NO BREACH OF THE CODE

CASE AUTH/3714/11/22

COMPLAINANT v GLAXOSMITHKLINE

Concerns about claims for Trelegy on GlaxoSmithKline's website

CASE SUMMARY

This case was in relation to the claim that Trelegy was 'A simple choice. One inhaler, easy to use and quick to teach'. made on the GlaxoSmithKline UK Limited's website for health professionals.
The Panel noted that the claim at issue was made up of several elements and, in its view, the allegations set out by the complainant in relation to the overall claim were based on its concerns regarding each of the separate elements of the claim. GlaxoSmithKline had broken down each element in its response and the Panel therefore considered each element in turn and made its rulings in this regard.

The Panel ruled no breach of the following Clauses of the 2021 Code because:

- **whilst it had some concerns regarding use of the claim 'easy to use', based on the complainant's narrow allegation that the device was not easy to use because of the number of steps for correct use, elderly patients with dexterity challenges would find opening the cover a challenge, and it was not always possible for elderly individuals with hearing challenges to listen for a click, it did not consider that the complainant had established that, within the context of the entire claim and the webpage which included details of the critical errors for Ellipta versus the comparator devices from van der Palen *et al*, 'easy to use' was misleading or incapable of substantiation as alleged.**
- **based on the complainant's narrow allegation that the Trelegy Ellipta was not 'quick to teach' considering the number of steps required, it did not consider that the complainant had established that, within the context of the entire claim and the webpage that referring to the inhaler as 'quick to teach' was misleading as alleged.**
- **it did not consider that the claim 'A simple choice' was misleading because it did not make any reference to why the inhaler was a simple choice as alleged.**
- **it did not consider that the complainant had established that referring to Trelegy Ellipta as 'A simple choice' within the context of the entire claim and webpage was misleading or that it could not be substantiated because it contained lactose and had a number of common side-effects. In the Panel's view, it was clear that reference to 'a simple choice' was in relation to the device and its dosing.**

No Breach of Clause 6.1	**Requirement that claims/information/comparisons must not be misleading**
No Breach of Clause 6.2	**Requirement that claims/information/comparisons must be capable of substantiation**
No Breach of Clause 5.1	**Requirement to maintain high standards at all times**

No Breach of Clause 2	Requirement that activities or materials must not bring discredit upon, or reduce confidence in, the pharmaceutical industry

This summary is not intended to be read in isolation.
For full details, please see the full case report below.

FULL CASE REPORT

An anonymous, contactable complainant, who described themselves as a health professional, complained that a claim about Trelegy made on the GlaxoSmithKline UK Limited's website for health professionals (PM-GB-FVU-WCNT- 200008 (V4.0) was misleading and could not be substantiated.

COMPLAINT

The complainant noted that on the website Trelegy was claimed to be a simple choice, easy to use and quick to teach and alleged that the claim could not be substantiated as the inhaler was not easy to use and required a number of steps for effective dose delivery. Not all patients would find it easy to use the inhaler considering elderly patients had challenges with dexterity and would find opening the cover of Trelegy a challenge. Patients would have to listen for a click which was not always possible for elderly individuals with hearing challenges. As there were a number of steps for correct use, the inhaler was not easy to use for patients especially instructions around inhaling from the inhaler. The choice of appropriate inhaler was dependent on patient preference and considering lactose was an excipient within the Trelegy inhaler, not all patients would want the inhaler if there was lactose intolerance reflecting that Trelegy was not a simple choice. The inhaler was not quick to teach considering the number of different steps that were required which would cause extra time in coaching inhaler technique to new patients and rechecking the technique at the same time. The claim was misleading and did not make any reference to why the inhaler was a simple choice considering the number of decisions that were required in choosing an inhaler for a patient. Trelegy had a number of common side effects which would cause the choice to use to be complex and not simple. The complainant alleged breaches of Clauses 6.1, 6.2 and 2.

When writing to GlaxoSmithKline, the Authority asked it to consider the requirements of Clauses 6.1, 6.2 and 2 of the 2021 Code as cited by the complainant and, in addition, Clause 5.1.

RESPONSE

GlaxoSmithKline explained that it was committed to following both the letter and the spirit of the ABPI Code and all other relevant regulations.

The anonymous complainant alleged that the claim that Trelegy was '*a simple choice, easy to use and quick to teach*' on the webpage in question (PM-GB-FVU-WCNT-200008 (V4.0)) could not be substantiated and was misleading. The complainant alleged breaches of Clauses 2, 6.1 and 6.2. The Authority also asked GlaxoSmithKline to consider Clause 5.1.

GlaxoSmithKline submitted that it had complied with the requirements of the Code and denied breaches of the cited clauses, and the reasons were detailed below.

GlaxoSmithKline stated that Trelegy (fluticasone furoate/vilanterol trifenatate/umeclidinium bromide) was indicated as a maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who were not adequately treated by a combination of an inhaled corticosteroid (ICS) and a long-acting β2-agonist (LABA) or a combination of a long-acting β2-agonist and a long-acting muscarinic antagonist (LAMA). Trelegy was delivered through the Ellipta dry powder inhaler which was the only available device for the delivery of Trelegy.

The claim in question was located on the 'Dosing and Device' page of the Trelegy Ellipta promotional website intended for health professionals. This page focussed on the Ellipta inhaler device, whereas other pages of the website focussed on clinical and safety data for the Trelegy medicinal product.

GlaxoSmithKline submitted that the overall claim in the heading of the 'Dosing and Device' webpage was '***A simple choice. One inhaler, easy to use and quick to teach***'. This claim was adjacent to an image of the Trelegy Ellipta inhaler device. The claim was referenced to the clinical paper, van der Palen J *et al*. NPJ Prim Care Med 2016; 26:16079. This was a multicentre, single visit, randomised, open-label, crossover study in patients naïve to the Ellipta device versus five comparator inhaler devices (Diskus/Accuhaler, metered dose inhalers (MDIs), Turbuhaler, Handihaler and Breezhaler). 567 COPD patients were each assessed in a crossover fashion using Ellipta and one of the other comparator devices.

A primary endpoint of the study was to assess the proportion of COPD patients making critical errors when using the Ellipta inhaler versus these other commonly used inhaler devices. Critical errors were defined as those likely to result in the inhalation of significantly reduced, minimal or no medication, as assessed by a trained investigator. The study also aimed to assess the teaching time required from a professional and patient preference for the inhalers.

GlaxoSmithKline submitted that as the complainant had made specific allegations about different components of the overall claim, for the purposes of this response, GlaxoSmithKline considered each component of the claim below.

'Easy to use'

GlaxoSmithKline noted that the complainant alleged that the 'claim could not be substantiated as the inhaler was not easy to use and required a number of steps for effective dose delivery. Not all patients would find it easy to use the inhaler considering elderly patients had challenges with dexterity and would find opening the cover of Trelegy a challenge. Patients would have to listen for a click which was not always possible for elderly individuals with hearing challenges. As there were a number of steps for correct use, the inhaler was not easy to use for patients especially instructions around inhaling from the inhaler.'

GlaxoSmithKline explained that in the van der Palen (2016) study, after reading the patient information leaflet (PIL), significantly fewer COPD patients made any critical errors with the Ellipta inhaler device compared with Diskus/Accuhaler (5% vs 44%), MDI (13% vs 60%), Turbuhaler (8% vs 44%), Handihaler (14% vs 48%) or Breezhaler (13% vs 46%); $p<0.001$ for all comparisons. These primary endpoint results were presented in a graphical format on the

webpage in question. While the 'easy to use' component of the claim referred to Ellipta specifically and did not make or imply any comparison with other inhaler devices, the Ellipta results from this study are relevant to substantiating the claim, as it showed that only between 5-14% of COPD patients using the Ellipta device made any critical errors which would have been likely to result in the inhalation of significantly reduced, minimal or no medication.

Furthermore, the study showed that after reading the PIL, most patients made no errors using the Ellipta inhaler (57–70% across the five sub studies), thus not requiring instruction from the nurse. To reiterate, the claim 'easy to use' as presented on the webpage referred to Ellipta and no comparison was implied with other devices, but the context from the source data in the van der Palen (2016) study was that the majority of patients did require nurse instruction for the other inhalers (65% Diskus/Accuhaler, 85% MDI, 71% Turbuhaler, 62% Handihaler and 56% Breezhaler). This context strengthens the case for describing Ellipta as 'easy to use'.

Study participants also completed an ease-of-use questionnaire. This showed that a larger proportion of patients in each sub-study rated the Ellipta inhaler very easy or easy to use compared with Diskus/Accuhaler (97% vs 60%), MDI (92% vs 44%), Turbuhaler (96% vs 55%), Handihaler (98% vs 38%) or Breezhaler (94% vs 55%). Larger proportions of patients responded that the Ellipta inhaler was very easy to use regarding each of the following characteristics – the dose counter, learning how to use the inhaler, handling the inhaler, preparing the inhaler for use and holding the inhaler while using it, compared with the proportions responding similarly for Diskus/Accuhaler, MDI, Turbuhaler, Handihaler and Breezhaler. Again, while no comparison with other devices was implied in the claim, this data indicated that between 92-98% of COPD patients felt that the Ellipta device was very easy or easy to use.

GlaxoSmithKline further noted that the complainant alleged that 'the inhaler was not easy to use and required a number of steps for effective dose delivery' and that 'as there were a number of steps for correct use, the inhaler was not easy to use for patients especially instructions around inhaling from the inhaler'. GlaxoSmithKline noted that all inhaler devices required a sequence of steps to be correctly performed by the user or carer in order to ensure delivery of the medicine. As well as the ease-of-use questionnaire detailed above, COPD patients in the van der Palen (2016) study completed preference questionnaires which showed the majority of patients preferred Ellipta vs each of the other five comparator inhalers for the criteria 'number of steps for correct use' ($p<0.001$). In contrast, the complainant had not shown any evidence to support their allegation that the number of steps required impacted negatively on the patients' perception of ease of use. All required steps were clearly laid out in the patient information leaflet (PIL).

The complainant alleged that 'elderly patients had challenges with dexterity and would find opening the cover of Trelegy a challenge' and therefore Trelegy Ellipta was not easy to use. The van der Palen (2016) patient preference questionnaire mentioned above also showed for the criteria 'ease of opening' that the majority of patients preferred Ellipta versus each of the five comparator inhalers ($p<0.001$). The mean age of the COPD population in this study was 67.3 years with a standard deviation of 8.3 years. Furthermore, the summary of product characteristics (SPC) of Trelegy Ellipta did not mention any special considerations for the elderly, in particular noting that no dose adjustment was required in elderly patients who were defined as aged 65 years or older. No upper age limit was mentioned in the SPC or PIL of Trelegy Ellipta. The complainant had provided no evidence to support their allegation that

elderly people would find opening the cover of the device to be a challenge impacting on ease of use.

The complainant alleged that 'patients would have to listen for a click which was not always possible for elderly individuals with hearing challenges'. The Trelegy Ellipta PIL stated in the step-by-step instructions section: 'Slide the cover down until you hear a "click." Your medicine is now ready to be inhaled. The dose counter counts down by 1 to confirm. If the dose counter does not count down as you hear the "click", the inhaler will not deliver medicine'. There was thus a visual dose counter indicator that the device was primed for use as well as the audible click. Therefore, if any patients were to have difficulties in hearing the click, there was an alternative means for them to confirm that the device was ready to use. Furthermore, the SPC and PIL of Trelegy Ellipta did not make mention of any special considerations being required for patients with hearing difficulties. GlaxoSmithKline had not made any specific claims around ease of use in patients with hearing difficulties, and the complainant had not provided any evidence that these patients would have difficulty using the device.

While not specifically referenced on the webpage in question, a recent paper Siler TM *et al*. 2022;17(8): e0273170, which was a pooled analysis of four Ellipta studies (including the aforementioned van der Palen (2016) paper) showed for an intention to treat population of 1232 patients (mean age 66.2 years): 'For the primary endpoint, 80.1% (n = 975/1217) of patients demonstrated correct use at study end (95% confidence interval [CI]: 77.8%–82.3%). For the secondary endpoint, 95.7% (n = 797/833) of patients rated placebo Ellipta dry powder inhaler use "easy"/"very easy" at study end (95% CI: 94.1%–97.0%). Correct use and "easy"/"very easy" user ratings remained high across younger (40–64 years) and older (≥65 years) age groups'. This study added to the broad body of evidence by demonstrating that across age groups, including 65 years and above, a large majority of COPD patients used the Ellipta device correctly and rated it 'easy' or 'very easy' to use.

GlaxoSmithKline referred the Panel to a previous Case AUTH/2701/2/14 . This case concerned a complaint about an advertisement for Relvar Ellipta. While the medicinal product was different from Trelegy, the Ellipta device was the same. The complaint was about a claim that Relvar Ellipta was 'delivered in a straightforward device'. The Panel accepted GlaxoSmithKline's position that the claim was not misleading and was capable of substantiation, and no breach was ruled. The claim in question was substantiated by a study which included a health professional's assessment of the COPD patients' correct usage, and a patient questionnaire on ease of use. The Panel considered this study and the usage steps described in the Relvar Ellipta PIL to reach its conclusion that the claim was not in breach of the Code. GlaxoSmithKline believed that the meaning of the claim 'delivered in a straightforward device' for Relvar Ellipta was like the current claim 'easy to use' for Trelegy Ellipta. GlaxoSmithKline asked the Panel to consider that the current claim also was based on a study where a health professional assessed COPD patients' correct usage of the Ellipta device, and the patients completed a questionnaire on ease of use, and the steps for usage were described in the Trelegy Ellipta PIL.

Taking the above information together, GlaxoSmithKline submitted that the 'easy to use' component of the claim was accurate, fair, objective, unambiguous and not misleading, based on an up-to-date evaluation of all the evidence. GlaxoSmithKline submitted that the claim met the requirements of Clause 6.1. The claim was capable of substantiation, and met the requirements of Clause 6.2.

'Quick to teach'

GlaxoSmithKline noted that the complainant alleged that 'the inhaler was not quick to teach considering the number of different steps that were required which would cause extra time in coaching inhaler technique to new patients and rechecking the technique at same time'.

This claim was also referenced to the van der Palen (2016) study which GlaxoSmithKline detailed above. This study measured time taken to correctly use the Ellipta device versus the other five devices. Three timepoints were measured: T1 was the time from when the patient started to read the PIL until using the inhaler (with no nurse support). T2 was the time from when the nurse started to demonstrate/instruct device use until up to three given instructions and demonstration of inhaler use. T3 was the sum of T1+T2 giving the time from when the patient started to read the PIL until up to three instructions and demonstration of inhaler use. Where no nurse support was required, T2 was recorded as 0.

For all comparisons of Ellipta versus the other five inhalers, 'median T1 could only be determined for the Ellipta inhaler because for the other inhalers, more than half of the patients could not perform correct use after reading the PIL only'. Comparisons could only be made at the T3 timepoint. The results were statistically significant for all comparisons in favour of Ellipta. The paper stated that 'median T3 was shorter for patients using the Ellipta inhaler compared with those using Diskus/Accuhaler (2.75 vs 3.93 min), MDI (3.79 vs 6.30 min), Turbuhaler (2.87 vs 7.80 min), Handihaler (4.32 vs 8.50 min) and Breezhaler (3.15 vs 8.44 min); all $p<0.001$'. While there was no comparison with other devices implied in the 'quick to teach' claim, this data showed that the median time taken to teach usage of Ellipta ranged from 2.75 - 4.32 minutes across the sub-studies, with over half of patients being competent by just reading the PIL without needing nurse instruction. This justified the use of the claim 'quick to teach' for Ellipta.

GlaxoSmithKline submitted that the 'quick to teach' component of the claim was accurate, fair, objective, unambiguous and not misleading. GlaxoSmithKline considered that the claim met the requirements of Clause 6.1. GlaxoSmithKline submitted that the claim was capable of substantiation, and met the requirements of Clause 6.2.

'A simple choice'

The complainant alleged that 'the choice of appropriate inhaler was dependent on patient preference and considering lactose was an excipient within the Trelegy inhaler, not all patients would want the inhaler if there was lactose intolerance reflecting that Trelegy was not a simple choice'. The complainant further alleged that 'the claim was misleading and did not make any reference to why the inhaler was a simple choice considering the number of decisions that were required in choosing an inhaler for a patient. Trelegy had a number of common side effects which would cause the choice to use to be complex and not simple'. GlaxoSmithKline had used the claim 'a simple choice' as the first component of the overall claim ***'A simple choice. One inhaler, easy to use and quick to teach'*** which was the headline of the webpage in question, the entire claim was intended to be read together. The latter sentence 'One inhaler, easy to use and quick to teach' explained why Trelegy Ellipta could be regarded as 'a simple choice'

It should be noted that GlaxoSmithKline had been deliberate in its use of the indefinite article '**A** simple choice', in acknowledgement that other choices are available for the treatment of COPD, although no specific alternatives or comparisons are mentioned in the headline.

An infographic further down the page demonstrated that there were many possible combinations of multiple inhaler triple therapy (comprising an ICS/LABA inhaler and separate LAMA inhaler) for COPD. These combinations might result in the patient needing to use different inhalers with different usage techniques and different dosing regimens. Trelegy Ellipta was positioned in the graphic as an alternative single inhaler triple therapy combining the three classes of medicinal product (ICS/LABA/LAMA). This formed the basis of the 'one inhaler' component of the headline claim which was one of the justifications for Trelegy Ellipta being 'a simple choice'.

Another section of the same page stated that 'the recommended and maximum dose is one inhalation of Trelegy Ellipta 92/55/22 micrograms once daily, at the same time each day' which was consistent with the Trelegy Ellipta SPC. Again, this provided further justification for the description of the product as 'a simple choice' in the headline claim.

Although the webpage in question did not mention lactose, the complainant alleged that 'the choice of appropriate inhaler was dependent on patient preference and considering lactose was an excipient within the Trelegy inhaler, not all patients would want the inhaler if there was lactose intolerance reflecting that Trelegy was not a simple choice'. The webpage in question was directed towards health professionals, not patients. The complainant had not provided any evidence that the presence of lactose as an excipient in Trelegy Ellipta would have a bearing on the health professional's understanding of the claim component 'a simple choice'. GlaxoSmithKline submitted that at no point had it implied that Trelegy Ellipta should be used in patients with lactose intolerance. The SPC for Trelegy Ellipta listed lactose as an excipient and stated that 'Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not use this medicinal product'. This information was also stated within the Trelegy Ellipta prescribing information (Enclosure 7) which could be found by following a single click link from the webpage. Furthermore, the PIL stated 'Trelegy Ellipta contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before using this medicine'. There was thus adequate information available for health professionals and patients to make the decision not to take the product in case of lactose intolerance.

The complainant alleged that 'Trelegy had a number of common side effects which would cause the choice to use to be complex and not simple'. GlaxoSmithKline took patient safety very seriously. The website in question had a very clear menu option 'Safety Data' in the top right. This menu option was designed to stay visible at the top of the page even when the user scrolled down. Clicking this prominent menu item took the health professional to a page where all common and other important side-effects of Trelegy Ellipta were listed. The Prescribing Information also listed this information and was accessible by a single click link. Given the similarity in adverse event profiles between the different triple therapy options available on the market for COPD, the complainant had not provided any evidence that this factor would cause the choice of inhaler to be complex as alleged, as the information about adverse events was readily available.

For the reasons given above, GlaxoSmithKline's position was that the 'a simple choice' component of the claim was accurate, fair, objective, unambiguous and not misleading. GlaxoSmithKline submitted that the claim met the requirements of Clause 6.1and was capable of substantiation, and met the requirements of Clause 6.2.

Clause 5.1

GlaxoSmithKline submitted that for the reasons given above, as it denied the complainant's alleged breaches, GlaxoSmithKline considered that high standards had been maintained and therefore it denied a breach of Clause 5.1.

Clause 2

GlaxoSmithKline submitted that for the reasons given above, as it denied all other alleged breaches, GlaxoSmithKline considered that it had not brought discredit upon, or reduced confidence in, the pharmaceutical industry and therefore denied a breach of Clause 2.

Conclusion

In closing, GlaxoSmithKline's position was that the claims on the website in question regarding 'a simple choice', 'easy to use', and 'quick to teach' were consistent with the requirements of Clauses 6.1 and 6.2 of the 2021 Code, and it denied breaches of those Clauses. Consequently, GlaxoSmithKline considered that it had maintained high standards and had not brought discredit upon or reduced confidence in the industry and it denied breaches of Clauses 5.1 and 2.

PANEL RULING

The Panel noted GlaxoSmithKline's submission that the claim ***'A simple choice. One inhaler, easy to use and quick to teach'*** was the heading of the 'Dosing and Device' webpage of the Trelegy Ellipta promotional website. GlaxoSmithKline stated that it had been deliberate in its use of the indefinite article '**A** simple choice', in acknowledgement that other choices were available for the treatment of COPD, although no specific alternatives or comparisons were mentioned in the headline. The claim was referenced to Van der Palen J *et al* which was a multicentre, single visit, randomised, open-label, crossover study in patients naïve to the Ellipta device versus five comparator inhaler devices (Diskus/Accuhaler, metered dose inhalers (MDIs), Turbuhaler, Handihaler and Breezhaler). 567 COPD patients, with and without asthma were each assessed in a crossover fashion using Ellipta and one of the other comparator devices. Below the claim alongside the image of the inhaler device, the recommended and maximum dose of Trelegy was given along with instructions if a dose was missed. This was followed by the claim 'Don't settle for a MDI, when you can give them the preferred, easy-to-use Ellipta device' which was also referenced to Van der Palen *et al* (2016) and a table comparing the critical errors of commonly used devices versus Ellipta which was adapted from Van der Palen *et al* (2016). Thus, in the Panel's view, the claim appeared to imply that Trelegy was a simple choice as it was one inhaler that was easy to use and quick to teach compared to the other inhaler choices.

A primary endpoint of Van der Palen *et al* (2016) was to assess the proportion of COPD patients making critical errors when using the Ellipta inhaler versus these other commonly used inhaler devices. Critical errors were defined as those likely to result in the inhalation of significantly reduced, minimal or no medication, as assessed by a trained investigator. The study also aimed to assess the teaching time required from a professional, and patient preference for the inhalers. The sequence of using the two inhaler devices within each substudy were randomised. After randomisation, patients were asked to read the Patient Information Leaflet 'PIL' of the first device and then were asked to perform inhaler use. Overall, errors made by the patient while using the first inhaler were recorded by a trained respiratory nurse. If the patient

made any errors in inhaler use after reading the PIL, the nurse demonstrated the correct use of the inhaler to the patient, and the patient was asked to perform the inhaler use again. If the patient continued to make errors in inhaler use, the nurse demonstrated the process again up to a maximum of three times. After completing the process with the first inhaler, the same procedures were followed for the second inhaler. The number of instructions (maximum three times) from the nurse that were needed to demonstrate correct inhalation technique was recorded. After completing the demonstration procedures of the two inhalers, the nurse asked the participant questions using two questionnaires; the ease-of-use questionnaire followed by the preference questionnaire.

The Panel noted that the claim at issue was made up of several elements and, in its view, the allegations set out by the complainant in relation to the overall claim were based on its concerns regarding each of the separate elements of the claim. GlaxoSmithKline had broken down each element in its response and the Panel therefore considered each element in turn and made its rulings in this regard.

'Easy to use'

The Panel noted that the complainant alleged that the claim could not be substantiated as the inhaler was not 'easy to use'. In this regard, the complainant alleged that 'not all patients would find it easy to use the inhaler considering elderly patients had challenges with dexterity and would find opening the cover a challenge and patients would have to listen for a click which was not always possible for elderly individuals with hearing challenges'. The complainant further alleged that 'as there were a number of steps for correct use, the inhaler was not easy to use for patients especially instructions around inhaling from the inhaler'.

The Panel noted GlaxoSmithKline's submission that all inhaler devices required a sequence of steps to be correctly performed by the user or carer in order to ensure delivery of the medicine.

The Panel further noted GlaxoSmithKline's submission that while the 'easy to use' component of the claim referred to Ellipta specifically and did not make or imply any comparison with other inhaler devices, the Ellipta results from the van der Palen study were relevant to substantiate the claim, as it showed that only between 5-14% of COPD patients using the Ellipta device made any critical errors which would have been likely to result in the inhalation of significantly reduced, minimal or no medication. The Panel noted GlaxoSmithKline's further submission that the study showed that after reading the PIL, 57–70% patients across the five sub studies made no errors using the Ellipta inhaler, thus not requiring instruction from the nurse and the majority of patients required nurse instruction for the other inhalers. The Panel noted, therefore, that this meant that 30-43% of patients across the five sub studies did make errors using the Ellipta inhaler after reading the PIL and 5-14% made critical errors. The Panel further noted that according to van der Palen, patients who had a critical error with both devices or who had no critical errors with both devices did not provide any information about the superiority of either device and only those patients who had critical error(s) in one device but not the other device were counted in the comparison.

The Panel noted GlaxoSmithKline's submission that study participants in van der Palen also completed an ease-of-use questionnaire which showed that a larger proportion of patients responded that the Ellipta inhaler was very easy to use regarding each of the following characteristics – the dose counter, learning how to use the inhaler, handling the inhaler, preparing the inhaler for use and holding the inhaler while using it, **compared** with the

proportions responding similarly for the comparators. Between 92-98% of COPD patients felt that the Ellipta device was very easy or easy to use compared to the comparators.

The Panel, noting the above, queried if the Ellipta device was easier to use than the other inhalers as opposed to being 'easy to use'.

The Panel further noted GlaxoSmithKline's submission that as well as the ease-of-use questionnaire detailed above, COPD patients in the van der Palen *et al* (2016) study completed preference questionnaires which showed the majority of patients preferred Ellipta vs each of the other five comparator inhalers for the criteria 'number of steps for correct use' ($p<0.001$). The Panel noted GlaxoSmithKline's submission that the Van der Palen J *et.al* (2016) patient preference questionnaire showed for the criteria 'ease of opening' that the majority of patients preferred Ellipta versus each of the five comparator inhalers ($p<0.001$). The mean age of the COPD population in this study was 67.3 years with a standard deviation of 8.3 years. The Panel further noted GlaxoSmithKline's submission that if any patients were to have difficulties in hearing the click, there was an alternative means for them to confirm that the device was ready to use; there was a visual dose counter indicator that the device was primed for use as well as the audible click.

The Panel noted GlaxoSmithKline's further submission that while not referenced on the webpage in question, a recent paper Siler TM *et al* which was a pooled analysis of four Ellipta studies (including the aforementioned van der Palen (2016) paper) showed for an intention to treat population of 1232 patients (mean age 66.2 years): 'For the primary endpoint, 80.1% (n = 975/1217) of patients demonstrated correct use at study end (95% confidence interval [CI]: 77.8%–82.3%). For the secondary endpoint, 95.7% (n = 797/833) of patients rated placebo Ellipta dry powder inhaler use "easy"/"very easy" at study end (95% CI: 94.1%– 97.0%). Correct use and "easy"/"very easy" user ratings remained high across younger (40–64 years) and older (≥65 years) age groups'. According to GlaxoSmithKline, this study added to the broad body of evidence by demonstrating that across age groups, including 65 years and above, a large majority of COPD patients used the Ellipta device correctly and rated it 'easy' or 'very easy' to use. The Panel noted that Siler *et al* stated that correct use and user ratings of 'easy' or 'very easy' of the placebo ELLIPTA DPI remained high with increasing age, including patients aged over 65 years. However, among the over 75 years age group, there was a slight trend towards a decrease in the proportion of patients demonstrating correct use of the placebo ELLIPTA DPI at study end and in the proportion finding its use 'very easy'. The Panel noted that according to Siler *et al*, notably, at study end, the study that enrolled patients who were naïve to the ELLIPTA inhaler showed an error rate of 30–43%, compared with an error rate of 3–24% among the three studies allowing prior but not recent use of the ELLIPTA inhaler. According to Siler *et al*, its limitations included that the possibility that the correct ease-of-use data in three of the studies were influenced by the patients' previous experience with the ELLIPTA inhaler which could not be discounted. However, while there were differences in correct use between each study, perception on ease-of-use appeared to be relatively unaffected. Furthermore, there were differences between studies in the number of times patients received correct use training, which could have introduced a possible source of inequity in instruction recall and potentially impacted on both correct use and perceived ease-of-use of the inhaler.

Noting its comments above, whilst the Panel had some concerns regarding use of the claim 'easy to use' it did not consider that the complainant had established that, within the context of the entire claim and the webpage which included details of the critical errors for Ellipta versus the comparator devices from van der Palen *et al*, 'easy to use' was misleading or incapable of

substantiation as alleged. Based on the complainant's narrow allegation that the device was not easy to use because of the number of steps for correct use, elderly patients with dexterity challenges would find opening the cover a challenge, and it was not always possible for elderly individuals with hearing challenges to listen for a click, the Panel ruled **no breach of Clauses 6.1 and 6.2**.

'Quick to teach'

The Panel noted that the complainant alleged that the inhaler was not 'quick to teach' considering the number of different steps that were required which would cause extra time in coaching inhaler technique to new patients and rechecking the technique at same time.

The Panel noted GlaxoSmithKline's submission that the claim 'quick to teach' was also referenced to van der Palen *et.al* (2016) which measured time taken to correctly use the Ellipta device versus the other five devices. Three timepoints were measured: T1 was the time from when the patient started to read the PIL until using the inhaler (with no nurse support). T2 was the time from when the nurse started to demonstrate/instruct device use until up to three given instructions and demonstration of inhaler use. T3 was the sum of T1+T2 giving the time from when the patient started to read the PIL until up to three instructions and demonstration of inhaler use. Where no nurse support was required, T2 was recorded as 0.

For all comparisons of Ellipta versus the other five inhalers, 'median T1 could only be determined for the Ellipta inhaler because for the other inhalers, more than half of the patients could not perform correct use after reading the PIL only'. Comparisons could only be made at the T3 timepoint. The results were statistically significant for all comparisons in favour of Ellipta. The 'median T3 was shorter for patients using the Ellipta inhaler compared with each of the five comparators, with a p value of all being $p<0.001$'. The median time taken to teach usage of Ellipta ranged from 2.75 - 4.32 minutes across the sub-studies, with over half of patients being competent by just reading the PIL without needing nurse instruction.

The Panel did not consider that the complainant had established that, within the context of the entire claim and the webpage that referring to the inhaler as 'quick to teach' was misleading as alleged. Based on the complainant's narrow allegation that the Trelegy Ellipta was not 'quick to teach' considering the number of steps required, the Panel ruled **no breach of Clauses 6.1 and 6.2**.

'A simple choice'

The Panel noted that the complainant alleged that 'the choice of appropriate inhaler was dependent on patient preference and considering lactose was an excipient within the Trelegy inhaler, not all patients would want the inhaler if there was lactose intolerance reflecting that Trelegy was not a simple choice'. The complainant further alleged that 'the claim was misleading and did not make any reference to why the inhaler was a simple choice considering the number of decisions that were required in choosing an inhaler for a patient. Further, Trelegy had a number of common side effects which would cause the choice to use to be complex and not simple.'

The Panel noted GlaxoSmithKline's submission that the claim 'a simple choice' was the first component of the overall claim 'A simple choice. One inhaler, easy to use and quick to teach' which was intended to be read together. According to GlaxoSmithKline, the latter sentence

'One inhaler, easy to use and quick to teach' explained why Trelegy Ellipta could be regarded as 'a simple choice'.

The Panel noted GlaxoSmithKline's submission that an infographic further down the webpage at issue demonstrated that there were many possible combinations of multiple inhaler triple therapy (comprising an ICS/LABA inhaler and separate LAMA inhaler) for COPD which might result in the patient needing to use different inhalers with different usage techniques and different dosing regimens. Trelegy Ellipta was positioned in the graphic as an alternative single inhaler triple therapy combining the three classes of medicinal product (ICS/LABA/LAMA). This formed the basis of the 'one inhaler' component of the headline claim. Another section of the same page stated that 'the recommended and maximum dose was one inhalation of Trelegy Ellipta 92/55/22 micrograms once daily, at the same time each day' which was consistent with the Trelegy Ellipta SPC. GlaxoSmithKline submitted that this provided further justification for the description of the product as 'a simple choice' in the headline claim. The Panel further noted the results of van der Palen *et al* in relation to the ease of use and the median time taken to teach usage of Ellipta versus the comparator inhalers. The Panel did not consider that the claim 'A simple choice' was misleading because it did not make any reference to why the inhaler was a simple choice as alleged and therefore **no breach of Clause 6.1** was ruled.

The Panel further noted GlaxoSmithKline's submission that although the webpage in question did not mention lactose, it was directed towards health professionals and the complainant had not provided any evidence that the presence of lactose as an excipient in Trelegy Ellipta would have a bearing on the health professional's understanding of the claim component 'a simple choice'. The Panel noted GlaxoSmithKline further submitted, among other things, that given the similarity in adverse event profiles between the different triple therapy options available on the market for COPD, the complainant had not provided any evidence that this factor would cause the choice of inhaler to be complex as alleged, as the information about adverse events was readily available.

The Panel did not consider that the complainant had established that referring to Trelegy Ellipta as 'a simple choice' within the context of the entire claim and webpage was misleading or that it could not be substantiated because it contained lactose and had a number of common side-effects. In the Panel's view, it was clear that reference to 'a simple choice' was in relation to the device and its dosing. The Panel therefore, based on the complainant's narrow allegation, ruled **no breach of Clauses 6.1 and 6.2**.

The Panel noted its comments and rulings of no breaches above and consequently ruled **no breach of Clauses 5.1 and 2**.

Complaint received **24 November 2022**

Case completed **24 October 2023**