CASE AUTH/3522/6/21 ***NO BREACH OF THE CODE***

HEALTH PROFESSIONAL v GLAXOSMITHKLINE

Promotion of Trelegy Ellipta

A health professional complained about the promotion of Trelegy Ellipta (fluticasone, umeclidinium and vilanterol) by GlaxoSmithKline UK Limited. The material at issue was an advertisement (ref PM-GB-FVU-JRNA-200003 (v2.0)) in the supplement for the British Thoracic Society's (BTS) Winter Meeting, February 2021 and an advertisement (ref PM-GB-RS-WCNT-210009) on the gskpro website.

Trelegy was indicated for maintenance treatment in adults with moderate-to-severe chronic obstructive pulmonary disease (COPD) who were not adequately treated by a combination of either an inhaled corticosteroid and a long-acting beta2-agonist (ICS+LABA) or of a long-acting beta2-agonist and a long-acting muscarinic antagonist (LABA + LAMA).

The detailed response from GlaxoSmithKline is given below.

In the BTS advertisement the first claim at issue was 'For patients with COPD on treatment with ICS/LABA who are symptomatic and at risk of an exacerbation*' which headed the advertisement and was referenced to the Trelegy summary of product characteristics (SPC). The asterisk led the reader to text immediately below the claim which read 'Has worsening of symptoms or has experienced an exacerbation treated with antibiotics or oral corticosteroid, in the past 12 months'.

The complainant alleged that the claim was not in line with the licensed indication for Trelegy; it was not accurate and could not standalone as Trelegy was only for moderate-to-severe COPD patients who were at risk of exacerbation and symptomatic. The claim 'For patients with COPD' implied any COPD patient, including those with mild disease, could be treated.

The Panel considered that health professionals would be familiar with the widely accepted and well-defined stepwise guidelines which existed for the treatment of COPD.

The Panel noted that the claim at issue was not simply 'For patients with COPD' as referred to by the complainant and that when read in full it was clear that the advertisement promoted Trelegy for its licensed indication ie COPD patients who were not adequately treated with combination therapy (ICS/LABA); patients already on dual therapy would, according to treatment guidelines, be those with moderate-to-severe COPD ie those for whom Trelegy was indicated – patients with mild COPD would only be treated with single therapy. The Panel thus did not consider that the advertisement promoted Trelegy for use COPD patients with mild disease, as alleged. In the Panel's view, the claim was not inconsistent with the particulars listed in the Trelegy Ellipta SPC and nor did it consider that it was misleading or that it could not be substantiated; no

breaches of the Code were ruled. The Panel did not consider that high standards had not been maintained and ruled no breach of the Code including of Clause 2.

The second claim at issue was 'Trelegy Ellipta provides your patients with superior improvements in lung function and health-related quality of life, and reduction in annual rate of exacerbations vs. Symbicort Turbohaler at 24 weeks'.

The complainant noted that Symbicort Turbohaler was available in a range of different strengths and that the claim did not make clear which strength of Symbicort Turbohaler, the improvements were shown against within the clinical trial. The clinical trial cited was only vs one strength of Symbicort Turbohaler so the evidence base was very specific but the claim was much broader.

The Panel noted that the advertisement was very clearly about the treatment of COPD and in that regard it noted GlaxoSmithKline's submission that only one dose of Symbicort Turbohaler was licensed for such use ie 400mcg budesonide/12mcg formoterol twice daily which could be delivered as one or two inhalations twice daily depending on which one of two presentations was prescribed (the third presentation and lowest dose of Symbicort Turbohaler (100mcg/6mcg) was only indicated for the treatment of asthma). As noted above, the Panel considered that health professionals would be familiar with the guidelines which existed for the treatment of COPD and be familiar with the place of Symbicort within those guidelines. The Panel noted that the clinical trial cited used one inhalation of Symbicort twice a day rather than the lower dose Turbohaler at two inhalations twice daily; in that regard the use of just one inhalation at a time of Symbicort would thus be the same as Trelegy which had a licensed dose of one inhalation, albeit once daily. Overall the Panel considered whilst it might have been helpful to include details of the administration of Symbicort, it did not consider that the claim was broader than the evidence as alleged and ruled no breach of the Code. The claim was substantiated by the clinical trial and therefore no breach was ruled. The Panel did not consider that high standards had not been maintained and ruled no breach of the Code including of Clause 2.

The advertisement on the gskpro website was for a promotional webinar entitled 'Single Inhaler Triple Therapy in COPD; Evidence to Action' and included a brief summary of the event. The complainant alleged that the advertisement implied that Trelegy was licensed for all COPD patients; further, statements such as 'The role of Single Inhaler Triple Therapy in the treatment of symptomatic COPD patients at risk of an exacerbation' were misleading to busy health professionals given that the licensed indication for Trelegy was not clarified on the page.

The Panel noted that the indication for Trelegy was not included on the material advertising the webinar. However the webpage referred to 'Single Inhaler Triple Therapy in COPD' in the heading with a reference to the evidence base for Trelegy in the first paragraph. At each citation of the brand name, the three constituent components of Trelegy were stated and so it was clear that Trelegy was a single inhaler triple therapy. The second paragraph of the material referred to the role of single inhaler triple therapy in the treatment of symptomatic COPD patients at risk of an exacerbation and webinar attendees were told to expect 'practical and informative advice on the treatment options for symptomatic COPD patients at risk of an exacerbation'. The Panel thus did not consider that the material implied that Trelegy could be used for any patient with COPD.

In addition to the material before them, the Panel considered that health professionals would be well aware of the stepwise approach to therapy and would know that triple therapy was for use in patients who were uncontrolled on dual therapy. The Panel thus considered that it was made clear that Trelegy was a triple therapy for treating certain COPD patients and not all COPD patients as alleged. The Panel did not consider that the material was inconsistent with the particulars listed in the Trelegy SPC. No breaches of the Code were ruled including of Clause 2.

A health professional complained about the promotion of Trelegy Ellipta (fluticasone, umeclidinium and vilanterol) by GlaxoSmithKline UK Limited. The material at issue was an advertisement (ref PM-GB-FVU-JRNA-200003 (v2.0)) in the supplement for the British Thoracic Society's (BTS) Winter Meeting, February 2021 (link provided) and an advertisement (ref PM-GB-RS-WCNT-210009) (link provided) on the gskpro website for a promotional webinar.

Trelegy was indicated for maintenance treatment in adults with moderate-to-severe chronic obstructive pulmonary disease (COPD) who were not adequately treated by a combination of either an inhaled corticosteroid and a long-acting beta2-agonist (ICS+LABA) or of a long-acting beta2-agonist and a long-acting muscarinic antagonist (LABA + LAMA).

A Advertisement in the BTS supplement

1 Claim 'For patients with COPD on treatment with ICS/LABA who are symptomatic and at risk of an exacerbation*'

This claim headed the advertisement and was referenced to the Trelegy summary of product characteristics (SPC). The asterisk led the reader to text immediately below the claim which read 'Has worsening of symptoms or has experienced an exacerbation treated with antibiotics or oral corticosteroid, in the past 12 months'.

COMPLAINT

The complainant alleged that the claim was not in line with the licensed indication for Trelegy. Further, the claim was not accurate and could not standalone as Trelegy was only for moderate-to-severe COPD patients who were at risk of exacerbation and symptomatic. The claim 'For patients with COPD' implied any COPD patient (eg a patient with mild COPD) as opposed to the precise indication. The complainant alleged breaches of Clauses 3.2, 7.2, 7.4, 9.1 and 2.

RESPONSE

GlaxoSmithKline explained that the pharmacological (and non-pharmacological) management of the estimated 1.2 million people in the UK diagnosed COPD was routinely provided by primary and secondary care practitioners. Well defined treatment pathways were published by the National Institute for health and Care Excellence (NICE), the Global Initiative for Chronic Obstructive Lung Disease (GOLD), the Primary Care Respiratory Society (PCRS-UK) and by NHS RightCare Pathway. Moreover, many local and regional clinical groups published their own guidelines based on the aforementioned advice. These guidelines and treatment algorithms made clear recommendations on the stepwise use of inhaled therapies, to manage patients with COPD of varying severity, from mild through to severe disease.

To exemplify, the current NICE COPD 'visual summary' or treatment algorithm (copy provided) recommended a step-up approach from short-acting single inhaled medications, through inhaled combination therapy of long-acting dual combinations, to triple therapy – three molecules, provided in 1 or 2 inhalers:

- **Single (inhaled) therapy**:
  - Short-acting beta2 agonists (SABA) and short-acting muscarinic antagonists (SAMA) as the initial empirical treatment to relieve breathlessness and exercise limitation – this was to manage mild COPD. If the patient remained 'uncontrolled' (or not adequately treated) despite this intervention, prescribers should consider 'stepping-up' to dual therapy (as well as other non-pharmacological interventions).

- **Dual (inhaled) therapy**:
  - inhaled long-acting beta-agonist (LABA) + long-acting muscarinic antagonists (LAMA), or, inhaled LABA + inhaled corticosteroids (ICS) – step-up option for patients with more advanced (moderate-to-severe) disease, who continued to experience breathlessness and exacerbations despite single inhaled therapy. If the patient remained 'uncontrolled' (or not adequately treated), prescribers should consider 'stepping-up' to triple therapy (as well as reviewing other non-pharmacological interventions).

- **Triple (inhaled) therapy (eg Trelegy Ellipta):**
  - LABA + LAMA + ICS – advocated in COPD patients who experienced acute episodes of worsening symptoms and COPD exacerbations, despite dual inhaled therapy ie the patient has moderate-to-severe (or very severe) COPD.

GlaxoSmithKline noted that GOLD international guidelines also recommended a similar stepwise treatment approach for COPD, commenting that worsening of airflow limitation (ie disease progression from mild to severe disease) was associated with increasing risk of symptoms, risk of exacerbations, hospitalisations and even death. Therefore moderate-to-severe COPD disease described patients who had ongoing symptoms and were at risk of an exacerbation. Only patients who remained symptomatic or at risk of exacerbation whilst receiving inhaled dual therapy were eligible for triple therapy – GlaxoSmithKline noted that that was the exact patient profile depicted in the materials at issue.

GlaxoSmithKline submitted that given these well-defined and widely acknowledged treatment pathways, primary and secondary care practitioners were very familiar with the appropriate use of the various classes of inhaled medicines to treat patients with COPD.

GlaxoSmithKline noted that the complainant alleged that the claim in the BTS advertisement, 'For patients with COPD on treatment with ICS/LABA who are symptomatic and at risk of an exacerbation*', was not in line with the Trelegy indication and that it could imply treatment of all COPD patients, regardless of disease severity, in breach of Clause 3.2. GlaxoSmithKline noted that the alleged breach of Clause 3.2 was a fundamental issue raised by the complainant, stemming from which, alleged breaches of Clauses 7.2, 7.4, 9.1 and 2 were inferred.

GlaxoSmithKline strongly challenged that assertion because:

1 The claim ‘For patients with COPD on treatment with ICS/LABA who are symptomatic and at risk of an exacerbation*’ was clear that it was not for all patients with COPD and was in line with Trelegy Ellipta’s indication as it stated that Trelegy was for use for patients as a ‘step-up’ intervention for COPD patients uncontrolled (not adequately treated) on inhaled dual combination therapy:

a) As a step-up treatment from inhaled dual combination therapy, Trelegy was clearly indicated for patients with moderate-to-severe COPD. GlaxoSmithKline maintained that the advertisement did not imply use of Trelegy to treat mild COPD as alleged; the claim clearly referred to patients already on dual therapy who were still symptomatic and at risk of exacerbations — which was moderate/severe COPD; those patients did not have mild COPD.

b) The asterisk led the reader to text immediately below the claim which defined an exacerbation as ‘Has worsening of symptoms or has experienced an exacerbation treated with antibiotics or oral corticosteroid, in the past 12 months’ – that clearly referred to a patient with moderate-to-severe COPD who was not adequately treated.

c) The above wording was in accordance with the marketing authorisation and was not inconsistent with the particulars listed in the SPC. Trelegy was indicated to treat moderate-to-severe COPD patients who were not adequately treated by ICS + LABA. The ‘step-up’ option to triple therapy from dual combination therapy was the exact patient profile depicted in the advertisement.

2 The licensed indication for Trelegy Ellipta was clearly marked on the advertisement in a blue box. Readers would thus be in no doubt that Trelegy Ellipta was indicated in adults with moderate-to-severe COPD who were not adequately treated by a combination of an ICS and a LABA, or a combination of a LAMA and a LABA ie excluding patients with mild COPD.

3 Finally, the prescribing information was also provided.

In summary, GlaxoSmithKline maintained that it was abundantly clear from the claim at the top of the advertisement, who the appropriate patient type was for treatment with Trelegy Ellipta. This was not inconsistent with licensed indication.

GlaxoSmithKline denied a breach of Clause 3.2; the BTS advertisement was in accordance with, and it did not promote indications not covered by the Trelegy Ellipta marketing authorisation. Moreover, GlaxoSmithKline did not understand why the complainant had alleged that the claim was misleading and not capable of substantiation, nor how it failed to maintain high standards and had brought the industry into disrepute. GlaxoSmithKline thus denied breaches of Clauses 7.2, 7.4, 9.1 and 2.

PANEL RULING

The Panel considered that health professionals would be familiar with the widely accepted and well-defined stepwise guidelines which existed for the treatment of COPD.

The Panel noted that the claim at issue read 'For patients with COPD on treatment with ICS/LABA who are symptomatic and at risk of an exacerbation' and not simply 'For patients with COPD' as referred to by the complainant. When the claim was read in full, the Panel considered that it was clear that the advertisement promoted Trelegy for its licensed indication ie COPD patients who were not adequately treated with combination therapy (ICS/LABA); patients already on dual therapy would, according to treatment guidelines, be those with moderate-to-severe COPD ie those for whom Trelegy was indicated – patients with mild COPD would only be treated with single therapy. The Panel thus did not consider that the advertisement promoted Trelegy for use in all COPD patients, including those with mild disease, as alleged. In the Panel's view, the claim was not inconsistent with the particulars listed in the Trelegy Ellipta SPC and no breach of Clause 3.2 was ruled. The Panel did not consider that the claim was misleading or that it could not be substantiated and so ruled no breach of Clauses 7.2 and 7.4. Given the circumstances, the Panel did not consider that high standards had not been maintained and ruled no breach of Clause 9.1. The Panel also ruled no breach of Clause 2.

2 Claim 'Trelegy Ellipta provides your patients with superior improvements in lung function and health-related quality of life, and reduction in annual rate of exacerbations vs. Symbicort Turbohaler at 24 weeks'

This claim was referenced to the Trelegy SPC and to Lipson *et al* (2017) and Lipson *et al* (2018).

COMPLAINT

The complainant noted that Symbicort Turbohaler was available in a range of different strengths and that the claim did not make clear which strength of Symbicort Turbohaler, the improvements were shown against within the clinical trial. The clinical trial referenced to the claim was only vs one strength of Symbicort Turbohaler so the evidence base was very specific but the claim was much broader. The complainant alleged breaches of Clauses 7.2, 7.3, 7.4, 9.1 and 2.

RESPONSE

GlaxoSmithKline strongly challenged the complainant's assertion because:

1 The claim was supported by a clearly referenced randomized, double-blind, double-dummy study, which compared 24 weeks of once-daily triple therapy (Trelegy Ellipta) with twice-daily ICS/LABA therapy (budesonide/ formoterol 400mcg/12mg; Symbicort Turbohaler) – the only licensed delivered dose as part of the overall posology and method of administration. Moreover, readers could refer to the study for more details if desired.

2 There were two licensed presentations of Symbicort Turbohaler (budesonide [BUD]/formoterol [FOR]) for the treatment of COPD:

a) Symbicort Turbohaler 400 mcg/12 mcg 1 inhalation twice daily
   i) this was the comparator in the head-to-head study

b) Symbicort Turbohaler 200 mcg/6 mcg 2 inhalations twice daily
   i) same equivalent dose of 400 mcg/12 mcg.

GlaxoSmithKline stated that, in its view, health professionals with experience in managing COPD would be aware that patients must achieve an inhaled delivered dose of 400mcg BUD/12mcg FOR, twice daily ie there was only one (equivalent) delivered dose indicated for COPD patients. It was common practice to refer to the 400/12 dose of Symbicort Turbohaler in COPD guidelines, as exemplified by the All Wales COPD Management and Prescribing Guideline. Moreover, the required delivered dose of 400mcg BUD/12mcg FOR (twice daily) was reflected in formulary references such as the British National Formulary (BNF) and Monthly Index of Medical Specialities (MIMS).

GlaxoSmithKline further noted that health professionals with experience in managing respiratory diseases, readily acknowledged that the lowest dose of Symbicort Turbohaler (100mcg/6mcg) was only indicated for the treatment of asthma and would not be an appropriate comparator in a COPD study.

GlaxoSmithKline thus maintained that the comparison was accurate, fair and balanced and not misleading; the company denied breaches of Clauses 7.2 or 7.3. The claim was substantiated by citing a robust clinical study, published in a high impact peer-reviewed journal (Lipson *et al*) and therefore not in breach of Clause 7.4.

GlaxoSmithKline submitted that it had maintained high standards and had not brought the industry into disrepute based on the claim and was therefore not in breach of Clauses 9.1 or 2.

PANEL RULING

The Panel noted that the advertisement was very clearly about the treatment of COPD and in that regard it noted GlaxoSmithKline's submission that only one dose of Symbicort Turbohaler was licensed for such use ie 400mcg budesonide/12mcg formoterol twice daily which could be delivered as one or two inhalations twice daily depending on which one of two presentations of Symbicort was prescribed (the third presentation and lowest dose of Symbicort Turbohaler (100mcg/6mcg) was only indicated for the treatment of asthma). As noted above, the Panel considered that health professionals would be familiar with the widely accepted and well-defined stepwise guidelines which existed for the treatment of COPD and be familiar with the place of Symbicort within those guidelines. The Panel noted that the clinical trial to which the claim at issue was referenced used one inhalation of Symbicort twice a day rather than the lower dose Turbohaler at two inhalations twice daily; in that regard the use of just one inhalation at a time of Symbicort would thus be the same as Trelegy which had a licensed dose of one inhalation, albeit once daily. Overall the Panel considered whilst it might have been helpful to include details of the administration of Symbicort, it did not consider that the claim at issue which compared the two medicines was broader than the evidence as alleged and ruled no breach of Clauses 7.2 and 7.3. The claim was substantiated by the clinical trial and therefore no breach of Clause 7.4 was ruled. Given the circumstances the Panel did not consider that high standards had not been maintained and ruled no breach of Clause 9.1. The Panel also ruled no breach of Clause 2.

B Advertisement for promotional webinar

The advertisement at issue was on the gskpro website and the webinar was entitled 'Single Inhaler Triple Therapy in COPD; Evidence to Action'. The advertisement included a brief summary of the webinar.

COMPLAINT

The complainant alleged that the advertisement for the webinar implied that Trelegy was licensed for all COPD patients. The complainant considered that statements such as 'The role of Single Inhaler Triple Therapy in the treatment of symptomatic COPD patients at risk of an exacerbation' were misleading to busy health professionals considering that the actual licensed indication for Trelegy was not clarified anywhere on the page. The complainant alleged breaches of Clauses 3.2, 9.1 and 2 as Trelegy could only be used in a particular cohort of patients as per the marketing authorisation.

RESPONSE

GlaxoSmithKline noted that the complainant had referred to material on a promotional website which advertised a webinar scheduled for 26 May 2021; the complaint had not referred to the webinar itself which was subject to a separate certification within GlaxoSmithKline. GlaxoSmithKline noted the title of the webinar and submitted that from the summary text, it was clear that a panel of expert respiratory physicians would be discussing the appropriate use (or positioning) of triple therapy to manage COPD.

The webinar advertisement was certified for promotional use before it was posted on the GlaxoSmithKline UK website. Online access to the advertisement was via the GlaxoSmithKline UK homepage for UK health professionals by selecting 'Webinars and Events' from the navigation menu. An email invitation with a direct link to the webpage was also sent to health professionals with a registered interest. The advertisement was intended only to be accessed by UK health professionals who had to click on 'I'm a UK healthcare professional' to access the webpage.

GlaxoSmithKline refuted the complainant's allegation that the wording 'The role of Single Inhaler Triple Therapy in COPD; Evidence to Action' could imply that triple therapy (and Trelegy Ellipta) was licensed for 'all COPD patients'. The company stated that there had been no breach of Clause 3.2 because:

1 The title did not imply that Trelegy Ellipta was licensed to treat all COPD patients, irrespective of disease severity. The title correctly outlined what would be discussed in the webinar – it made no reference directly or indirectly to Trelegy.

2 Trelegy Ellipta was referred to within the context of the management of 'symptomatic COPD patients at risk of an exacerbation'. As explained in point A1 above, following the stepwise use of single and combination inhaled therapies, that was the appropriate population for triple therapy and was not inconsistent with the licensed indication or the particulars listed in the Trelegy SPC.

3 Prescribing information of Trelegy Ellipta and other relevant COPD inhaled medicines were available for download via a single click link on the webinar advertisement, which clearly stated the indication for use of Trelegy Ellipta. The link was located in a prominent, easy to access part of the webpage.

GlaxoSmithKline noted that the supplementary information to Clause 3.2 stated that the promotion of indications not covered by the marketing authorisation for a medicine was

prohibited by that clause. As demonstrated above, this was not the case. The webinar advertisement did not imply or promote Trelegy Ellipta for all COPD patients.

In accordance with GlaxoSmithKline policies and to ensure high standards of Code compliance were maintained, the post was reviewed prior to publication by a registered physician who was an experienced ABPI signatory. GlaxoSmithKline denied a breach of Clauses 3.2, 9.1 and 2.

PANEL RULING

The Panel noted that the indication for Trelegy was not included on the material advertising the webinar. However, the webpage referred to 'Single Inhaler Triple Therapy in COPD' in the heading with a reference to the evidence base for Trelegy in the first paragraph. At each citation of the brand name, the three constituent components of Trelegy were stated and so it was clear that Trelegy was a single inhaler triple therapy. The second paragraph of the material referred to the role of single inhaler triple therapy in the treatment of symptomatic COPD patients at risk of an exacerbation and the summary of the webinar ended with a statement that webinar attendees could expect 'practical and informative advice on the treatment options for symptomatic COPD patients at risk of an exacerbation'. The Panel thus did not consider that the material implied that Trelegy could be used for any patient with COPD. In addition to the material before them, the Panel considered that health professionals would be well aware of the stepwise approach to therapy and would know that triple therapy was for use in patients who were uncontrolled on dual therapy. The Panel thus considered that it was made clear that Trelegy was a triple therapy for treating certain COPD patients and not all COPD patients as alleged. The Panel did not consider that the material was inconsistent with the particulars listed in the Trelegy SPC. The Panel ruled no breach of Clause 3.2 of the Code as alleged and consequently no breach of Clauses 9.1 and 2 of the Code.

Complaint received **14 June 2021**

Case completed **3 August 2021**