CASE AUTH/3432/12/20

COMPLAINANT v GLAXOSMITHKLINE

Promotion of respiratory medicines

An anonymous, contactable complainant raised concerns about the promotion of respiratory medicines by GlaxoSmithKline UK Limited. The complainant referred to four medicines: Trelegy (fluticasone/umeclidinium/vilanterol), Anoro (umeclidinium/vilanterol), Incruse (umeclidinium) and Relvar (fluticasone/vilanterol), that were each delivered via the Ellipta device. Seretide (fluticasone/salmeterol) and Serevent (salmeterol) were also referred to on one of the materials at issue. All of the medicines were variously indicated for chronic obstructive pulmonary disease (COPD) and/or asthma.

The detailed response from GlaxoSmithKline is given below.

1 Invitation to a promotional meeting on inhaler techniques and devices

The complainant alleged that an invitation to a respiratory promotional meeting lacked the mandatory information. The complainant noted that at the bottom of the page, Trelegy, Anoro, Relvar and Incruse were mentioned but the generic names were not listed for any of the medicines and more importantly there was no adverse event reporting statement or black triangles which were needed for Incruse, Anoro and Trelegy. The complainant did not consider that the material appeared to have been certified given the lack of mandatory information.

The Panel noted that the bottom right-hand corner of the invitation to a respiratory promotional meeting titled 'Inhaler Technique & Devices Workshop' provided by GlaxoSmithKline listed the brand names for Trelegy, Anoro, Relvar and Incruse but did not include the corresponding non-proprietary names or an inverted black triangle for Trelegy, Anoro and Incruse. Breaches of the Code were ruled as acknowledged by GlaxoSmithKline. Relvar Ellipta did not need a black triangle and thus the Panel ruled no breach of the Code in relation to Relvar Ellipta. The Panel noted that whilst the adverse event reporting statement was included within the prescribing information, which was hosted on external links from the invitation, there was no reference to it on the meeting invitation itself. The Panel considered that this was particularly important given that three of the four products were subject to additional monitoring, and therefore it ruled a breach of the Code; In reaching its decision on this point, the Panel did not consider that a separate adverse event reporting statement was needed for each product promoted as alleged.

The Panel noted that both the certificate for the Asthma and COPD promotional meetings invite template and the final invitation to the meeting provided by GlaxoSmithKline included the same job bag number and date of preparation (PM-GB-UCV-BRF-190006, September 2019). This gave the impression that the final populated template had been approved but from GlaxoSmithKline's response that was not so.

The Panel noted that it was not unacceptable to use certified templates for invitations but the arrangements must be such that the company could be confident that the completed template complied with the Code. Instructions to representatives were important in this regard. In the Panel's view, altering fields such as the agenda, which was likely to be directly relevant to whether material was Code compliant and might meaningfully change the nature of the original certified invitation template, was different to the population of fields related to administrative details. In the Panel's view, in the particular circumstances of this case, the final invitation had not been certified prior to being issued and a breach of the Code was ruled.

The Panel ruled a breach of the Code as high standards had not been maintained.

The Panel noted its rulings above and although it considered that it was unacceptable to omit the adverse event reporting statement and black triangle, where relevant within the invitation in question, they could, nonetheless, be viewed when the prescribing information was accessed from the links within the invitation. The Panel considered that the rulings of breaches adequately covered this matter and an additional ruling of a breach of Clause 2 would be disproportionate in the particular circumstances of this case. A ruling of a breach of Clause 2 was used as a sign of particular censure and reserved for such use. The Panel, on balance, ruled no breach of Clause 2.

2 Invitation to a promotional meeting on asthma control

The complainant alleged that another promotional meeting invitation to a meeting titled 'Optimising asthma control in your practice', implied that Trelegy Ellipta was licensed for asthma but it was only licensed for COPD.

The Panel noted GlaxoSmithKline's submission that the digital invitation at issue was intended to be printed and distributed to health professionals. It appeared to the Panel that, if printed the invitation was a 6 page gate-folded booklet and that the front cover of the invitation included an image of a pair of lungs, the title 'Optimising asthma control in your practice' and the Trelegy Ellipta brand logo at the bottom of the page.

The Panel noted that the agenda on the invitation listed two separate sessions, one titled 'Optimising asthma control in your practice' and one titled 'Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol): The only single daily inhalation triple therapy for COPD'.

In the Panel's view, it was not unreasonable to consider that a busy health professional reading the first page of the invitation might assume that Trelegy Ellipta was a treatment option for asthma, given the heading. It would have only been upon reading the agenda that one might have been made aware from the session 'Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol): The only single daily inhalation triple therapy for COPD' that Trelegy Ellipta was licensed for COPD. The Panel also considered that the impression from the agenda might have led health professionals to believe that Trelegy was licensed for both asthma and COPD.

In the Panel's view, the invitation implied that Trelegy was licensed for asthma which was not so; a breach of the Code was ruled.

The Panel ruled a breach of the Code as high standards had not been maintained. The Panel considered that any reference to Trelegy on an invitation for an asthma-focussed meeting was wholly inappropriate given that Section 4.4, Special warning and precaution for use of the Trelegy SPC, stated that it should not be used in patients with asthma since they had not been studied in that patient population. The Panel considered that the implied suggestion otherwise was such as to reduce confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel noted that it was not unacceptable to use certified templates for invitations but the arrangements must be such that the company could be confident that the completed template complied with the Code. Instructions to representatives were important in this regard. In the Panel's view, altering fields such as the agenda, which was likely to be directly relevant to whether material was Code compliant and might meaningfully change the nature of the original certified invitation template, was different to population of fields related to administrative details. In the Panel's view, in the particular circumstances of this case, the final invitation had not been certified prior to being issued and a breach of the Code was ruled.

3 On-demand webinar

The complainant noted that an on-demand webinar entitled 'Winter is Coming – COPD patient optimisation in the context of COVID-19' (ref PM-GB-UCV-VID-200012, September 2020 could be accessed via a Google search and it was important to note the route of access within the context of the first mention of generic names. The complainant stated that when Trelegy Ellipta was first mentioned three times it did not have a generic name or black triangle anywhere next to the three mentions on the slide. Anoro and Relvar were also first mentioned on the same slide but again there was no generic name or black triangle for Anoro.

The Panel noted GlaxoSmithKline's submission that the on-demand video could be searched for via Google, however when landing on the page via a Google search, the first mention of the product was within the video-on-demand and at that point, the black triangle and the non-proprietary name were clearly displayed.

The Panel further noted that the complainant referred to a slide at 29 minutes and 31 seconds into the webinar, which mentioned Trelegy Ellipta three times with no generic name or black triangle and did not include the generic name or black triangle for Anoro Ellipta either.

The Panel noted that a screenshot of the video at 26 seconds provided by GlaxoSmithKline, described as Slide 2, included the licensed indications, non-proprietary names, and inverted black triangles, where relevant, for Trelegy Ellipta, Anoro Ellipta, Relvar Ellipta, Incruse Ellipta, Seretide and Serevent. The Panel noted that the complainant bore the burden of proof and that he/she had not established that the required obligatory information was not included as alleged. No breaches of the Code were ruled in relation to each medicine. The Panel consequently ruled no further breaches of the Code including Clause 2 in this regard.

4 Patient resource material

The complainant noted that on the GSKPro website, there was, within the patient resources, a one-page leaflet on how to use the Ellipta device available in different languages. However, none of the five pdf guides included the adverse event reporting details as required by the Code, which was of concern as patients might take the Ellipta device with one of the black triangle Ellipta products (eg Anoro, Incruse) but yet were not provided with information on how to report adverse effects.

The Panel noted that the patient leaflet at issue was intended to provide instructions for patients on how to use the Ellipta inhaler.

The Panel noted that whilst the leaflet did not refer to a specific medicine and thus the black triangle which was related to a specific medicines was not required to be included, the ultimate audience of the leaflet was members of the public who had been prescribed one of the four licensed medicines used with an Ellipta device and thus, in the Panel's view, the leaflet should have included an adverse event reporting statement and a breach of the Code was ruled.

5 Claim for Trelegy

The complainant further referred to claims regarding exacerbation reduction for Trelegy Ellipta within the GSKPro website (ref PM-GB-FVU-WCNT-200013, September 2020). The complainant noted that on the first part of the page, there was a claim that Trelegy Ellipta delivered superior reduction in annual rate of moderate/severe exacerbations vs an inhaled corticosteroid/long-acting beta agonist (ICS/LABA); there was a bubble next to the bar chart which stated 44% reduction. The complainant alleged that that was relative risk reduction and not absolute risk reduction which had to be shown.

The Panel noted that the relative risk reduction was in a bubble, to the right of the graph. The Panel noted GlaxoSmithKline's submission that the graph represented the absolute values from the referenced clinical study (Lipson *et al* 2017); the absolute values on each bar of the chart were of the same size and prominence as the relative risk reduction.

The Panel considered that the graph included the absolute values with similar prominence to the relative risk reduction and therefore no breaches of the Code was ruled. The Panel noted its rulings above and did not consider that high standards had not been maintained.

6 Claim about the cost-effectiveness of Trelegy

The complainant alleged thatthe claim that Trelegy was a cost-effective single inhaler triple therapy, on the GSKPro website, was not accurate as no cost-effective analysis had been done and the reference provided for the claim (MIMS) was purely the price of the inhaler as opposed to actual cost-effectiveness which was much broader than simply the price of a product.

The Panel noted that the webpage at issue had the heading 'Trelegy Ellipta Price' beneath which was a graph which compared Trelegy Ellipta with other branded multiple inhaler triple therapy combinations in COPD; the graph was a bar chart which was headed 'A cost-effective single inhaler triple therapy for COPD' and illustrated the price differential between Seretide, Fostair, Symbicort and Trelegy; Trelegy was markedly lower visually.

The Panel noted GlaxoSmithKline's submission that in July 2019, the National Institute for Health and care Excellence (NICE) updated its guideline on the diagnosis and management of COPD, which also took into account clinical and cost-effectiveness outcomes of a treatment. The Panel noted GlaxoSmithKline's submission that two Trelegy Ellipta COPD studies had been included in the review and whilst it did not make a recommendation in favour of single or multiple inhaler devices, NICE did state that using a single inhaler device was more cost-effective than using more than one inhaler to deliver triple therapy. The section headed 'Cost effectiveness and resource use' discussed indirect costs and the application of its economic model.

The Panel noted that the complainant bore the burden of proof and considered that, on the evidence before it, the complainant had not established that there was no cost-effective analysis as alleged. Based on the very narrow allegation, the Panel thus ruled no breach of the Code.

An anonymous contactable complainant raised concerns about the promotion of respiratory medicines by GlaxoSmithKline UK Limited. The complainant referred to four medicines: Trelegy (fluticasone/umeclidinium/vilanterol), Anoro (umeclidinium/vilanterol), Incruse (umeclidinium) and Relvar (fluticasone/vilanterol), that were each delivered via the Ellipta device. Seretide (fluticasone/salmeterol) and Serevent (salmeterol) were also referred to on one of the materials at issue. All of the medicines were variously indicated for chronic obstructive pulmonary disease (COPD) and/or asthma.

When writing to GlaxoSmithKline, the Authority asked it to consider the requirements of Clauses 2, 3.2, 4.3, 4.9, 4.10, 7.2, 9.1, 14.1 and 26.3 as cited by the complainant.

1 Invitation to a promotional meeting on inhaler techniques and devices

COMPLAINT

The complainant alleged that an invitation to a respiratory promotional meeting lacked the mandatory information (a link to the meeting invitation was provided). The meeting, which took place at a named conference centre in late October 2019, was an 'Inhaler Technique & Devices Workshop' with presentations from a named independent respiratory trainer and a named GlaxoSmithKline sales representative. The complainant noted that at the bottom of the page, four medicines were mentioned: Trelegy, Anoro, Relvar and Incruse. The complainant alleged that the generic names were not listed for any of the medicines and more importantly there was no adverse event reporting statement or black triangles which were needed for Incruse, Anoro and Trelegy. The complainant alleged breaches of Clauses 4.3 (4 times), 4.9 (4 times), 4.10 (4 times), 9.1 and 2. Further, the complainant did not consider that the material appeared to have been certified given the lack of mandatory information; a breach of Clause 14.1 was alleged.

RESPONSE

GlaxoSmithKline stated that the invitation was generated using the company's iMAIL system which allowed representatives to populate key information into reviewed and certified invitation templates from pre-selected fields. Those fields were venue, meeting title, agenda, speaker details and timings of the meeting. The invitation once generated was distributed to health professionals. The template for the invitation in question was reviewed and certified on 4 September 2019.

GlaxoSmithKline submitted that during its investigation for this complaint, it was noted that on 14 October 2019, internal controls identified that on iMAIL invitations, the link for the prescribing information did not contain the black triangle for Trelegy Ellipta, Anoro Ellipta and Incruse Ellipta or the non-proprietary name for those products and Relvar Ellipta. At that time Relvar Ellipta no longer required a black triangle.

GlaxoSmithKline stated that on 14 October 2019, action was taken to immediately stop the creation and sending of any further invitations; an internal review was conducted to understand how the error had occurred and to put appropriate actions in place to rectify the issue and additional training was provided on the Code requirements before any further materials could be developed.

GlaxoSmithKline's internal review identified that these invitations had been generated for meetings from 4 September to 14 October 2019.

GlaxoSmithKline regretted that the approved invitation (ref PM-GB-UCV-BRF-190006 Sept 2019) did not contain the black triangle and the non-proprietary names for Trelegy Ellipta, Anoro Ellipta and Incruse Ellipta and the non-proprietary name for Relvar Ellipta. When GlaxoSmithKline identified the issue, it immediately stopped the use of the invitations. GlaxoSmithKline stated that health professionals could access the prescribing information from the link within the invitation and that all mandatory information was available at the meeting.

GlaxoSmithKline confirmed that the version of the invitation available on the link at the time of the complaint matched that of GlaxoSmithKline's records. The version sent by the Panel was an incomplete version of the same document. GlaxoSmithKline also confirmed that the prescribing information link for Incruse in the invitation linked to the UK prescribing information on GSKPro and a copy was provided. GlaxoSmithKline did not understand how the Panel accessed a non-UK Incruse document following the link in the invitation.

GlaxoSmithKline stated that the adverse event reporting statement was available and was present within the prescribing information for each product and so health professionals were able to access information about reporting adverse events. GlaxoSmithKline denied a breach of Clause 4.9 as the adverse event report statement was present.

GlaxoSmithKline also denied a breach of Clause 14.1; the template was certified.

GlaxoSmithKline accepted that the invitation breached Clause 4.3 and 4.10, therefore the company had not maintained the high standards that were required and it accepted a breach of Clause 9.1.

GlaxoSmithKline denied a breach of Clause 2 and submitted that Clause 2 was a sign of particular censure and reserved for such matters. GlaxoSmithKline stated that it was aware of its obligations under the Code and regretted that this error had occurred.

PANEL RULING

The Panel noted that the material at issue was an invitation to a respiratory promotional meeting in late October 2019 titled 'Inhaler Technique & Devices Workshop' which appeared to be

published on a CCG website. The bottom right corner had four links to the prescribing information for Trelegy, Anoro, Relvar and Incruse.

The Panel noted that the PDF of the invitation downloaded by the case preparation manager from the link provided by the complainant was dated 11 September 2019 and appeared to be cut off such that a job code could not be seen. The Panel noted that the invitation provided by GlaxoSmithKline was dated 9 September 2019 and included the job code and date (ref PM-GB-UCV-BRF-190006 Sept 2019). The Panel queried why the dates were different but noted that otherwise the visible content was identical. The Panel based its rulings on the invitation provided by GlaxoSmithKline which appeared to be complete.

The Panel noted that the bottom right-hand corner of the invitation listed the brand names for Trelegy, Anoro, Relvar and Incruse which were all available in Ellipta inhalers, but did not include the corresponding non-proprietary names as required by Clause 4.3 and a breach was ruled in relation to each as acknowledged by GlaxoSmithKline. The Panel noted GlaxoSmithKline's submission that its internal review identified that these invitations had been generated for meetings from 4 September 2019 to 14 October 2019; Trelegy, Anoro and Incruse at the time were subject to additional monitoring but the invitation did not include an inverted black triangle for each of the three medicines as required by Clause 4.10 and a breach was ruled in relation to each, as acknowledged by GlaxoSmithKline. The complainant acknowledged that Relvar Ellipta did not need a black triangle and then cited Clause 4.10 in relation to each of the four products. The Panel thus ruled no breach of Clause 4.10 in relation to Relvar Ellipta. The Panel considered that each promotional item must be capable of standing alone and Clause 4.9 stated that all promotional material must include the prominent adverse event reporting statement. The Panel noted that whilst the adverse event reporting statement was included within the prescribing information, which was hosted on external links from the invitation, there was no reference to it on the meeting invitation itself. The Panel considered that this was particularly important given that three of the four products were subject to additional monitoring, and therefore it ruled a breach of Clause 4.9. In reaching its decision on this point, the Panel did not consider that a separate adverse event reporting statement was needed for each product promoted as implied by the complaint.

Clause 14.1 stated, *inter alia*, that promotional material must not be issued unless its final form, to which no subsequent amendments will be made, has been certified by one person on behalf of the company in the manner provided for by this clause, subject to the provisions of the supplementary information to this clause where relevant.

The Panel noted that both the certificate for the Asthma and COPD promotional meetings invite template and the final invitation to the 22 October 2019 meeting provided by GlaxoSmithKline included the job bag number PM-GB-UCV-BRF-190006, September 2019. This gave the impression that the final populated template had been approved but from GlaxoSmithKline's response that was not so.

The Panel noted that it was not unacceptable to use certified templates for invitations but the arrangements must be such that the company could be confident that the completed template complied with the Code. Instructions to representatives were important in this regard. In the Panel's view, altering fields such as the agenda, which was likely to be directly relevant to whether material was Code compliant and might meaningfully change the nature of the original certified invitation template, was different to the population of fields related to administrative

details. In the Panel's view, in the particular circumstances of this case, the final invitation had not been certified prior to being issued and a breach of Clause 14.1 was ruled.

The Panel noted its rulings above and considered that high standards had not been maintained. The Panel was also concerned that the governance of the iMAIL invitations appeared to be poor during the relevant period. A breach of Clause 9.1 was ruled.

The Panel noted its rulings above including a breach of Clauses 4.9 and 9.1 and although it considered that it was unacceptable to omit the adverse event reporting statement and black triangle, where relevant within the invitation in question, they could, nonetheless, be viewed when the prescribing information was accessed from the links within the invitation. The Panel considered that the rulings of breaches adequately covered this matter and an additional ruling of a breach of Clause 2 would be disproportionate in the particular circumstances of this case. A ruling of a breach of Clause 2 was used as a sign of particular censure and reserved for such use. The Panel, on balance, ruled no breach of Clause 2.

2 Invitation to a promotional meeting on asthma control

COMPLAINT

The complainant provided a link to an invitation to a meeting at a named venue which took place on 4 July 2019 and was titled 'Optimising asthma control in your practice'. The complainant noted that there was a picture of the lungs with the meeting title and the logo for Trelegy Ellipta. The complainant stated that Trelegy Ellipta was only licensed for COPD although the invitation implied that it was licensed for asthma. The complainant alleged breaches of Clauses 3.2, 14.1, 9.1 and 2. The complainant was concerned that GlaxoSmithKline had already breached the Code with regard to the lack of generic names and off-label promotion in several other cases but continued with the same practices.

RESPONSE

GlaxoSmithKline noted that the link provided by the complainant was to an invitation to a promotional meeting organised by a named representative. The invitation was intended to be printed and distributed to health professionals.

GlaxoSmithKline submitted that at the time the meeting occurred, it was promoting Relvar Ellipta in asthma and Trelegy Ellipta in COPD (copies of summaries of product characteristics (SPCs) provided) in line with the marketing authorisations for each.

GlaxoSmithKline confirmed that the version of the invitation available on the link at the time of the complaint matched GlaxoSmithKline's records. The version sent by the PMCPA was an incomplete version of the same document.

As a result of a thorough internal investigation, GlaxoSmithKline confirmed the following:

- the meeting, 'Optimising asthma control in your practice' was mainly about asthma control and included the appropriate use of Relvar Ellipta. That was followed by a second presentation promoting Trelegy Ellipta in COPD. The meeting was intended to cover both asthma and COPD
- the meeting was cancelled by GlaxoSmithKline

- the COPD representative and the key account manager for asthma had left GlaxoSmithKline by early 2020
- meeting titles and agenda items were only available in the iMAIL system after approval from the marketing and medical teams.

GlaxoSmithKline submitted that the invitation was created through the iMAIL system which had been in place for over 20 years. Through the system, the brand logo and the prescribing information were auto-populated based on the role of the representative and the selection of the meeting information. In this case, the COPD representative (as could be seen from his/her contact details) created the invitation for the meeting. In this case the representative and the key account manager had proposed to have a joint meeting covering both asthma and COPD.

GlaxoSmithKline submitted that the meeting was not intended to promote Trelegy for use in asthma.

GlaxoSmithKline further noted that the meeting pre-dated its decision to submit for a licence for Trelegy in asthma. GlaxoSmithKline stated that there was no briefing or expectation of representatives to attempt to promote in asthma and submitted that the Trelegy session was clearly on COPD and there was no link to Trelegy in asthma in the meeting or the invitation. There were clearly two discreet sessions. GlaxoSmithKline denied that this in anyway promoted Trelegy for the use in asthma and it was clear on the invitation that the Trelegy session related to COPD. Furthermore, the meeting was cancelled.

GlaxoSmithKline regretted that the title of the meeting solely related to asthma, however there was no promotion of Trelegy in the use of asthma in this invitation. Furthermore, GlaxoSmithKline submitted that the complainant had provided no evidence that demonstrated promotion of Trelegy in asthma.

GlaxoSmithKline noted that the iMAIL system had been replaced by Veeva Events Management system (VEM) in July 2020. This provided GlaxoSmithKline with a modern system to generate invitations with more appropriate controls in place. GlaxoSmithKline conducted ongoing testing of the system to ensure it continued to meet its requirements for governance and compliance. GlaxoSmithKline stated that it was fully committed to its requirements and obligations under the Code and would only promote its medicines in accordance with the terms of the marketing authorisation as set out in Clause 3.2. GlaxoSmithKline denied a breach of Clause 3.2.

GlaxoSmithKline denied a breach of Clause 14.1. The templates were approved for promotional activities by an experienced final signatory (copy provided). The final signatory left GlaxoSmithKline in March 2020.

GlaxoSmithKline submitted that it maintained a system for approving invitations which was of a high standard and in that regard, it refuted a breach of Clause 9.1.

GlaxoSmithKline had taken a full and thorough review of its systems and processes with respect to invitations. Since November 2019 it had invested in significant Code training for head office staff and meetings training across head office and field teams.

GlaxoSmithKline respectfully denied a breach of Clause 2 and noted that a finding of a breach of that clause was a sign of particular censure and reserved for such matters.

PANEL RULING

The Panel noted GlaxoSmithKline's submission that the digital invitation at issue was intended to be printed and distributed to health professionals. It appeared to the Panel that, if printed the invitation was a 6 page gate-folded booklet and that the front cover of the invitation included an image of a pair of lungs, the title 'Optimising asthma control in your practice' and the Trelegy Ellipta brand logo at the bottom of the page. The invitation had been published on a local pharmaceutical committee website.

The Panel noted that the invitation was generated through GlaxoSmithKline's iMAIL system and that the brand logo and prescribing information were auto-populated based on the role of the representative creating it and the selection of the meeting information; the invitation at issue was generated by the COPD representative and the joint asthma and COPD meeting was to be conducted by the representative and a key account manager.

The Panel noted GlaxoSmithKline's submission that the meeting was cancelled. The Panel noted GlaxoSmithKline's submission that there was no briefing or expectation of representatives to attempt to promote Trelegy in asthma, and that whilst it regretted the title of the meeting solely related to asthma, the Trelegy session was clearly on COPD and there was no link to Trelegy in asthma on the invitation or in the meeting.

The Panel noted that the agenda on the invitation listed two separate sessions, one titled 'Optimising asthma control in your practice' and one titled 'Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol): The only single daily inhalation triple therapy for COPD'.

In the Panel's view, it was not unreasonable to consider that a busy health professional reading the first page of the invitation might assume that Trelegy Ellipta was a treatment option for asthma, given the heading. It would have only been upon reading the agenda that one might have been made aware from the session 'Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol): The only single daily inhalation triple therapy for COPD' that Trelegy Ellipta was licensed for COPD. The Panel also considered that the impression from the agenda might have led health professionals to believe that Trelegy was licensed for both asthma and COPD.

The Panel considered both the immediate and overall impression given to a busy health professional. In the Panel's view, the invitation implied that Trelegy was licensed for asthma which was not so; a breach of Clause 3.2 was ruled.

The Panel noted its comments and ruling above and considered that high standards had not been maintained. A breach of Clause 9.1 was ruled. The Panel considered that any reference to Trelegy on an invitation for an asthma-focussed meeting was wholly inappropriate given that Section 4.4, Special warning and precaution for use of the Trelegy SPC, stated that they should not be used in patients with asthma since they had not been studied in that patient population. The Panel considered that the implied suggestion otherwise was such as to reduce confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel noted that it was not unacceptable to use certified templates for invitations but the arrangements must be such that the company could be confident that the completed template complied with the Code. Instructions to representatives were important in this regard. In the Panel's view, altering fields such as the agenda, which was likely to be directly relevant to

whether material was Code compliant and might meaningfully change the nature of the original certified invitation template, was different to population of fields related to administrative details. In the Panel's view, in the particular circumstances of this case, the final invitation had not been certified prior to being issued and a breach of Clause 14.1 was ruled.

3 On-demand webinar

COMPLAINT

The complainant provided a link to an on-demand webinar entitled 'Winter is Coming – COPD patient optimisation in the context of COVID-19' (ref PM-GB-UCV-VID-200012, September 2020). The complainant noted that the webinar could also be accessed via a Google search and so it was important to note the route of access within the context of the first mention of generic names. The webinar was conducted with different health professionals and lasted 57 minutes, 31 seconds. At 29 minutes and 31 seconds the focus of the webinar switched to pharmacological options. The complainant stated that Trelegy Ellipta was first mentioned three times at that point on the slide but it did not have a generic name or black triangle anywhere next to the three mentions on the slide. In addition, Anoro and Relvar were also first mentioned on the same slide at that time but again there was no generic name or black triangle for Anoro. The complainant alleged breaches of Clause 4.3 (3 times) and 4.10 (twice), 9.1 and 2.

RESPONSE

GlaxoSmithKline submitted that the webinar was held on 16 September 2020 and an on- demand video of the event was subsequently made available on GSKPro, a company website for health professionals. Health professionals had to self-declare their professional status in order to access GSKPro. GlaxoSmithKline confirmed that the on-demand video could be searched for via Google, however when landing on the page via a Google search, the first mention of the product was within the video-on-demand and at that point, the black triangle and the non-proprietary name were clearly displayed. The item was certified as a promotional item by a final signatory.

GlaxoSmithKline submitted that the webinar was of a panel of respiratory experts discussing how the NHS could prepare for significant pressures in winter with seasonal flu and COVID-19; the webinar was chaired by a GlaxoSmithKline physician.

GlaxoSmithKline submitted that all mandatory information was provided during the webinar including licensed indications for ease of use for the audience. Furthermore, clarity was provided on the different licences in one place at the beginning of the webinar. GlaxoSmithKline noted that the complainant had not mentioned that at 25 seconds, slide 2 provided comprehensive information about the licensed indication for Trelegy Ellipta, Anoro Ellipta, Relvar Ellipta, Incruse Ellipta, Seretide and Serevent, including all the appropriate mandatory information, the non-proprietary name for all the listed medicines along with the black triangle for Trelegy Ellipta, Anoro Ellipta and Incruse Ellipta (copy provided). In addition, the presenter also informed the audience that further information was available on the GSKPro website under the 'Key Documents' section (copy provided) including the generic name, black triangle for the relevant products and a link to the prescribing information. Furthermore, clarity was provided on the different licences in one place at the beginning of the webinar.

GlaxoSmithKline denied a breach of Clause 4.3 as the non-proprietary name appeared immediately adjacent to the brand name at its first appearance in a size that was readily visible

on slide 2. The non-proprietary name for all the products was also available on the 'Key Documents' section of the webpage.

GlaxoSmithKline also denied a breach of Clause 4.10 as the black triangle was present for Trelegy Ellipta, Anoro Ellipta and Incruse Ellipta on slide 2 of the video, at the first mention of the medicines. This information was also available on the 'Key Documents' sections of the webpage.

GlaxoSmithKline therefore also denied breaches of Clauses 9.1 and 2.

PANEL RULING

The Panel noted that health professionals needed to self-declare their health professional status in order to access GSKPro.com webpage where the video was hosted. The Panel noted that it did not have a copy of the on-demand video before it but had been provided with certain screenshots. The Panel noted GlaxoSmithKline's submission that the on-demand video could be searched for via Google, however when landing on the page via a Google search, the first mention of the product was within the video-on-demand and at that point, the black triangle and the non-proprietary name were clearly displayed.

The Panel further noted that the complainant referred to a slide at 29 minutes and 31 seconds into the webinar, which mentioned Trelegy Ellipta three times with no generic name or black triangle and did not include the generic name or black triangle for Anoro Ellipta either. The Panel, however, noted GlaxoSmithKline's submission that 25 seconds into the webinar, on Slide 2, all mandatory information was included.

The Panel noted that a screenshot of the video at 26 seconds provided by GlaxoSmithKline, described as Slide 2, included the licensed indications, non-proprietary names, and inverted black triangles, where relevant, for Trelegy Ellipta, Anoro Ellipta, Relvar Ellipta, Incruse Ellipta, Seretide and Serevent. The Panel noted that the complainant bore the burden of proof and that he/she had not established that the required obligatory information was not included as alleged. No breach of Clause 4.3 was ruled in relation to Trelegy Ellipta, Anoro Ellipta, Relvar Ellipta, and Incruse Ellipta and no breach of Clause 4.10 was ruled in relation to Trelegy Ellipta, Anoro Ellipta and Incruse Ellipta. The Panel noted its rulings and consequently ruled no breach of Clauses 9.1 and 2 in this regard.

4 Patient resource material

COMPLAINT

The complainant noted that on the GSKPro website, there was, within the patient resources, a one-page leaflet on how to use the Ellipta device available in different languages. However, none of the five pdf guides had the adverse event reporting in breach of Clause 26.3 (5 times). The complainant stated that this was very worrying as patients might take the Ellipta device with one of the black triangle Ellipta products (eg Anoro, Incruse) but yet were not provided with information on how to report adverse effects. The complaint provided a link to the English language leaflet.

RESPONSE

GlaxoSmithKline submitted that the 'How to use the Ellipta inhaler' patient leaflet (copy provided), was only available through the GSKPro site. The GSKPro site was intended for health professionals and they had to self-declare that they were health professionals in order to access the site. The leaflet was for health professionals to share with patients and was available in English, Urdu, Punjabi, Gujarati, Polish and Welsh.

The leaflet provided instructions on how to use the Ellipta device and useful advice for patients who might be new to the Ellipta device or who would benefit from useful instruction on how to use it. The leaflets were non-promotional and non-branded. Importantly the leaflet was not about any specific medicine but was related to the use of the Ellipta device itself. GlaxoSmithKline noted that Clause 26.3 stated 'Any material which related to a **medicine** and which was intended for **patients taking that medicine** must include the statement…' (emphasis added). The clause then referred to the specific wording to be used which differed if the medicine was subject to additional monitoring (such as a black triangle). There were four licensed products for use in the Ellipta device of which three had additional monitoring requirements, therefore it would not be appropriate to have that information on the leaflet. The patient information leaflet which related to the medicine intended to be taken by the patient and supplied with the dispensed medicine, contained information about how to report adverse events by the patient and was a more appropriate place for that information.

GlaxoSmithKline submitted that as the 'How to use the Ellipta inhaler' leaflet did not relate to a specific medicine and therefore did not require the adverse event reporting statement. GlaxoSmithKline took adverse event reporting and patient safety extremely seriously. Health professionals could also download the patient information leaflet from GSKPro.

GlaxoSmithKline denied a breach of Clause 26.3.

PANEL RULING

The Panel noted that the patient leaflet at issue was intended to provide instructions for patients on how to use the Ellipta inhaler.

Clause 26.3 stated that any material which relates to a medicine and which is intended for patients taking that medicine must include the statement below or a similar one:

> 'Reporting of side effects' If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the package leaflet. You can also report side effects directly via the Yellow Card Scheme at [a web address which links directly to the MHRA Yellow Card site]. By reporting side effects you can help provide more information on the safety of this medicine.'

It further stated that when the material relates to a medicine which is subject to additional monitoring an inverted black equilateral triangle must be included on it together with the statement below or a similar one:

> 'This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See [a web address which links directly to the MHRA Yellow Card site] for how to report side effects.'

The Panel noted GlaxoSmithKline's submission that the leaflet did not relate to a specific medicine but the Ellipta device itself. The Panel further noted GlaxoSmithKline's submission that there were four licensed products for use in the Ellipta device of which only three had additional monitoring requirements (black triangle) and it would therefore not be appropriate to have that information on the leaflet for the Ellipta device.

The Panel noted that whilst the leaflet did not refer to a specific medicine and thus the black triangle which was related to a specific medicines was not required to be included, the ultimate audience of the leaflet was members of the public who had been prescribed one of the four licensed medicines used with an Ellipta device and thus, in the Panel's view, the leaflet should have included an adverse event reporting statement as required by Clause 26.3; a breach of Clause 26.3 was ruled.

5 Claim for Trelegy

COMPLAINT

The complainant referred to claims regarding exacerbation reduction for Trelegy Ellipta within the GSKPro website (ref PM-GB-FVU-WCNT-200013, September 2020) (link provided). The complainant noted that on the first part of the page, there was a claim that Trelegy Ellipta delivered superior reduction in annual rate of moderate/severe exacerbations vs an inhaled corticosteroid/long-acting beta agonist (ICS/LABA); there was a bubble next to the bar chart which stated 44% reduction. The complainant alleged that that was relative risk reduction and not absolute risk reduction which had to be shown. Breaches of Clauses 7.2 and 9.1 were alleged.

RESPONSE

GlaxoSmithKline submitted that the webpage referenced by the complainant was available on GSKpro.com. GSKPro was a website intended for health professionals and contained promotional and non-promotional content. Health professionals had to self-declare their health professional status to access the site.

GlaxoSmithKline submitted that the webpage in question (copy provided) showed the annual rate of moderate/severe exacerbations for Trelegy Ellipta vs an ICS/LABA. The x and y axes were clearly labelled, with legible text and there were no unusual scales or suppressed zeros. The graph represented the absolute values from the referenced clinical study (Lipson *et al* 2017, copy provided). The absolute values on each bar of the chart were of the same size and prominence as the relative risk reduction. In a bubble, to the right of the graph, was the relative risk reduction and the P value for the relative risk reduction. The material was certified by a final signatory.

GlaxoSmithKline noted that the supplementary information to Clause 7.2 stated:

> 'Referring only to relative risk, especially about risk reduction, can make a medicine appear more effective than it actually is. To assess the clinical impact of an outcome, the reader also needs to know the absolute risk involved. In that regard relative risk should never be referred to without also referring to the absolute risk. Absolute risk can be referred to in isolation.'

GlaxoSmithKline believed there was a clear representation of the absolute values on the page and graph in the material. The company noted that the font size and colour were similar to that of the relative risk reduction and there was an accurate scale on the graph with clear legibility. GlaxoSmithKline refuted a breach of Clause 7.2 as absolute values and relative risk values were clearly prominent and visible to the health professional. GlaxoSmithKline did not consider that the information was misleading.

GlaxoSmithKline also denied a breach of Clause 9.1. The material in question had undergone rigorous and diligent review and approval and met the requirements of the Code.

PANEL RULING

The Panel noted the complainant's allegation that the webpage at issue included a relative risk reduction of 44% but no absolute risk reduction.

The Panel noted that the relative risk reduction was in a bubble, to the right of the graph. The Panel noted GlaxoSmithKline's submission that that the graph represented the absolute values from the referenced clinical study (Lipson *et al* 2017, copy provided); the absolute values on each bar of the chart were of the same size and prominence as the relative risk reduction.

The Panel noted that the supplementary information to Clause 7.2 stated that referring only to relative risk, especially with regard to risk reduction, can make a medicine appear more effective than it actually is. In order to assess the clinical impact of an outcome, the reader also needs to know the absolute risk involved. In that regard, relative risk should never be referred to without also referring to the absolute risk. Absolute risk can be referred to in isolation.

The Panel considered that the graph included the absolute values with similar prominence to the relative risk reduction and therefore no breach of Clause 7.2 was ruled.

The Panel noted its rulings above and did not consider that high standards had not been maintained. No breach of Clause 9.1 was ruled.

6 Claim about the cost-effectiveness of Trelegy

COMPLAINT

The complainant provided a link to a page on the GSKPro website which included a claim that Trelegy was a cost-effective single inhaler triple therapy. The complainant alleged that the claim was not accurate as no cost-effective analysis had been done and the reference provided for the claim (MIMS) was purely the price of the inhaler as opposed to actual cost-effectiveness which was much broader than simply the price of a product.

RESPONSE

By way of background, GlaxoSmithKline submitted that in July 2019, the National Institute for Health and care Excellence (NICE) updated its guideline on the diagnosis and management of COPD (which included emphysema and chronic bronchitis) in the over 16s (NG115). The guideline aimed to help those with COPD to receive an earlier diagnosis so that they could benefit from treatments to reduce symptoms, improve quality of life and keep them healthy for longer. The NICE review also took into account clinical and cost-effectiveness outcomes of a

treatment (link provided). The 2019 update included a section providing the rationale and recommendations for the use of triple therapy for patients with COPD. NICE specifically mentioned the following in the 2019 COPD guideline.

> 'The committee did not make a recommendation in favour of single or multiple inhaler devices as the included evidence did not show a meaningful difference in clinical effectiveness between triple therapy compared to dual therapy based on the number of devices. From the economic evidence, using a single inhaler device was more cost effective, but the committee agreed that there were circumstances where using more than one inhaler to deliver triple therapy may be more appropriate for a particular person with COPD. Finally, the committee had already made a recommendation about the factors to be considered when choosing an inhaler device and these included minimising the numbers and types of inhalers where possible and cost so an additional recommendation on this issue was unnecessary.'

GlaxoSmithKline noted that Trelegy was approved by the European Medicines Agency (EMA) in November 2017 and from the full NICE COPD guideline, GlaxoSmithKline confirmed two Trelegy Ellipta COPD studies had been included in the review NICE had completed for the 2019 COPD guideline. Therefore, Trelegy Ellipta was included in the above review of the single inhaler triple therapy economic evidence review the NICE committee had completed in July 2019.

GlaxoSmithKline subsequently created GSKpro.com, a website intended for health professionals; access to the site was only granted after health professionals self-declared their health professional status. The site contained key Trelegy information and a claim that it was 'A cost-effective single inhaler triple therapy for COPD'. That claim was based on an interpretation from the NICE COPD guideline issued in July 2019, which quoted 'From the economic evidence, using a single inhaler device was more cost effective'. Therefore, GlaxoSmithKline believed that the cost-effective claim in the webpage represented the review NICE had conducted of single inhaler triple therapy in 2019.

As stated above, in July 2019, NICE updated its COPD in over 16s: diagnosis and management guideline [NG115]. Included in that guideline was the reference to economic evidence, that using a single inhaler device was more cost effective than using more than one inhaler to deliver triple therapy. NICE also confirmed in its guideline, that the NICE reviews considered clinical and cost-effectiveness outcomes of a treatment. GlaxoSmithKline confirmed from the full COPD 2019 updated NICE guideline, that Trelegy Ellipta indicated for COPD, was part of that review.

GlaxoSmithKline acknowledged that the NICE committee did not make a recommendation in favour of single or multiple inhaler devices, as the included evidence for the July 2019 triple therapy review for COPD did not show a meaningful difference in clinical effectiveness between triple therapy vs dual therapy based on the number of devices. However, NICE did state that using a single inhaler device was more cost-effective than using more than one inhaler to deliver triple therapy. NICE acknowledged that triple therapy could be achieved via a single inhaler or by more than one inhaler.

GlaxoSmithKline submitted that this was the basis on which it made the claim, a cost-effective single inhaler triple therapy for COPD, on the website material in question. Clause 7.6 stated that when promotional material referred to published studies, clear references must be given. The NICE document referenced above was not a published study and so did not meet that criterion and the requirement to reference the NICE COPD guideline on the Trelegy webpage in

question by the complainant. In line with Clause 7.5, if substantiation for the claim in question was requested by members of the health professions or other relevant decision makers, GlaxoSmithKline would provide the NICE COPD guideline and the references in the material. The references adjacent to the claim in question were MIMS and data on file which listed the moving annual total of different combinations of multiple inhaler dual and triple therapies (copy provided).

GlaxoSmithKline acknowledged that in future it would be useful to cite the NICE COPD guidelines as an additional reference to add clarity to the claim 'A cost effective single inhaler triple therapy for COPD', however, this would not be considered as a breach of the Code.

GlaxoSmithKline noted that the webpage was certified and a copy of the certificate was provided.

GlaxoSmithKline stated that it was its intention to always ensure COPD patients were appropriately treated and its materials were produced in line with the Code. Therefore, GlaxoSmithKline refuted the content in question by the complainant and believe it was accurate and reflective of the latest NICE COPD guideline [NG115].

PANEL RULING

The Panel noted that the complainant had not cited any specific clauses in relation to this matter, and that GlaxoSmithKline had not referred to any of the Clauses raised by the case preparation manager in its response. The Panel noted that the company had been asked to consider the requirements of Clause 7.2 which it considered was relevant to the complainant's allegation and decided that it would make its rulings on that basis.

The Panel noted that the webpage at issue, on GSKPro.com, had the heading 'Trelegy Ellipta Price' beneath which was a graph which compared Trelegy Ellipta with other branded multiple inhaler triple therapy combinations in COPD; the graph was a bar chart which was headed 'A cost-effective single inhaler triple therapy for COPD' and illustrated the price differential between Seretide, Fostair, Symbicort and Trelegy; Trelegy was markedly lower visually.

The Panel noted that the term 'cost-effective' meant more than just a comparison of the acquisition costs, both direct and indirect costs should be taken into account such as resource. Other factors such as relative efficacy and incidence of side effects might also be relevant.

The Panel noted GlaxoSmithKline's submission that in July 2019, the National Institute for Health and care Excellence (NICE) updated its guideline on the diagnosis and management of COPD, which also took into account clinical and cost-effectiveness outcomes of a treatment. The Panel noted GlaxoSmithKline's submission that two Trelegy Ellipta COPD studies had been included in the review and whilst it did not make a recommendation in favour of single or multiple inhaler devices, NICE did state that using a single inhaler device was more cost-effective than using more than one inhaler to deliver triple therapy.

The Panel noted that the NICE Guidelines stated that the recommendation on how to choose drugs and inhalers covered factors that prescribers routinely considered, so was not a change in practice. However, minimising the number and type of inhaler devices and avoiding unnecessary within-class switching might produce cost savings through lower upfront spending and better symptom control. The section headed 'Cost effectiveness and resource use' discussed indirect costs and the application of its economic model.

The Panel noted that the complainant bore the burden of proof and considered that, on the evidence before it, the complainant had not established that there was no cost-effective analysis as alleged. Based on the very narrow allegation, the Panel thus ruled no breach of Clause 7.2.

Complaint received **28 November 2020**

Case completed **6 September 2021**