CASE AUTH/3469/2/21

COMPLAINANT v TAKEDA

'ASH 2020 Highlights' online meeting

An anonymous contactable complainant, who described him/herself as an oncologist in the UK, complained about an online meeting, 'ASH [American Society of Hematology] 2020 Highlights' on 21 January 2021 organised by Takeda UK Limited.

Ninlaro (ixazomib) was indicated in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who had received at least one prior therapy. Takeda also marketed Adcetris (brentuximab vedotin) which was indicated in certain patients with Hodgkin lymphoma, systemic anaplastic large cell lymphoma, and cutaneous T-cell lymphoma.

The complainant stated that the topics were very good and there were four or five top speakers who spoke and answered questions. There was more time speaking and only a few minutes for questions and answers which was quite disappointing, but perhaps organised like that because of Covid.

The complainant was surprised that Takeda had run meetings where medicines which did not have a licence were discussed eg ixazonib for first line use in myeloma. The complainant queried whether there were rules that forbade companies from doing that. The complainant queried if the medicines were safe if the Medicines and Healthcare products Regulatory Agency (MHRA) had not given them the OK. The complainant knew this was common in oncology but questioned whether Takeda wanted health professionals to prescribe its medicines after the meeting as it certainly felt like it. The names of the medicines also had a black triangle and queried whether Takeda was saying that health professionals should report side effects for unlicensed medicines? The complainant was also surprised to see an advertisement for the meeting on Twitter which was how he/she registered in the first place. Did that mean companies should not be talking about medicines online?

The detailed response from Takeda is given below.

The Panel noted the broad definition of promotion in the Code and that although the promotion of a medicine prior to the grant of its marketing authorisation was prohibited, the Code permitted companies to undertake certain activities with regard to unlicensed medicines and/or indications. The legitimate exchange of medical and scientific information during the development of a medicine was not prohibited provided that this did not constitute promotion. Informal PMCPA guidance stated that companies must ensure that such activities constituted a genuine exchange of information and were not promotional. The legitimate exchange of scientific information during the development of a medicine should involve debate that enhanced the current state of scientific

knowledge. To avoid being seen as promotional, it should not be a one-way flow of information.

The Panel noted that slide 10 stated that the meeting was an interactive meeting and encouraged attendees to submit questions and some of the speakers included a slide titled questions at the end of their presentations to encourage questions. Materials advertising the meeting referred to it as being an interactive virtual meeting and invitedquestions and discussion from the audience. The invitation included that there would be dedicated time for Q&A and discussion with the speakers. It went on to state that to ensure a lively debate and help attendees make the most of the scientific exchange meeting, it encouraged them to fully partake in the discussion and Q&A sessions with the expert speakers following each presentation. Similarly the registration page encouraged readers to take part in the Q&A and discussion following each presentation. Further tweets sent by the speakers included I hope you can join us to debate and discuss key haemato-oncology data from ASH'.

The Panel noted that the briefing to the chair and speakers stated that the overall objectives of the meeting would be to exchange and discuss new clinical research, advances and challenges in the management of haematological malignancies including lymphoma and myeloma. In addition the service brief for the Chair highlighted that their responsibilities included, *inter alia*, chairing the scientific exchange session at the end of the meeting programme and taking questions from the webinar audience. The brief to speakers stated 'Please include the relevant abstracts from ASH that you believe will be of most interest to UK/Ireland clinical practice. Please ensure that in your presentation the licence status of any medicines is made clear. The Panel noted Takeda's submission that there was no request to discuss data on Takeda products if indeed any was available in the therapeutic area. However, the brief to speakers included a reference to lymphoma and myeloma, two areas in which Takeda had interests and licensed medicines. The invitation included the speakers' names and topics, these being multiple myeloma, low grade lymphoma, high grade lymphoma and Hodgkin's lymphoma.

The Panel further noted Takeda's submission that a verbal briefing call with the chair and speakers highlighted various points including that the meeting was a scientific exchange meeting, meaning it should include 2 way discussion and debate as opposed to a 1 way presentation followed by Q&A.

The Panel noted that after each 20 minute presentation 5 minutes were set aside for Q&A and a further 15 minutes was set aside for a panel discussion at the end of the meeting. The Panel noted that each speaker had between 43 and 92 slides and queried whether this number of slides could have been properly presented within 20 minutes thus leaving the allotted time for Q&As. In this regard the Panel noted that 53% of the attendees provided feedback and three of the comments related to providing more time for questions and discussion. The lowest score was in relation to whether adequate time was given for discussion. The Panel noted the list of seventeen questions asked by delegates of which two appeared not to be questions related to the meeting content.

The Panel further noted the number of attendees at the session (192) and queried whether the company could be confident that all delegates were each able to meaningfully contribute to a discussion that enhanced the current state of scientific knowledge.

The Panel noted that despite encouragement by both Takeda and the speakers, there was very little evidence of any legitimate scientific exchange.

The Panel noted Takeda's submission that the style and tone of the slides and presentation was scientific and no use of brand names was included. Further that the meeting covered a broad number of topics and medicines, which included information on two Takeda medicines and the company's submission that this did not take up an undue proportion of the information presented and all unlicensed information was clearly stated as such on the relevant slides. In the Panel's view, the presentation did not overall give disproportionate emphasis to Takeda's products. The topics presented appeared to relate to lymphoma or myeloma rather than haematological malignancies including lymphoma or myeloma as in the brief from Takeda.

The Panel noted that the presentation gave attendees the opportunity to talk to the Takeda oncology medical team after the meeting. The Panel considered that the presentation was likely to raise interest in relation to all of the products referred to including Takeda's and thus it might be argued that Takeda was soliciting questions about its medicines including for an unlicensed indication. In the Panel's view, it was reasonable to assume that, on the balance of probabilities, attendees might ask about Takeda's medicines.

The nature and depth of discussion was fundamental to the legitimate exchange of medical and scientific information. The Panel queried whether the arrangements for the presentation were conducive to the legitimate exchange of scientific information during the development of a medicine. In the Panel's view, the cumulative effect of the large number of detailed slides presented within a short period of time, the lack of discussion, and the question mark over whether all 192 attendees could contribute to scientific debate was such that, on balance, the meeting was not the legitimate exchange of scientific and medical information during the development of a medicine.

The Panel noted that ixazonib was a licensed medicine and that its alleged promotion for first line use in myeloma, was an unlicensed indication. The Panel noted its comments above that the meeting did not constitute legitimate exchange of medical and scientific information and therefore could not take the benefit of the relevant supplementary information. The Panel noted that the meeting discussed the unlicensed use of ixazonib for first line use in myeloma and, in the Panel's view, promoted it for an unlicensed indication. The Panel ruled a breach of the Code. It ruled no breach in relation to the alleged promotion of an unlicensed medicine.

The Panel considered that high standards had not been maintained and a breach of the Code was ruled.

The Panel did not consider that the promotional nature of the meeting had been disguised and ruled no breach of the Code.

With regard to the advertisement for the meeting on Twitter, the Panel was unclear what the complainant's allegation was in this regard. The Tweets linked to the registration site which required delegates to confirm that they were UK/Ireland health professionals. The Panel thus ruled no breach of the Code in that regard.

The Panel noted Takeda's submission that for best practice it decided to use the black triangle symbol where its medicines which had an existing licence were mentioned (ixazomib and brentuximab vedotin). Takeda considered it diligent to include a reminder to report adverse events and that the products were subject to additional monitoring. However, any slides with unlicensed indications for a Takeda medicine were clearly marked as such. The Panel did not consider that by including the black triangle in relevant slides, Takeda failed to maintain high standards and no breach of the Code was ruled.

The Panel noting its comments and ruling above did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 which was a sign of particular censure and was reserved for such use. No breach of the Code was ruled.

An anonymous contactable complainant, who described him/herself as an oncologist in the UK, complained about an online meeting he/she attended 'ASH [American Society of Hematology] 2020 Highlights' on 21 January 2021 organised by the oncology team of Takeda UK Limited.

Ninlaro (ixazomib) was indicated in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who had received at least one prior therapy. Takeda also marketed Adcetris (brentuximab vedotin) which was indicated in certain patients with Hodgkin lymphoma, systemic anaplastic large cell lymphoma, and cutaneous T-cell lymphoma.

COMPLAINT

The complainant stated he/she could remember reading that the medical team organised the meeting and in that regard he/she asked 'Aren't they the representatives of the company who sell drugs to doctors like me?'.

The complainant stated that the topics were very good and there were four or five top speakers who spoke and answered questions. There was more time speaking and only a few minutes for questions and answers which was quite disappointing, but perhaps organised like that because of Covid.

The complainant stated that it was only after he/she consulted some of his/her colleagues that he/she realised that what Takeda had done might not be right. He/she commented that he/she might be totally wrong but was told to email the ABPI.

The complainant stated that he/she had attended several other company meetings in the past but was surprised that Takeda had run meetings where medicines which did not have a licence were discussed eg ixazonib for first line use in myeloma. The complainant queried whether there were rules that forbade companies from doing that or if it was allowed because of Covid and there were currently not many other educational talks happening? The complainant queried if the medicines were safe if the Medicines and Healthcare products Regulatory Agency (MHRA) had not given them the OK. The complainant knew this was common in oncology but questioned whether Takeda wanted health professionals to prescribe its medicines after the meeting as it certainly felt like it. The names of the medicines also had a black triangle which he/she thought meant that health professionals should report side effects and queried whether Takeda was saying that health professionals should report these for unlicensed medicines?

The complainant was also surprised to see an advertisement for the meeting on Twitter which was how he/she registered in the first place. Did that mean companies should not be talking about medicines online?

The complainant stated that he/she was not an expert in laws about pharmaceutical company meetings but it did not seem right to him/her that one company had one set of rules and another company had another set.

When writing to Takeda, the Authority asked it to consider the requirements of Clauses 2, 3.1, 3.2, 9.1 and 12.1 of the Code.

RESPONSE

Takeda explained that the complainant had referred to the Takeda-organised and funded, CPD-accredited ASH 2020 Highlights meeting, held on 21 January 2021 from 7-9pm. The non-promotional meeting was organised by the medical department of Takeda's UK oncology team.

The objective of the meeting was to create an interactive forum for expert clinicians to consider and debate recent advances in research, in the field of haematological malignancies. The Takeda medical team went to great lengths to ensure that the meeting complied with the Code and was conducted in a non-promotional, scientific exchange format, which would fulfil the requirements around the legitimate exchange of medical and scientific information (LEMS). The meeting involved presentations by expert speakers, each with individual dedicated time for Q&A and discussion, ending with a further interactive panel discussion. Delegates were able to ask questions of and make comments to the speakers throughout the entire meeting. Due to the Covid-19 pandemic and lockdown restrictions, the meeting was held live via an online platform; it was one of a series of two meetings with the second meeting being held on 25 January 2021. Each meeting had a faculty of regional and national expert speakers which allowed delegates to choose the meeting that was the most relevant and convenient for them to attend.

The Takeda oncology medical team organised the event, funded it and selected the Chair with speaker selection being driven by the Chair except where he/she requested suggestions from Takeda for suitable speakers on a particular topic. The event was intended for health professionals from the UK and Ireland with a clinical specialty in haemato-oncology only and this was clearly stated on the invitation to the event. On the registration site the following statement was prominent: 'This content is intended for healthcare professionals from the UK and Ireland with a clinical specialty in haemato-oncology only' and delegates were asked to confirm that they were a UK or Ireland health professional. Registration details were checked to ensure that either an NHS email address was used or else individuals were emailed to confirm their health professional status. There were 192 health professional delegates to the meeting.

The ASH congress in December 2020 (to which the meeting related) was a fully virtual event due to the Covid-19 pandemic and therefore it was anticipated that the delegates to the meeting in question would be either those that had attended the ASH congress and wanted an opportunity to hear experts summarising their own highlights and discuss and ask questions of the faculty, or those who were unable to attend the ASH congress due to clinical commitments. Takeda noted that the congress was held in pacific time (GMT minus 8 hours) but with catch up content available for viewing on demand by registered delegates. The medical team was aware from feedback received from health professionals previously that virtual congress attendance did not always offer the same opportunity for full engagement with content due to challenging

time zones and conflicts with clinical and personal commitments. Therefore, it seemed even more important in 2021 to provide high quality highlights of the 2020 congress.

Takeda stated that speakers were asked via their service briefs to select relevant abstracts from ASH for the topic they were asked to speak on with no request to discuss data on Takeda products if indeed any was available in the therapeutic area. The service briefs signed by the speakers (copies provided) included the following:

- Confirmation that the event was organised by the medical department at Takeda
- The meeting would be via webinar due to the current Covid-19 restrictions
- It would be attended virtually by UK/Ireland health professionals with an interest in haemato-oncology
- The overall objectives of the meeting on 21 January were to exchange and discuss new clinical research, advances and challenges in the management of haematological malignancies including lymphoma and myeloma
- Confirmation of the topics they were speaking on and that the sessions were to last 20 minutes with 5 minutes for audience questions and answers immediately after their presentations and a panel session at the end of the programme
- Speakers were asked to include the relevant abstracts from ASH that they believed would be of most interest to UK/Ireland clinical practice
- Speakers were asked to make clear in their presentations the licence status of any medicines.

The service brief for the Chair (copy provided) highlighted in addition to the overall meeting objectives, that his/her responsibilities included ensuring the speakers adhered to time, managing questions from the audience and chairing the panel discussion and scientific exchange.

Alongside the service brief, a verbal briefing call, supported by a briefing guidance document (copy provided) for the medical scientific liaison (MSL) delivering the briefing, was also held with the Chair and speakers; the following points were highlighted during those calls:

- That the meeting was a scientific exchange meeting, meaning it should include two-way discussion and debate as opposed to a one-way presentation followed by questions and answers
- That the objective of the meeting was to present and discuss new clinical research, advances and challenges in the management of haematological malignancies
- To discuss, share and debate the key highlights from ASH and the implications on local practice, in relation to the management of haematological malignancies
- To increase the knowledge of, and facilitate discussion and scientific exchange amongst health professionals involved in the management of haematological malignancies
- To provide an opportunity for health professionals who were unable to attend the congresses to increase their knowledge and engage in scientific exchange, discussion and debate
- For any health professionals who did attend the congresses, the meeting provided an opportunity for debate, discussion and scientific exchange on the highlights

The chair opened the meeting and at the outset, highlighted the purpose of the meeting and spent 12 seconds on the opening disclaimer slide (slide 6) over which he/she said 'The meeting is sponsored by Takeda. Takeda has not had any input into the slides.....the panel has produced their own slides and they had been reviewed by Takeda. But it is their independent opinion'. There were four presentations:

1. Multiple myeloma: 93 slides in total with 6 slides on a Takeda product (ixazomib) with a clear statement on the first slide that 'Ixazomib is not licensed for frontline use in patients with multiple myeloma.'

2. Low-grade lymphoma/chronic lymphocytic leukaemia: 62 slides with no data on Takeda products

3. High-grade lymphoma: 67 slides with 3 slides on a Takeda product (brentuximab vedotin) with a clear statement on the first slide that 'Brentuximab vedotin is licensed in combination with cyclophosphamide, doxorubicin and prednisone (CHP) in adult patients with previously untreated systemic anaplastic large cell lymphoma only' (SPC provided).

4. Hodgkin lymphoma: 45 slides with 6 slides on a Takeda product (brentuximab vedotin) in older Hodgkin lymphoma patients with the following statement appearing on both the initial slide and the conclusion slide 'Brentuximab vedotin is not licensed or funded for the frontline treatment of patients with Hodgkin lymphoma as monotherapy or in combination with dacarbazine, bendamustine or nivolumab'. There were also 7 slides on a Takeda product (brentuximab vedotin) used for the treatment of Hodgkin lymphoma in the consolidation setting in combination with nivolumab with the following statement made on the first and concluding slides: 'Brentuximab vedotin (BV) is not licensed or funded as consolidation therapy in combination with nivolumab in patients with Hodgkin lymphoma'

There were 285 slides in total which formed the showreel for the webinar of which the first 3 slides were shown on a loop whilst delegates waited for the meeting to start. Therefore, of the 282 slides shown once the meeting had started, 22 had information on Takeda products in an unlicensed setting constituting 7.8% of the total content. Takeda reiterated that the meeting was a non-promotional, medically-organised, scientific exchange event and it was clearly stated in the advertisement, registration site and at the meeting that both licensed and investigational agents would be discussed. Any slides detailing Takeda products in an unlicensed indication were clearly marked as such. There was no greater prominence given to Takeda medicines than any other medicine.

Takeda submitted that for best practice it decided to use the black triangle symbol where its medicines which had an existing licence were mentioned (ixazomib and brentuximab vedotin), as the team knew that many delegates would be health professionals who used those medicines in licensed indications. Takeda considered it diligent to include that reminder to report adverse events and that those products were subject to additional monitoring. However, any slides with unlicensed indications for a Takeda medicine were clearly marked as such.

The agenda clearly outlined that all speakers had been allotted 25 minutes - 20 minutes for the presentation followed by 5 minutes for live Q&A and discussion. At the end of the webinar there was a 15 minute additional panel discussion to allow the audience to ask further questions of

the chair and speakers and there were many questions asked during that panel discussion that were submitted by the attendees to the webinar. A list of the questions submitted during the meeting was provided. Importantly, delegates could submit questions before the start of the webinar and at any time during it. Whilst delegates waited for the webinar to start, one of the slides provided guidance on how to submit questions using the engagement panel of the platform. When the chair showed the slide that gave instructions as to how to submit questions he/she also stated 'We want to make this a very interactive session. It is obviously different not all being in the same room together but we will try and get through any questions you send in'. At the end of each presentation, an on-screen prompt appeared on the webinar platform, signaling the beginning of the live Q&A session and inviting the audience to submit questions via the engagement panel. In all, 35 minutes of the 120 minute agenda were assigned to Q&A or discussion, ie 29% of the agenda time.

In the meeting itself, speakers spoke for 95 minutes and 55 seconds of the total 121 minute 23 second meeting. The panel discussion session started as planned at 1 hour and 45 minutes.

Feedback was sought on the meeting and the feedback form, which was available at the end of the webinar, was completed by 53% of delegates. The rating scale was out of 7 and some of the feedback question responses relevant to the complaint were:

- 'The meeting was relevant to my educational needs' was rated 6.56/7
- 'The meeting has enhanced my knowledge' was rated 6.60/7
- 'Adequate time was given for discussion' was rated 5.82/7

Takeda noted that the verbatim comments in the feedback received were very positive. Three of the comments referenced the fact that more time for discussion and questions would be of benefit and this was reflective of the fact that a lot of questions were received in response to the meeting and presentations. Takeda submitted that it was pleased with the high level of engagement but took into account the feedback that for any future meetings, it might need to allow even more discussion time.

Takeda UK stated that it had an active 'MSL Ways of Working' standard operating procedure (SOP) (ref PROC-0011902 2.0; SOP-TUK-MI-607, copy provided) which detailed specific guidance in section 4.6.3 on MSL led medical education meetings. Section 4.6.3 included the following elements which were relevant to the meeting in question:

- MSLs might organise non-promotional medical education events to support continued education amongst health professionals eg therapy area updates, scientific exchange meetings.

- The content of such medical meetings might be developed/delivered by either Takeda (eg MSL/medical advisor) or a key opinion leader/steering committee and was subject to the approval/certification process to ensure that content was appropriate, factually accurate, fair and balanced. However, it was important that these meetings were devised in such a way that any off-licence Takeda data was unlikely to take up a substantial proportion of the agenda. Therefore, meeting topics such as wide-ranging post-Congress updates were likely to be acceptable, whereas meetings focused on areas where off-licence Takeda products/data were likely to constitute a large proportion of the meeting content were unlikely to be approved

- For all medical/scientific exchange meetings, sufficient time should be allowed for two-way discussion and scientific debate (ie to allow exchange).

Takeda submitted that given the Covid-19 pandemic, it wanted to ensure that health professionals were made aware of the educational meeting and it used invites emailed by its MSL team, Twitter, RCPath and Doctors.net to advertise the meetings in a compliant manner. Advertisements made clear that the meetings were for health professionals only and only health professionals were then able to register for the events. Takeda provided copies of the content put out by the platforms above, and noted that it had been certified before use. No commercial colleagues (sales or marketing) were involved in the organisation or advertising of the meeting or attended the meeting.

Takeda noted the complainant's reference to Tweets and noted that those Tweets were fully certified, did not mention any Takeda or other company products and made clear the event was for health professionals only. The Tweets linked to the registration site which required delegates to confirm that they were UK/Ireland health professionals and the registration portal made clear that 'The meeting will include discussion of both investigational and licensed agents'.

With regard to Clause 2, Takeda considered that it had demonstrated that the meeting was conducted in line with both internal SOP and Code guidance to fulfill the requirements of 'legitimate exchange of medical and scientific information' and was a highly regarded interactive educational and scientific exchange meeting which allowed delegates to hear from experts and discuss new developments and the evolutions in the field of haematological malignancies without any undue focus on unlicensed Takeda products or indications. This was supported by the feedback from delegates, chair and speakers (see below).

With regard to Clause 3.1, Takeda considered that the information provided demonstrated that the meeting was an example of the legitimate exchange of medical and scientific information and did not constitute the promotion of any Takeda products given the nature of the meeting and how it was organised and executed. Takeda made every effort to encourage scientific exchange and discussion including via appropriate briefing of the chair and speakers, clear time for discussion in the agenda and the opportunity to submit comments and questions both before and during the meeting. The meeting was solely organised by the medical team of Takeda UK and was conducted as a non-promotional, scientific exchange meeting.

With regard to Clause 9.1, Takeda considered that it had shown that it aimed at all times to provide high quality, fair and balanced, non-promotional medical education to haemato-oncologists during the meeting. Takeda stated that it went to great lengths to ensure that the meeting complied with the Code and was conducted in a non-promotional, scientific exchange format, which would fulfil the requirements around the legitimate exchange of medical and scientific information.

With regard to Clause 12.1, Takeda reiterated that the meeting was a non-promotional, medically-organised, scientific exchange meeting and was approved as such. There was no intent to promote any Takeda medicines during the meeting. The style and tone of the slides and presentation was scientific and no use of brand names was included. The meeting covered a broad number of topics and medicines, which included information on two Takeda medicines, however, this did not take up an undue proportion of the information presented and all unlicensed information was clearly stated as such on the relevant slides. The purpose of this

meeting was solely to support scientific exchange and the education of health professionals. Takeda noted that it was stated on the invitation, the registration site and meeting materials that the meetings were organised by the medical team and that, as a congress update, the meeting would contain information on both investigational and licensed agents.

Takeda submitted that in organising the meeting, the medical team used prior case precedent to guide it and, by taking learnings from previous cases on the topic, put appropriate guardrails in place so that Takeda could deliver these non-promotional medical educational events in a compliant manner.

Takeda provided feedback and comment from its chair and all speakers who included abstracts on Takeda medicines within their presentations:

Chair

'I have chaired and presented at these meetings for several years. I have previously selected the abstracts independently, choosing the most relevant for a UK audience in terms of current practice and also important data which may be relevant for lymphoma practice in the future. I have not had the abstracts selected for me. The slides were reviewed by Takeda prior to the meeting and I have not had any additional abstracts added or significant change of content. The feedback had been consistently excellent in that colleagues find this of significant educational value.'

Speaker

'I am shocked and surprised you have had a complaint placed about the post ASH educational meeting held virtually on Thursday 21 January 2021. I can confirm you had never asked for editorial control over the abstracts or data I present. We did not discuss my presentation except to make sure it was accurate. This had been the case for the 4-5 meetings POST-ASH meetings we had held in [named area]. The abstracts I selected were the top myeloma abstracts at the meeting and this year I presented data on 16 -17 abstracts. Four mentioned off-label Janssen product use, 4 mentioned Celgene/BMS off label data, 3 abstracts mentioned off label use of an Amgen product and 3 mentioned off label use of GSK products. There was only one abstract I discussed that included a Takeda product and this was in my clinical opinion (and that of many others) one of the most important abstracts at ASH 2020. I have always been struck through these meetings at how there was no attempt to exert editorial control or any pressure to include an abstract on a Takeda product. The universally fabulous feedback we get from these meetings is a testament to this and I know we have never had any criticism of the balance of the meeting from our audience. It has been a fantastic academic collaboration to put on these highly successful meetings which has a first class faculty. As a KOL and speaker at a number of meetings I could honestly say this was the least bias meeting I had been involved in.'

Speaker

'I can confirm that when I prepared the talk for the [named area] ASH highlights meeting 2021, I had full control over what I included and how it was discussed. There was no input from Takeda apart from approving the slides that I submitted. These meetings were highly educational, as reflected by the feedback and there was plenty of time for questions and discussion. These meetings were particularly important in the current circumstances when fewer people were able to take study leave to attend congresses even when they were virtual.'

Speaker

'I am quite flabbergasted by the complaint. In my view, there was no doubt that it was entirely unfounded. Personally, I never deemed the annual 'post ASH meeting' held in [named area] in late January as a company sponsored promotional event; instead, it had been a meeting organised by Haematologists and sponsored by Takeda with the aim of providing an ASH update on the latest developments in the field. Since this meeting was started more than 5 years ago, all presenters had been able to select the topics and presentations freely, typically focusing on the most important ASH abstracts. Hence, in this setting I consider it justifiable, if important results relating to non-licensed medicines were presented, even if the rights to those medicine/s were owned by the sponsor of the meeting.'

Takeda provided associated certificates from its electronic approval system, all the documents referred to above and the Ninlaro (ixazomib) and Adcetris (brentuximab vedotin) summaries of product characteristics (SPC). The company submitted that although only requiring examination under the Code, all the materials for the meeting underwent single certification as non-promotional items; the signatory was a UK registered pharmacist.

For the reasons detailed above Takeda did not consider that the meeting in question was in breach of Clauses 2, 3.1, 3.2, 9.1 and 12.1 of the Code.

PANEL RULING

The Panel noted Takeda's explanation that the Takeda-organised and funded, CPD-accredited ASH 2020 Highlights meeting held on 21 January 2021 referred to by the complainant was one of a series of two non-promotional meetings organised by the medical department of Takeda's UK oncology team.

The Panel noted that according to the MSL Ways of Working Standard Operating Procedure (SOP), MSLs could organise non-promotional medical education events to support continued education amongst health professionals which included therapy area updates and scientific exchange meetings as examples. The SOP stated that the content of such medical meetings may be developed/delivered by either Takeda (eg MSL/Medical Advisor) or a KOL/steering committee and was subject to the approval/certification process to ensure that content was appropriate, factually accurate, fair and balanced. It went on to state that it was important that these meetings were devised in such a way that any off-licence Takeda data was unlikely to take up a substantial proportion of the agenda. Therefore meeting topics such as wide-ranging post-congress updates were likely to be acceptable, whereas meetings focussed on areas where off-licence Takeda products/data were likely to constitute a large proportion of the meeting content, were unlikely to be approved. The SOP required that for all medical/scientific exchange meetings, sufficient time should be allowed for two-way discussion and scientific debate (ie to allow exchange).

The Panel noted the broad definition of promotion at Clause 1.2 of the Code. The Panel also noted that although Clause 3 prohibited the promotion of a medicine prior to the grant of its marketing authorization, the Code permitted companies to undertake certain activities with regard to unlicensed medicines and/or indications. The supplementary information to Clause 3 provided additional details including a statement that the legitimate exchange of medical and scientific information during the development of a medicine was not prohibited provided that this did not constitute promotion which was prohibited by Clause 3 or any other clause. The

PMCPA Guidance about Clause 3 provided informal guidance stating that companies must ensure that such activities constituted a genuine exchange of information and were not promotional. The legitimate exchange of scientific information during the development of a medicine should involve debate that enhanced the current state of scientific knowledge. To avoid being seen as promotional, it should not be a one-way flow of information.

The Panel noted that slide 10 of the chair's presentation, stated that it was an interactive meeting and encouraged attendees to use the engagement panel present on the right hand side of their screens to submit questions and some of the speakers included a slide titled questions at the end of their presentations to encourage questions. One of the materials advertising the meeting referred to it as being an interactive virtual meeting and another stated that speakers would invite questions and discussion from the audience. The invitation invited readers to join these interactive and engaging virtual meetings from the 62nd ASH annual meeting and exposition 2020 and included that there would also be dedicated time for Q&A and discussion with the speakers. It went on to state that to ensure a lively debate and help attendees make the most of the scientific exchange meeting, it encouraged them to fully partake in the discussion and Q&A sessions with the expert speakers following each presentation. Similarly the registration page encouraged readers to take part in the Q&A and discussion following each presentation. Further the tweets sent by the speakers on behalf of Takeda stated, *inter alia*, 'I will be speaking at a Takeda organised webinar 'ASH 2020 Highlights' on Thursday 21 January 2021,7pm-9pm. I hope you can join us to debate and discuss key haemato-oncology data from ASH'.

The Panel noted that the briefing to the chair and speakers stated that the overall objectives of the meeting on 21 January 2021 would be to exchange and discuss new clinical research, advances and challenges in the management of haematological malignancies including lymphoma and myeloma. In addition the service brief for the chair highlighted that their responsibilities included ensuring the speakers adhered to time, chairing the panel discussion and scientific exchange session at the end of the meeting programme and taking questions from the webinar audience. The chair was also responsible for reminding the audience at the end of the meeting to complete the electronic feedback forms. The brief to speakers stated 'Please include the relevant abstracts from ASH that you believe will be of most interest to UK/Ireland clinical practice. Please ensure that in your presentation the licence status of any medicines is made clear (eg if any data on an unlicensed medicine or unlicensed indication of a licensed medicine is included this must be made clear to the audience either verbally or as a note on the relevant slide'. The Panel noted Takeda's submission that there was no request to discuss data on Takeda products if indeed any was available in the therapeutic area. However, the brief to speakers included a reference to lymphoma and myeloma, two areas in which Takeda had interests and licensed medicines. The invitation included the speakers names and topics, these being multiple myeloma, low grade lymphoma, high grade lymphoma and Hodgkin's lymphoma.

The Panel further noted Takeda's submission that a verbal briefing call by the medical scientific liaison (MSL) with the chair and speakers highlighted the following points:

- That the meeting was a scientific exchange meeting, meaning it should include 2 way discussion and debate as opposed to a 1 way presentation followed by Q&A

- That the objective of the meeting was to present and discuss new clinical research, advances and challenges in the management of haematological malignancies

- To discuss, share and debate the key highlights from ASH and the implications on local practice, in relation to the management of haematological malignancies

- To increase the knowledge of and facilitate discussion and scientific exchange amongst health professionals involved in the management of haematological malignancies

- To provide an opportunity for health professionals who were unable to attend these congresses to increase their knowledge and engage in scientific exchange, discussion and debate

- For any health professionals who did attend these congresses, the meeting provided an opportunity for debate, discussion and scientific exchange on the highlights

The Panel noted that after each 20 minute presentation 5 minutes were set aside for Q&A and a further 15 minutes was set aside for a panel discussion at the end of the meeting. The Panel noted that each speaker had between 43 and 92 slides and queried whether this number of slides could have been properly presented within 20 minutes thus leaving the allotted time for Q&As. In this regard, the Panel noted Takeda's submission that in the meeting itself, speakers spoke for 95 minutes and 55 seconds of the total 121 minute 23 second meeting and the discussion session started as planned at 1 hour and 45 minutes. It was not clear whether this included the 5 minutes Q&A at the end of each presentation. It thus appeared that the speakers' presentations ran over time and thus there might not have been the full allotted time for questions. In this regard the Panel noted that 53% of the attendees provided feedback and three of the comments related to providing more time for questions and discussion. The lowest score of 5.82 out of 7 was in relation to whether adequate time was given for discussion. The Panel noted the list of seventeen questions asked by delegates of which two appeared not to be questions related to the meeting content but rather an answer to where the delegate was joining from and a thank you.

The Panel further noted the number of attendees at the session (192) and queried whether the company could be confident that all delegates were each able to meaningfully contribute to a discussion that enhanced the current state of scientific knowledge.

The Panel noted that despite encouragement by both Takeda and the speakers, there was very little evidence of any legitimate scientific exchange.

The Panel noted Takeda's submission that the style and tone of the slides and presentation was scientific and no use of brand names was included. Further that the meeting covered a broad number of topics and medicines, which included information on two Takeda medicines and the company's submission that this did not take up an undue proportion of the information presented and all unlicensed information was clearly stated as such on the relevant slides. The Panel noted Takeda's submission there were 285 slides in total which formed the showreel for the webinar of which the first 3 slides were shown on a loop whilst delegates awaited the start of the meeting. Of the 282 total slides shown once the meeting had commenced, 22 slides had information on Takeda products in an unlicensed setting constituting 7.8% of the total content. The first speaker's presentation included 93 slides in total with 6 slides on a Takeda product (ixazomib) with a clear statement on the first slide that 'Ixazomib is not licensed for frontline use in patients with multiple myeloma.'. In this regard the Panel noted that the speaker stated that he/she presented data on 16 -17 abstracts; four which mentioned off-label Janssen product use, 4 which mentioned Celgene/BMS off label data, 3 abstracts which mentioned off label use of an

Amgen product and 3 which mentioned off label use of GlaxoSmithKline products. There was only 1 abstract he/she discussed that included a Takeda product.

The second speaker had 62 slides with no data on Takeda products.

The third speaker had 67 slides with 3 slides on a Takeda's product (brentuximab vedotin) with a clear statement on the first slide that 'Brentuximab vedotin is licensed in combination with cyclophosphamide, doxorubicin and prednisone (CHP) in adult patients with previously untreated systemic anaplastic large cell lymphoma only'.

The final speaker had 45 slides with 6 slides on a Takeda product (brentuximab vedotin) in older Hodgkin lymphoma patients with the following statement appearing on both the initial slide and the conclusion slide 'Brentuximab vedotin is not licensed or funded for the frontline treatment of patients with Hodgkin lymphoma as monotherapy or in combination with dacarbazine, bendamustine or nivolumab'. There were also 7 slides on a Takeda product (brentuximab vedotin) used for the treatment of Hodgkin lymphoma in the consolidation setting in combination with nivolumab with the following statement made on the first and concluding slides: 'Brentuximab vedotin (BV) is not licensed or funded as consolidation therapy in combination with nivolumab in patients with Hodgkin lymphoma'.

In the Panel's view, the presentation did not overall give disproportionate emphasis to Takeda's products. The topics presented appeared to relate to lymphoma or myeloma rather than haematological malignancies including lymphoma or myeloma as in the brief from Takeda.

The Panel noted that the presentation gave attendees the opportunity to talk to the Takeda oncology medical team after the meeting when a separate 'room' would be open for 15 minutes for the Takeda team to answer your questions ask for further information on the topics discussed during this meeting. The Panel considered that the presentation was likely to raise interest in relation to all of the products referred to including Takeda's and thus it might be argued that Takeda was soliciting questions about its medicines including for an unlicensed indication. In the Panel's view, it was reasonable to assume that, on the balance of probabilities, attendees might ask about Takeda's medicines.

The nature and depth of discussion was fundamental to the legitimate exchange of medical and scientific information. The Panel noted its comments above and queried whether the arrangements for the presentation were conducive to the legitimate exchange of scientific information during the development of a medicine. In the Panel's view, the cumulative effect of the large number of detailed slides presented within a short period of time, the lack of discussion, and the question mark over whether all 192 attendees could contribute to scientific debate was such that, on balance, the meeting was not the legitimate exchange of scientific and medical information during the development of a medicine.

The Panel noted that ixazonib was a licensed medicine and that its alleged promotion for first line use in myeloma, an unlicensed indication, would fall under Clause 3.2 rather than Clause 3.1. The Panel thus ruled no breach of Clause 3.1 in this regard. The supplementary information to Clause 3.2 Unauthorized indications made it clear that the promotion of indications not covered by the marketing authorisation for a medicine was prohibited by this clause. The supplementary information referring to the legitimate exchange of information during the development of a medicine was not limited to medicines without a marketing authorisation, although the Panel noted the relative difficulties of establishing that a medicine

that already had a marketing authorisation was in development in relation to an unlicensed indication. Each case would be considered on its individual merits. The Panel noted its comments above that the meeting did not constitute legitimate exchange of medical and scientific information and therefore could not take the benefit of the relevant supplementary information. The Panel noted that the meeting discussed the unlicensed use of ixazonib for first line use in myeloma and, in the Panel's view, promoted it for an unlicensed indication. The Panel ruled a breach of Clause 3.2 of the Code.

The Panel considered that high standards had not been maintained and a breach of Clause 9.1 was ruled.

The Panel noted that promotional material did not need to be labelled as such, however, it must not be disguised. The Panel noted that it was clear that it was a Takeda organised meeting and that both investigational and licensed medicines would be discussed. In the Panel's view, health professionals would be aware that the meeting was being run by Takeda and, on the balance of probabilities, would be likely to assume that it would include material on Takeda's medicines and therefore be promotional. The Panel did not consider that the promotional nature of the meeting had been disguised. No breach of Clause 12.1 was ruled.

The Panel noted that the complainant was surprised to see an advertisement for the meeting on Twitter which was how he/she registered in the first place and queried whether that meant companies should not be talking about medicines online? The Panel was unclear what the complainant's allegation was in this regard and it was not for the Panel to make out a complainant's allegation. The Panel noted Takeda's submission that the Tweets were fully certified, did not mention any Takeda or other company products and made clear the event was for health professionals only. The Tweets linked to the registration site which required delegates to confirm that they were UK/Ireland health professionals and the registration portal made clear that 'The meeting will include discussion of both investigational and licensed agents'. The Panel thus ruled no breach of Clause 9.1 in that regard.

The Panel noted Takeda's submission that for best practice it decided to use the black triangle symbol where its medicines which had an existing licence were mentioned (ixazomib and brentuximab vedotin), as the team knew that many delegates would be health professionals who used those medicines in licensed indications. Takeda considered it diligent to include that reminder to report adverse events and that those products were subject to additional monitoring. However, any slides with unlicensed indications for a Takeda medicine were clearly marked as such. The Panel did not consider that by including the black triangle in relevant slides, Takeda failed to maintain high standards and no breach of Clause 9.1 was ruled.

The Panel noting its comments and ruling above did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 which was a sign of particular censure and was reserved for such use. No breach of Clause 2 was ruled.

Complaint received **2 February 2021**

Case completed **23 July 2021**