**CASE/0257/08/24** *NO BREACH OF THE CODE*

# COMPLAINANT v GSK

## Alleged unlicensed promotion of Trelegy Ellipta in a COPD medicines optimisation toolkit

### CASE SUMMARY

**This case was in relation to a GSK COPD (chronic obstructive pulmonary disease) medicines optimisation toolkit. The complainant alleged that it promoted Trelegy Ellipta (fluticasone furoate, umeclidinium, vilanterol) for an unlicensed indication because the licence was specific to moving from dual inhaler use to triple therapy, and did not cover moving patients from multiple inhaler triple therapy to single inhaler triple therapy.**

**The outcome under the 2021 Code was:**

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|---|---|
| **No Breach of Clause 2** | **Requirement that activities or materials must not bring discredit upon, or reduce confidence in, the pharmaceutical industry** |
| **No Breach of Clause 5.1** | **Requirement to maintain high standards at all times** |
| **No Breach of Clause 11.2 (x2)** | **Requirement that a medicine must be promoted in accordance with the terms of its marketing authorisation and must not be inconsistent with the particulars listed in its summary of product characteristics** |

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

### FULL CASE REPORT

A complaint about GSK was received from an anonymous, contactable complainant who described themselves as a health professional. The complainant later became non-contactable.

### COMPLAINT

The complaint wording is reproduced below with some typographical errors corrected:

> "A GSK COPD medicines optimisation toolkit promotes Trelegy for off-label use. The toolkit job code and date of preparation are PM-GB-UCV-LBND-230006 | April 2024. Trelegy is licensed as maintenance treatment in those not adequately treated on ICS/LABA or LABA/LAMA. Thus the license for Trelegy is very specific to dual inhaler step up only. Trelegy does not have a license to step up those patients who are not adequately treated on multiple inhaler therapy. In the toolkit, there is a MITT optimisation page. The following is claimed on this page alongside an image of a Trelegy inhaler – 'Modelled data suggests that there are 175 Patients with COPD

prescribed multiple inhaler triple of quad+* therapy in an average 48,000 patient population (Average population in a PCN).** Optimising inadequately treated patients offers benefits for patients, the NHS and the environment.' There is a financial impact page which claims the following – 'There is an opportunity to optimise patients currently being treated with triple therapy in multiple inhalers or Quad+ to Single Inhaler Triple Therapy'. These claims on both the MITT optimisation and Financial impact pages of the tool actively promote a switch to Trelegy from those patients on multiple inhaler triple therapy. However this is outside the licenced indication as the licence does not cover a move to Trelegy from those patients not adequately treated on multiple inhaler triple therapy. If there was such a licence, then triple therapy inhalers on the market would have a step up from multiple inhalers for those patients not adequately treated incorporated within their licensed indications in the SPC and requested the regulators for such an approval. There were breaches of clause 11.2 (promotion of indications not covered by marketing authorisation), 5.1 and 2."

When writing to GSK, the PMCPA asked it to consider the requirements of Clauses 2, 5.1 and 11.2 of the 2021 Code.

**GSK'S RESPONSE**

The response from GSK is reproduced below with some typographical errors corrected:

"Thank you for your letter dated 8th August 2024 wherein you informed GSK that an anonymous complainant has alleged off-label promotion of Trelegy within a GSK COPD medicines optimisation toolkit (PM-GB-UCV-LBND-230006, approved April 2024). GSK take all complaints very seriously and is committed to following both the letter and the spirit of the ABPI Code of Practice and all other relevant regulations. GSK considers it noteworthy that this is the fourth anonymous allegation of an identical nature within an 8-week period, each alleging off-label promotion of Trelegy for patients on multiple inhaler triple therapies (Case AUTH/3922/6/24; Case AUTH/3923/6/24; Case/0257/08/24; Case/0266/08/24). GSK has submitted a rebuttal defending all cases, with evidence supportive of the promotion of Trelegy for patients not adequately treated on multiple inhaler triple therapy.

**COPD medicines optimisation toolkit (PM-GB-UCV-LBND-230006)**

The material at issue is a digital interactive pdf ('toolkit'), intended for use by UK HCPs, approved for promotional use in April 2024. The interactivity refers to functionality within the toolkit whereby users can navigate different sections using tabs, or access more detailed slides/clinical papers through embedded links within the text (e.g. studies FULFIL, IMPACT, INTREPID) or access prescribing information, GSK contact webpage and the MHRA yellow card reporting site.

The toolkit is hosted and can be downloaded from two GSK landing webpages. One landing page (PM-GB-RS-WCNT-230024) is designed to quantify downloads from GSK distributed emails, while the second, identical, landing webpage (PM-GB-RS-WCNT-230025) quantifies downloads from GSK approved third party emails/banners. The landing pages are part of [URL provided], however the main site has not been live since July 2023. HCPs can only access these landing pages, and hence the toolkit, by clicking on a direct link in a GSK or third-party email/banner. Outside of these direct links, the landing pages can only be accessed if a person has the full URL address. It

cannot be found via a google search. Access to these landing pages requires completion of a verification step in a pop-up screen. Viewers must select if they are a UK HCP/person making decisions relevant to UK healthcare provision or a member of the UK public, whereby they are redirected. The landing pages are headed with the GSK logo, the intended audience (For UK Healthcare Professionals only) and the promotional nature of the content.

Prior to accessing or downloading the content within the toolkit, a further self-verification step, using an additional pop-up, is required. It specifies the need for name, email, job title and professional number (GMC, NMC, GPhC) and identifies only email addresses with the domain name 'nhs.net'.

The toolkit is intended to support HCPs who have a role in the optimisation of COPD medicines across a primary care network (PCN). These HCPs could be PCN pharmacists, Clinical Directors (often General Practitioners), Prescribing Advisors (Pharmacists) or Medicine Optimisations Managers (Pharmacists).

The homepage cites three opportunities for optimisation within COPD:

- Patients on Triple therapy (ICS/LABA + LAMA) or Quad+*, in separate inhalers.

**Quad+ is defined as COPD patients prescribed four or more inhalers.*

- Patients on LAMA or LABA who may benefit from stepping up to LAMA/LABA maintenance treatment.
- Newly diagnosed patients who may benefit from LAMA/LABA as initial maintenance treatment.

Aligned to these opportunities, the toolkit aims to provide relevant information on GSK's single inhaler triple therapy Trelegy and GSK's dual bronchodilator inhaler Anoro. Trelegy is a triple therapy combination of the inhaled corticosteroid fluticasone furoate, the long-acting muscarinic antagonist (LAMA) umeclidinium and the long-acting β 2-agonist (LABA) vilanterol. Anoro is a combined dual bronchodilator inhaler containing the long-acting muscarinic antagonist (LAMA) umeclidinium and the long-acting β 2-agonist (LABA) vilanterol.

To avoid any misinterpretation that this deck is advocating or supporting a 'switch service' the opening page states that any medicine optimisation project '*must involve a therapeutic review and patient choice/consent of a medicine change at each step. By using this tool you are confirming that it will only be used for such medicines optimisation implementation projects involving all such elements*'. In addition, a prominent boxed statement, 'GSK does not advocate switch programmes. A clinical therapy review should occur before any change of medication', can be seen within the financial impact and environmental impact pages.

**Allegation and PMCPA Clauses for consideration**

The complainant alleges that the toolkit promotes Trelegy for off-label use, namely as a '*step up treatment for those patients who are not adequately treated on multiple inhaler therapy*'. They cite two claims, which are on separate tabs, as alleged evidence that GSK is actively promoting '*a switch to Trelegy from those patients on multiple inhaler triple therapy', which 'is outside the licenced indication.*'

1. Claim on MITT optimisation tab, adjacent to image of Trelegy inhaler:

*'Modelled data suggests that there are 175 Patients with COPD prescribed multiple inhaler triple or quad+* therapy in an average 48,000 patient population (Average population in a PCN).***
*Optimising inadequately treated patients offers benefits for patients, the NHS and the environment.'*
**Quad+ is defined as COPD patients prescribed four or more inhalers.*
***The 48,000 patient population has been taken as the average size of a PCN in England.*

2. Claim on Financial impact tab:
'*There is an opportunity to optimise patients currently being treated with triple therapy in multiple inhalers or Quad+ to Single Inhaler Triple Therapy*'.

GSK was asked to consider Clauses 11.2, 5.1 and 2. Clause 11.2 states: '*The promotion of a medicine must be in accordance with the terms of its marketing authorisation and must not be inconsistent with the particulars listed in its summary of product characteristics...*'

**Triple therapy and Trelegy SmPC**

Triple inhaler therapy for managing COPD involves the use of two bronchodilators—a long-acting beta-agonist (LABA) and a long-acting muscarinic antagonist (LAMA)—alongside an inhaled corticosteroid (ICS). This treatment can be delivered either through multiple inhalers (MITT) or a single inhaler that combines all three medications (SITT). The terminology MITT (multiple inhaler triple therapy) or SITT (single inhaler triple therapy) simply indicates the number of inhalers prescribed to the patient. It does not denote different classes of medications, and there is no specific licence for MITT or SITT as distinct treatments.

Trelegy is a once daily SITT containing the LAMA umeclidinium (UMEC), LABA vilanterol (VI) and ICS fluticasone furoate (FF). Trelegy is delivered through the Ellipta device and marketing authorisation was granted on 15th Nov 2017.

Section 4.1 of the SmPC states the therapeutic indication as follows: '*Trelegy Ellipta is indicated as a maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by a combination of either an inhaled corticosteroid and a long-acting β 2-agonist or a combination of a long-acting β 2-agonist and a long-acting muscarinic antagonist*'.

Please note that throughout this response, reference to COPD will substitute for moderate to severe COPD unless otherwise stated.

GSK acknowledges that in promoting Trelegy for '*COPD patients who are not adequately treated by a combination of either an inhaled corticosteroid and a long-acting β 2-agonist or a combination of a long-acting β 2-agonist and a long-acting muscarinic antagonist*' that this could include COPD patients on MITT as noted by the complainant. GSK can confirm that a careful and considered assessment of all relevant information was undertaken by GSK prior to the inclusion of any data on multiple inhaler triple therapy within Trelegy promotional material, to ensure compliance with Clause 11.2.

**Section 5.1 Pharmacodynamic properties**

The clinical efficacy and safety of Trelegy is supported by three Phase 3 studies, FULFIL, IMPACT and Study 200812 and detailed in Section 5.1 of the SmPC. Relevant text has been bolded for emphasis.

> '*5.1 Pharmacodynamic properties*
> *Clinical efficacy and safety*
> *The efficacy of Trelegy Ellipta (92/55/22 micrograms), administered as a once-daily treatment, has been evaluated in patients with a clinical diagnosis of COPD in two, active-controlled studies and in a single, non-inferiority study. All three studies were multicentre, randomised, double-blind studies that required patients to be symptomatic with a COPD Assessment Test (CAT) score ≥ 10 and on daily maintenance treatment for their COPD for at least three months prior to study entry.*
> *FULFIL (CTT116853) was a 24-week study (N=1,810), with an extension up to 52 weeks in a subset of subjects (n=430), that compared Trelegy Ellipta (92/55/22 micrograms) with budesonide/formoterol 400/12 micrograms (BUD/FOR) administered twice-daily.' ….*
> *'IMPACT (CTT116855) was a 52-week study (N=10,355) that compared Trelegy Ellipta (92/55/22 micrograms) with fluticasone furoate/vilanterol 92/22 micrograms (FF/VI) and umeclidinium/vilanterol 55/22 micrograms (UMEC/VI).'….*
> *'At study entry**, the most common COPD medications reported in the FULFIL and IMPACT studies were ICS+LABA+LAMA (28%, 34% respectively)**, ICS+LABA (29%, 26% respectively), LAMA+LABA (10%, 8% respectively) and LAMA (9%, 7% respectively). These patients may have also been taking other COPD medications (e.g. mucolytics or leukotriene receptor antagonists).'*
> *Study 200812 was a 24-week, non-inferiority study (N=1 055) that **compared Trelegy Ellipta (92/55/22 micrograms) with FF/VI (92/22 micrograms) + UMEC (55 micrograms), co-administered once daily as a multi-inhaler therapy** in patients with a history of moderate or severe exacerbations within the prior 12 months.*'

As stated in the SmPC above, all three Phase III studies supporting the clinical efficacy and safety of Trelegy included a significant proportion of patients previously treated with multiple inhaler triple therapy.

In FULFIL, 28% of patients (n=513) were previously on a combination of ICS+LABA+LAMA, making it one of the largest cohorts of patients in the study. A subgroup analysis for FULFIL, published by Halpin et al, confirmed that irrespective of the class of prior COPD medication received, treatment with Trelegy demonstrated a significantly greater improvement in lung function compared to BUD/FOR at 24 and 52 weeks. In addition, Trelegy, when compared to BUD/FOR, reduced the mean annual exacerbation rate up to week 24 (range 24–63%) in all prior medication subgroups, except LAMA+LABA (annual exacerbation rate reduction −44%).

In IMPACT, 34% (n=3563) of patients were previously treated on a combination of ICS+LABA+LAMA, making it the largest proportion of patients within the study. Details on medication combinations at trial entry are provided in Table S4 in the Supplementary Appendix of the primary manuscript. A post hoc analysis of IMPACT by

Singh et al, analysed the primary and secondary endpoints across the COPD medication subgroups.

This showed that COPD patients previously treated with ICS+LAMA+LABA, who were randomised to Trelegy had significantly reduced annual moderate/severe and annual severe exacerbation rates, significantly improved lung function (FEV1) and significantly improved quality of life (SGRQ) versus either comparator FF/VI or UMEC/VI.

The third study referred to in Section 5.1 of the SmPC, Study 200812, was a 24-week, non-inferiority study (N=1 055) which directly compared the SITT Trelegy to the same triple therapy molecules, ICS/LABA (FF/VI) + LAMA (UMEC), delivered using multiple inhalers. Of the 1055 patients, 445 (42%) were patients being treated with multiple inhaler triple therapy at baseline. The mean change from baseline in trough FEV1 at Week 24 was 113 mL (95% CI 91, 135) for Trelegy and 95 mL (95% CI 72, 117) for FF/VI + UMEC; the between-treatment difference of 18 mL (95% CI -13, 50) confirmed that single inhaler triple therapy with Trelegy was considered non-inferior to FF/ VI + UMEC (MITT). At Week 24, the proportion of responders based on St George's Respiratory Questionnaire Total score (a disease specific quality of life questionnaire) was 50% (FF/UMEC/VI) and 51% (FF/VI + UMEC); the proportion of responders based on the Transitional Dyspnea Index focal score was similar (56% both groups).

A similar proportion of patients experienced a moderate/severe exacerbation in the FF/UMEC/VI (24%) and FF/VI + UMEC (27%) groups; the hazard ratio for time to first moderate/ severe exacerbation with FF/UMEC/VI versus FF/VI + UMEC was 0.87 (95% CI 0.68, 1.12). The incidence of adverse events was comparable in both groups (48%); the incidence of serious adverse events was 10% (FF/UMEC/VI) and 11% (FF/VI + UMEC).

In summary, all three clinical studies which support the registrational efficacy and safety of Trelegy, and are referenced in the SmPC, enrolled a substantial number of patients who were being treated with multiple inhaler triple therapy at baseline. The Phase III sub analyses in patients being treated with MITT at baseline, prior to randomisation, confirmed that Trelegy demonstrated superior efficacy and quality of life scores when compared to the dual bronchodilator combination (BUD/FOR, UMEC/VI) or ICS/LABA combinations (FF/VI). Study 200812 confirmed that delivering Trelegy through a single inhaler was at least as effective and posed no additional safety risk compared to administering the three components through two separate inhalers. GSK therefore concluded that the promotion of Trelegy in COPD patients not adequately treated on multiple (open) triple therapy is in accordance with the terms of the Trelegy marketing authorisation and not inconsistent with the particulars listed in the Trelegy SmPC as required under Claure 11.2.

**Section 4.1 Therapeutic Indications**

'*Trelegy Ellipta is indicated as a maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by a combination of either an inhaled corticosteroid and a long-acting β 2-agonist or a combination of a long-acting β 2-agonist and a long-acting muscarinic antagonist*'.

This indication is the same for all UK SITTs and no SITT inhaler has MITT stated as part of the indication. Similarly, no dual combination or monotherapy COPD inhalers have a licence which states use as part of a MITT regimen. Patients on MITT are not on a combination therapy as per a licensed indication, but rather on two separate medicines independently, each prescribed for their respective indications for COPD.

All COPD patients on triple therapy, either MITT or SITT, have failed to be adequately treated by either a LABA/LAMA or ICS/LABA. This treatment paradigm is seen within national guidelines, including the NICE COPD treatment algorithm which has a series of step wise, evidence-based treatment recommendations. Dual maintenance therapy (LABA/LAMA or ICS/LABA depending on phenotype) is recommended by NICE for use in COPD patient who are limited by symptoms or have experienced exacerbations despite treatment with short acting bronchodilators. If despite these treatments a patient still has day-to-day symptoms that adversely impact their quality of life, or one severe or two moderate exacerbations within a year, then NICE recommend considering triple therapy.

The Trelegy indication, and that of all other SITTs, specifies ‘not adequately treated’ as opposed to an objective endpoint such as lung function or exacerbation risk. This terminology reflects the complexity in managing COPD, where different factors often beyond the choice of molecule can negatively impact the clinical outcome for an individual patient. MITT is inherently complex for patients.

Data from the NHS site www.RightBreathe.com on COPD inhalers licenced in the UK, shows the degree of choice available. Currently there are:

- 8 different LABA inhalers
- 8 different LAMA inhalers
- 5 different dual bronchodilator LABA/LAMA inhalers
- 14 different combination ICS/LABA inhalers

This means there could be as many of 112 different on-licence combinations of MITT available for prescription. A patient on MITT is likely to have a daily routine which incorporates different dosing regimens (one or two puffs either once or twice daily) and/or different inhalation techniques for each separate inhaler.

There is consistent evidence, including within the UK, that MITT is associated with low adherence and persistence. Sansbury at al showed that around three-quarters of patients discontinued MITT in the UK before reaching the end of a 12-month observation period. As per the 2024 GOLD strategic report, non-adherence to COPD medication has been associated with poor symptom control, increased risk of exacerbation, increased healthcare utilization and costs, decreased health-related quality of life and higher mortality risk. This contrasts with real-world data showing that patients initiating SITT have improved adherence and/or treatment persistence compared with MITT. In a large retrospective cohort study analysing UK primary and secondary care databases, Halpin et al demonstrated that patients initiating SITT (either Trelegy or Trimbow pMDI), had significantly better adherence and persistence compared with patients initiating MITT at 6,12- and 18-months post-initiation ($p<0.001$ for all comparisons) and that these improvements persisted for at least 18 months following treatment initiation. A study by Van der Palen has shown that COPD patients make substantially fewer critical errors with a single placebo Ellipta inhaler versus triple

therapy delivered through multiple inhalers (Diskus+Handihaler or Turbuhaler+Handihaler).

A wealth of real-world evidence now exists in support of potential clinical and economic benefits of SITTs versus MITT. Spanish data from Alcázar-Navarrete et al showed that at 12-month follow-up, SITT patients had a 37% improvement in persistence compared with MITT patients, leading to a 33% risk reduction in all-cause mortality and a 32% risk reduction in the incidence of exacerbations. Similar improvement in clinically relevant outcomes was reported in a European 24-week multicentre, randomized, open-label, phase IV effectiveness study which showed treatment with the SITT Trelegy resulted in significantly more patients gaining health status improvement and greater lung function improvement versus non-Ellipta MITT. A recently published UK study which examined patient data from linked primary and secondary databases also showed that patients who had changed from MITT to SITT (Trelegy) had significantly decreased the rate of COPD exacerbations, COPD-related healthcare resource use and direct medical costs in the 6 months following the switch compared with the 6 months prior.

The potential advantages of SITTs are reflected in the most recent UK and global guidelines and strategy documents. The 2023 Primary Care Respiratory Society (PCRS) guideline on Triple Therapy for COPD states:

> *'Consider a single inhaler triple therapy device to improve adherence, reduce inhaler technique errors and reduce inhaler burden.'*

Similarly, the 2024 Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy document, based on the best-available evidence, states:

> *'Although patient preferences may vary, prescribing strategies that could help improve adherence often include selecting devices with a similar inhalation technique (in the case of multiple inhalers) and combination therapy.'*

NICE makes recommendations within section 1.2.19, Inhaled combination therapy, on what the choice of drugs and inhalers should be based on, namely:

> - *how much they improve symptoms,*
> - *the person's preference and ability to use the inhalers,*
> - *the drugs' potential to reduce exacerbations,*
> - *their side effects,*
> - *their cost.*
>
> *Minimise the number of inhalers and the number of different types of inhalers used by each person as far as possible.*

From the patient perspective, new advances such as SITTs were developed to address a clinical need. The prevalence of COPD increases with age and the average age of patients with moderate to severe COPD who entered the Trelegy registration studies was between 63.8-66.3 (+/- 8.6) years. It is not unreasonable that some patients who clinically need a LAMA, LABA and an ICS can struggle with the complexity of 2 different inhalers with different techniques i.e. a DPI inhaler which requires a fast and deep inhalation to disaggregate the dry powder and an MDI which requires a slow and steady inhalation of aerosol particles, combined with different dosing regimens i.e one puff vs two puffs, either once daily vs twice daily. GSK considers that, supported by the evidence presented, these patients should have the option of receiving the same

classes of medicine in one single inhaler. Even for patients with simpler MITT regimens, e.g. Relvar and Incruse which both use the same device, there are practical advantages and efficiencies to be gained by reducing the number of inhalers to one.

Were the alleged complaint to be found in breach, such patients would be out of scope for the promotion of all SITTs, pharmaceutical advances developed specifically to meet their needs. The use of SITT instead of MITT in appropriate patients means cost saving for the NHS. Although the NICE guidelines did not make a recommendation in favour of single or multiple inhaler devices, the NICE committee did comment on the economic evidence that using a single inhaler device for triple therapy in COPD was more cost effective. Fewer inhalers to use and dispose of, particularly pMDIs which make up 70% of prescribed inhalers in the UK and contain potent greenhouse propellant gases, helps the NHS meet its carbon emission targets. The British Thoracic Society position statement on The Environment and Lung Health 2020 sets out a number of recommendations including the importance of using low carbon inhalers such as propellant-free DPIs or reusable Soft Mist Inhalers where possible and improved recycling/disposal schemes.

In summary, GSK considers that the phrase 'not adequately treated' allows clinicians to prescribe Trelegy for patients with COPD who are clinically impacted by factors such as poor adherence, device errors and poor inhalation technique, inconvenience, or even cost. As all MITT patients are on a combination of an ICS, a LABA and a LAMA when such patients are not adequately treated despite their current therapy, be that due to poor adherence, device errors, poor inhalation techniques, inconvenience or even cost, GSK considers that such MITT patients are within the scope of the Trelegy licenced indication and aligned to Clause 11.2 of the Code.

**Clauses 5.1 and 2**

- Clause 5.1 states: *High standards must be maintained at all times.*
- Clause 2 states: *Activities or materials must never be such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry.*

As set out in the scientific and clinical rationale above GSK has carefully and consciously considered the requirements of the Code. These data were evaluated prior to taking any decision to promote Trelegy for COPD patients not adequately treated with multiple inhaler triple therapy. Consequently, it is GSK's belief that high standards have been maintained and that this activity does not bring discredit to the industry. GSK strongly denies breaches of Clauses 5.1 and 2.

**Conclusion**

Based on the factors described above, GSK remains confident that the promotion of Trelegy for patients not adequately treated on multiple inhaler triple therapy is firstly, in accordance with the Trelegy indication and not inconsistent with the particulars of the SmPC; secondly, clinically sound and in the best interest of appropriate COPD patients based on available evidence supporting SITT versus MITT and the clinical unmet need; and finally, consistent with national and international recommendations. For these reasons, GSK strongly refutes the allegation and denies any breach of Clauses 11.2, 5.1 and 2 in relation to the COPD medicines optimisation toolkit."

**PANEL RULING**

The complainant alleged that a GSK COPD (chronic obstructive pulmonary disease) medicines optimisation toolkit promoted Trelegy Ellipta for an unlicensed indication.

The medicines optimisation toolkit was an interactive pdf, which users could navigate using tabs and embedded links. The complainant cited statements on two pages of the toolkit: one on the 'MITT optimisation' page and one on the 'Financial impact' page.

The Panel noted the content of the 'MITT optimisation' page. The following text, including that cited by the complainant, appeared on the left side of the page:

> "*Patient Outcomes*
> *Optimising COPD Patients on triple therapy or Quad+ (ICS/LABA + LAMA)*
> *In two separate inhaler devices (Multiple Inhaler Triple Therapy)*
>
> *Modelled data suggests that there are 175 Patients with COPD prescribed multiple inhaler triple or quad+* therapy in an average 48,000 patient population (Average population in a PCN).***
> *Optimising inadequately treated patients offers benefits for patients, the NHS and the environment.*
>
> * Quad+ is defined as COPD patients prescribed four or more inhalers.
> ** The 48,000 patient population has been taken as the average size of a PCN in England."

On the right-hand side of the page, information about the INTREPID study was presented, including a graph. There was a link to the page of the toolkit titled 'INTREPID Safety' and a link to view the graph at a larger size.

In relation to the 'Financial impact' page, the complainant cited the following statement:

> "*There is an opportunity to optimise patients currently being treated with triple therapy in multiple inhalers or Quad+ to Single Inhaler Triple Therapy*"

This statement appeared beneath the main heading of the page, which was:

> "*Financial outcomes of optimising patients from Multiple Inhaler Triple Therapy to Single Inhaler Triple Therapy*"

The remainder of the 'Financial impact' page presented cost saving opportunity information. There was also an outline box stating "GSK does not advocate switch programmes. A clinical therapy review should occur before any change of medication."

The complainant alleged that the two statements they cited constituted promotion of Trelegy for off-label use because the licence was "very specific to dual inhaler step up only. Trelegy does not have a licence to step up those patients who are not adequately treated on multiple inhaler therapy."

Section 4.1 of the Trelegy summary of product characteristics stated that Trelegy Ellipta was indicated as a maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by a combination of an ICS/LABA or a combination of a LABA/LAMA.

The Panel bore in mind GSK's submission that the medicines optimisation toolkit was not advocating or supporting a "switch service" and the statement on the first page that read: "This tool is intended to support your medicine optimisation implementation projects, which involve a therapeutic review and patient choice/consent of a medicine change at each step. By using this tool you are confirming that it will only be used for such medicines optimisation implementation projects involving all such elements."

GSK submitted that, in relation to triple therapy for managing COPD, the terminology MITT (multiple inhaler triple therapy) or SITT (single inhaler triple therapy) indicated the number of inhalers prescribed to the patient rather than denoting different classes of medications. GSK submitted that there was no specific licence for MITT or SITT as distinct treatments and that patients on MITT were not on a combination therapy as per a licensed indication, but rather on two separate medicines independently, each prescribed for their respective indications for COPD.

The Panel noted GSK's detailed submission regarding relevant guidelines, the efficacy of Trelegy Ellipta, SITTs and the three Phase III registration studies referred to in the Trelegy Ellipta summary of product characteristics which included patient cohorts that had transferred to Trelegy Ellipta from MITT.

GSK submitted that the phrase "not adequately treated" allows clinicians to prescribe Trelegy Ellipta for patients with COPD who are clinically impacted by factors such as poor adherence, device errors and poor inhalation technique, inconvenience, or even cost. In the Panel's view, however, the phrase was used within section 4.1 of the Trelegy Ellipta summary of product characteristics in relation to patients not adequately treated by a combination of an ICS/LABA or a combination of a LABA/LAMA; it did not refer to patients not adequately treated by a triple therapy. The Panel disagreed with GSK's submission that the phrase allowed clinicians to prescribe Trelegy Ellipta for patients with COPD who are impacted by cost.

The Panel considered that the primary issue to consider was whether promoting "optimising" patients currently being treated with MITT by moving to a SITT (Trelegy Ellipta) was outside Trelegy Ellipta's licensed indication; whether it was merely a change in the delivery mechanism for triple therapy or whether GSK needed to be satisfied that all MITT patients satisfied the requirement set out in section 4.1 of the Trelegy Ellipta summary of product characteristics, namely that they were not adequately treated by LAMA/LABA or ICS/LABA therapy. The Panel noted the complainant's use of the phrase "step up" in reference to a patient changing from MITT to SITT but considered that this was not the appropriate wording in this context, as the components of the therapy (LAMA/LABA plus ICS) were the same in both cases.

The Panel bore in mind GSK's submission that all COPD patients on triple therapy, either MITT or SITT, have failed to be adequately treated by either a LABA/LAMA or ICS/LABA and that this treatment paradigm is seen within national guidelines, including the NICE COPD treatment algorithm which has a series of stepwise, evidence-based treatment recommendations.

The Panel considered in principle that it was not necessarily unacceptable to promote a switch from MITT to Trelegy Ellipta. Whether such a claim was acceptable would depend on the circumstances of each case; context was important. The Panel considered that, in the context of this medicines optimisation toolkit, the complainant had not established that the two phrases cited meant that Trelegy Ellipta had been promoted in a manner that was inconsistent with its licensed indication. The Panel therefore ruled **no breach of Clause 11.2** in relation to each phrase in question.

Noting its ruling of no breach above, the Panel did not consider that there were any additional factors that indicated that GSK had failed to maintain high standards or had brought discredit upon, or reduced confidence in, the pharmaceutical industry. The Panel therefore ruled **no breach of Clauses 5.1 and 2**.

**Complaint received** **4 August 2024**

**Case completed** **24 June 2025**