca's submission that there would be real educational value in bringing together haematologists who prescribed acalabrutinib through the early access programme (EAP). In this regard, the Panel noted that the Code stated that meetings must have a clear educational content; the Panel noted that this applied to all meetings irrespective of whether they were promotional or non-promotional.

The Panel noted that the footer of the first webinar slide stated, 'This non-promotional webinar has been organised and funded by AstraZeneca UK'. The Panel noted that the second slide described the webinar as non-promotional and referred to AstraZeneca supporting an educational forum for consultant haematologists enrolled on the early access programme. The second bullet point stated that the agenda and content of the meeting had been developed in collaboration with the faculty. In relation to the faculty, the Panel noted AstraZeneca's submission that having decided to address certain matters by holding a meeting, it then established a steering committee and selected and contracted with three haematologists, all of whom were participating in the EAP to become steering committee members. An additional speaker, recommended by one of the steering committee members, who also participated in the EAP, was used to allow for the presentation of the differing challenges that existed in the management of CLL patients across secondary and tertiary centres.

The Panel noted that during the webinar, five patient case studies were shared by the four haematologists including treatment outcomes and key takeaways. The slides highlighted when a treatment approach was potentially inconsistent with the acalabrutinib SPC.

The Panel noted that there was no reference to prescribing information on the slides, however, the second slide contained an adverse event reporting statement.

The Panel noted that the treatment outcomes in Case Study 1 stated that the patient tolerated acalabrutinib well, no adverse events were reported and that there was improvement in lymph nodes. A key takeaway was stated as 'Elevated lymphocyte count and manageable safety profile were reported in this patient with renal comorbidities who was treated with acalabrutinib'.

In Case Study 2, and a further case which was stated as being a 'comparative case study', despite side-effects, the management of the patient included continuing with acalabrutinib and managing the side-effects. The treatment outcomes of Case Study 2 included that there was 'very significant reduction in lymphadenopathy', 'spleen is now normal' and 'at least excellent partial response, possibly complete'.

In Case Study 3, the patient had acalabrutinib stopped due to side-effects but then later restarted with a key takeaway message being 'Patients experiencing infections may be considered for acalabrutinib, but dose adjustments may be needed to appropriately manage the patient'. A comparative Case Study referred to reducing the dose of acalabrutinib to manage a particular side-effect and eventually the patient returned to full dose of acalabrutinib. It was stated that the goal was to continue acalabrutinib and maintain remission.

The Panel considered that all the case studies presented, although discussing the management of side-effects, were overall positive about the use of acalabrutinib. The case studies were detailed and referred to treatment effectiveness in addition to the management of side-effects.

In the Panel's view, AstraZeneca appeared to have classified the meeting in question as non-promotional in the same way that an investigator meeting for clinical trials might be classified; however, the Panel considered that there were fundamental differences between a meeting for investigators involved in a clinical trial and a meeting for health professionals who had previously been involved in an early access programme for a medicine which now had a marketing authorisation; one such difference being the current relationship between the company and the health professionals involved.

The Panel noted the broad definition of promotion in Clause 1.2 and considered that the proactive presentation of acalabrutinib data which, although mainly discussing the management of adverse events, shared overall positive experiences of acalabrutinib use, could not be anything other than the promotion of acalabrutinib. In the Panel's view, neither the role of the Steering Committee nor that the audience was restricted to consultant haematologists who had participated in the EAP meant that the webinar was non promotional as implied by AstraZeneca. In the Panel's view, the webinar slides were promotional material; the webinar slides had been examined and not certified and therefore a breach of Clause 14.1 was ruled.

The Panel considered that in referring to the meeting as non-promotional in all of the associated materials, including the invitation to the meeting and the meeting slides, the promotion of Calquence had been disguised and the Panel ruled a breach of Clause 12.1.

Complaint received **7 June 2021**

Case completed **29 April 2022**