CASE/0377/11/24

COMPLAINANT v ASTRAZENECA

Allegations about a Trixeo promotional video

CASE SUMMARY

This case was in relation to a promotional video which was hosted on an AstraZeneca website. The video featured a health professional sharing their experiences of Trixeo, including their rationale for pharmaceutical interventions in COPD which included reviewing clinical studies and their observations of patient quality of life. The health professional went on to discuss a patient case study involving a switch from another inhaler to Trixeo.

The complainant made several allegations relating to: misleading information, lack of safety considerations or side effects, the use of a hanging comparison and the use of an exaggerated claim.

The outcome under the 2024 Code was:

Breach of Clause 5.1 (x2)	**Failing to maintain high standards**
Breach of Clause 6.1 (x2)	**Making a misleading claim**
Breach of Clause 14.4	**Making an exaggerated claim that could not be substantiated**

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 6.1	**Requirement that information/claims/ comparisons must not be misleading**
No Breach of Clause 6.2	**Requirement that information/claims/comparisons must be capable of substantiation**

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 AstraZeneca UK Limited was received from an anonymous contactable complainant who described themselves as a health professional and later became non-contactable.

COMPLAINT

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

> "A promotional video about Trixeo that is hosted on a website is misleading and risks patient safety. The video is on the following platform; [URL provided] [material identification code and date of preparation]. In this video, the nurse consultant between 45 and 51 seconds verbalises that the Ethos study improved lung function. This is misleading as the primary endpoint of Ethos was not lung function. Furthermore in the Ethos study there was increased pneumonia in the Trixeo group. An increase in pneumonia would actually harm lung function. Therefore, the video should have been explicit about what the primary objective of the study was as well as provided discussion of safety data. There was actually zero mention of any safety data which means video is not fair and is unbalanced. Discussion of pneumonia increase on the Trixeo arm within the trial, considering the broad improvement in lung function claimed by the nurse was pivotal. There is also no mention of what the improvement in lung function was vs, rendering this a hanging comparison. There are breaches of clauses 6.1, 6.2, 5.1 and 2. At 55 seconds to 58 seconds there is a claim about a patient that Trixeo changed their life. This is an exaggerated claim which is in breach of clause 14.4 and 5.1. It is shocking to see such videos being approved and hosted considering promotion should be balanced."

When writing to AstraZeneca, the PMCPA asked it to consider the requirements of Clauses 6.1, 6.2, 14.4, 5.1 and 2 of the 2024 Code.

ASTRAZENECA'S RESPONSE

The response from AstraZeneca is reproduced below:

> "We are writing to you in response to your letter dated 2 December 2024, concerning a complaint from a healthcare professional (HCP) with respect to a Trixeo promotional video on the [named] website. The complainant's allegations can be broken down as follows:
>
> 1. Nurse in the video states (45-51s) that Ethos study improved lung function. This is misleading as the primary endpoint of ETHOS was not lung function. In the ETHOS study there was increased pneumonia in the Trixeo group, which would harm lung function. Therefore, the video should have been explicit about what the primary objective of the study as well as provided safety data.
> 2. There was zero mention of safety data which means the video is not fair and is unbalanced.
> 3. No mention of what the improvement in lung function was v. [versus], rendering this a hanging comparison.
> 4. At 55-58s there is a claim about a patient that Trixeo changed their life. This is an exaggerated claim.
>
> AstraZeneca have been asked to consider clauses 2, 5.1, 6.1, 6.2 and 14.4 of the 2024 ABPI Code ('the Code'). We will address each of the complainant's allegations according to the relevant clauses.
>
> **Background**

This video (Using Trixeo in Clinical Practice - [named health professionals] experience, [material identification number]) is hosted on an AZ website [URL provided]. This website hosts several educational resources for nurses, including videos of nurses recounting their experience of using Trixeo in practice. This complaint is referring to one of these videos. The title of this video is 'Using Trixeo in your clinical practice – [named health professionals] experience' and is clearly subtitled '[named health professionals] speaks about [their] experience of using TRIXEO in clinical practice and shares a patient case study', ensuring that the purpose of the video is clear from the outset. The purpose of the video was not to discuss the details of the ETHOS study but to share real world experiences of using Trixeo from a respiratory nurse.

HCPs have been directed to this website via an e-mail link sent to delegates following a National Nurse meeting. Each component of this website has been individually reviewed and certified by an experienced Nominated Signatory, including each of the videos. The Nominated Signatory who approved this video is registered with the [named regulatory body].

The website includes a single-click, direct link to the Trixeo prescribing information (PI) at the top of the page [screenshot provided of the webpage where the video was hosted].

AstraZeneca Response to the Allegations

1. *Nurse in the video states (45-51s) that Ethos study improved lung function. This is misleading as the primary endpoint of ETHOS was not lung function. In the ETHOS study there was increased pneumonia in the Trixeo group, which would harm lung function. Therefore, the video should have been explicit about what the primary objective of the study as well as provided safety data.*

As described above, the purpose and intention of the video was clear from the outset, to share HCP experience using Trixeo. The video was not designed to educate on the clinical parameters or data for Trixeo. Should the HCP viewing the video want to access this, they can do so via the prescribing information (clearly signposted at the beginning of the video).

The statement '*The ETHOS data showed in patients with moderate to severe COPD that it improved lung function*' is accurate and substantiated by the ETHOS study. The ETHOS study did include a pre-specified pulmonary function test sub-study, assessing lung function in a subset of the patients in the ETHOS study. This sub-study included 3088 patients of the ETHOS intent-to-treat population. The primary endpoints of this sub-study included change from baseline in morning pre-dose trough FEV1 at week 24 and over 24 weeks for Trixeo vs LABA/LAMA, and FEV1 AUC(0-4h) post-dose at week 24 and over 24 weeks for Trixeo vs LABA/ICS. Other lung function endpoints included change from baseline for these endpoints at 52 weeks, onset of action and rate of decline of these endpoints over 52 weeks. The study demonstrated statistically significant improvements for Trixeo vs comparators for all primary endpoints. We therefore maintain that the statement '*The ETHOS data showed in patients with moderate to severe COPD that it improved lung function*' is accurate and not misleading with regards to the ETHOS data.

Provision of safety data was not relevant to this HCP's clinical experience and therefore wasn't mentioned in the video. AstraZeneca did ensure important safety information was included by adding a prominent statement at the beginning of the video referring the reader to PI (including safety information), which was available via one single click link at the top of the webpage where the video is hosted. The PI has a prominent statement at the top **'Consult Summary of Product Characteristics before prescribing'** and includes pneumonia as a possible side effect within the PI itself (within the subsection of **undesirable events)**. [screenshots of Trixeo prescribing information provided]

It is important to note that pneumonia and lung function are two separate study observations and un-related to one another.

We therefore ascertain that there has been no breach of clause 6.1, 6.2, 5.1 or 2 of the Code regarding this allegation.

2. *There was zero mention of safety data which means the video is not fair and is unbalanced.*

The video is based on the speaker's clinical experience with Trixeo, which is clear from the outset. PI is also clearly signposted at the beginning of the video, and the PI includes the prominent statement **'Consult the Summary of Product Characteristic before prescribing'** at the top. We do not agree that the video is therefore unbalanced as it accurately reflects the experience of that HCP.

Based on this, we ascertain that there has been no breach of clause 5.1 or 2 of the Code regarding this allegation.

3. *No mention of what the improvement in lung function was v., rendering this a hanging comparison.*

The HCP states that '*The ETHOS data showed in patients with moderate to severe COPD that it improved lung function*'. It is clear that improved lung function seen with Trixeo is compared with the comparator arms of the ETHOS study. It would be broadly understood by the audience that the improvement referred to by the HCP is change in lung function from baseline vs. dual therapy.

We therefore deny a breach of clause 6.1 in relation to this allegation.

4. *At 55-58s there is a claim about a patient that Trixeo changed their life. This is an exaggerated claim.*

The speaker states: '*…and this patient, I was very pleased to hear, said that it actually changed their life...*'. The statement that Trixeo 'changed their life' is a reflection of what the HCP has been told about a patient experience using the medicine. The HCP does not state that it will change all patients lives; it is specific to this patient and their circumstances, which would be different for different patients. This statement is not a claim of special merit and presented in the context of this patient only. This phrase could have many different meanings in how it has changed their life; it is not a claim about Trixeo's clinical benefit, but a patient's lived experience about using Trixeo. We, therefore do not agree that this is an exaggerated claim.

AstraZeneca does not agree that this results in a breach of the Code. Therefore, we refute the breach of clauses 14.4 or 5.1 of the Code in relation to this allegation.

Summary of AstraZeneca's position

In summary:

- The intention of the video is to share HCP experience using Trixeo and not to discuss the ETHOS data. It is valuable for HCPs to hear about others experiences using medicines in addition to considering all of the relevant efficacy/safety/dosing information before prescribing Trixeo.
- Lung function was studied in ETHOS and is mentioned appropriately. It is not discussed in detail, as this was not the purpose of the video. The purpose of the video was clear to the viewer from the outset.
- Prescribing information was clearly signposted at the beginning of the video. It also includes the prominent statement 'Consult Summary of Product Characteristics before prescribing' at the top.
- Use of the phrase '*[Trixeo]... changed their life*' is non-specific and used in the context of one patient's feedback.
- This video is complete for its intended purpose and does not pose any risk to patient safety.

AstraZeneca takes its responsibilities under the Code very seriously. Based on the above detailed response, we maintain that the video is appropriately reflecting on HCP experience using Trixeo and therefore, **we refute breach of clauses 6.1, 6.2 and 14.4 of the Code.** We strongly deny that this video jeopardises patient safety in any way, and therefore also refute **5.1 and 2 of the Code**".

PANEL RULING

This case was in relation to a short promotional video (1m10s) titled "Using Trixeo In Your Clinical Practice", which was hosted on an AstraZeneca website among other similar resources featuring health professionals sharing their experiences of Trixeo. The video was subtitled "[named health professional] speaks about [their] experience of using TRIXEO in clinical practice and shares a patient case study". The health professional described their rationale for pharmaceutical interventions in COPD which included reviewing clinical studies and their observations of patient quality of life. They went on to discuss a patient case study involving a switch from another inhaler to Trixeo, which had a positive impact, and that part of their decision to prescribe Trixeo was based on the ETHOS data published in the GOLD 2024 strategy.

The Panel noted that the video was a Trixeo promotional item for which AstraZeneca was responsible under the Code. It was well-established that if companies' materials within the scope of the Code, contained interviews with patients or health professionals, such published interviews should comply with the Code and the pharmaceutical company would be responsible for their content. To permit otherwise would allow companies to circumvent the requirements. The Panel noted that AstraZeneca had complete editorial control over the content of the video.

The complainant made several allegations which the Panel considered in order:

1. Mention of improved lung function and the omission of there being increased pneumonia in the Trixeo group

The complainant alleged that the health professional's statement, "The ETHOS data showed in patients with moderate to severe COPD, it improved lung function", was misleading as the primary endpoint of the ETHOS study was not lung function.

The ETHOS study was a randomised controlled trial in patients with moderate to severe COPD, for which the primary endpoint was the annual rate of moderate or severe exacerbations (the estimated mean number per patient per year). The Panel noted a subset of patients in the modified intent-to-treat (mITT) population of the ETHOS study were included in a pre-specified pulmonary function test (PFT) sub-study that assessed lung function (Rabe *et al.*, 2021).

The Panel considered while the complainant appeared to refer to the main ETHOS study (Rabe et al., 2020), the data mentioned by the health professional referred to the published sub-study which assessed lung function, according to AstraZeneca (Rabe *et al.*, 2021).

The primary endpoints in the sub-study were change from baseline in morning pre-dose trough forced expiratory volume in one second (FEV1) for Trixeo triple therapy versus glycopyrrolate/formoterol fumarate *(*GFF) and FEV_1 area under the curve from 0 to 4 hours ($AUC_{0–4}$) for Trixeo *versus* budesonide/formoterol fumarate (BFF) at week 24. The Panel accepted AstraZeneca's submission that the sub-study was pre-specified and demonstrated statistically significant improvements for Trixeo versus comparators (dual therapy) for the primary endpoints.

The Panel further noted the complainant's reference to increased pneumonia in the Trixeo arm of the ETHOS study and that this would allegedly harm lung function. In this regard, the Panel observed the Rabe et al., 2020 included the following incidences of confirmed pneumonia: 3.5% in the 320-µg–budesonide triple-therapy Trixeo group; 4.2% in the 160-µg–budesonide triple-therapy Trixeo group; 4.5% in the ICS/LABA budesonide–formoterol group; and 2.3% in the LAMA/LABA glycopyrrolate–formoterol group.

While the Panel observed the ETHOS study reported a higher incidence of pneumonia with the Trixeo arms compared to glycopyrrolate–formoterol, the LAMA/LABA dual therapy group, the Panel accepted AstraZeneca's submission that this was a separate study observation. The complainant had not established that they were related in a manner such that it mitigated the primary finding of the sub-study for improved lung function.

In this context, the Panel considered the health professional's brief reference to improved lung function was consistent with the findings of the pre-specified ETHOS sub-study. The PFT sub-study was pre-specified and had been conducted concurrently with the ETHOS trial, as opposed to being a post hoc analysis, for example.

The Panel considered it might have been helpful to have provided context around the main ETHOS study and its primary endpoint, along with clarification that lung function was a pre-specified endpoint of the concurrent sub-study. Nonetheless, in the Panel's view, the complainant had not established that reference to improved lung function was misleading on the narrow basis that this was not the primary endpoint of the main ETHOS study. Nor had the complainant established the claim was not capable of substantiation. The Panel ruled **no breaches of Clauses 6.1 and 6.2.**

2. Lack of safety considerations or side effects

The complainant alleged that there was no mention of safety data which meant the video was not fair and balanced. It appeared, in part, that the complainant's reference to the omission of safety data related to the increased incidence of pneumonia.

AstraZeneca submitted that the purpose of the video was clear from the outset and that it was based on the speaker's clinical experience with Trixeo. AstraZeneca further submitted that prescribing information was clearly signposted at the beginning of the video and included the prominent statement *"Consult the Summary of Product Characteristic before prescribing"* at the top.

Clause 6.1 required information and claims to be balanced and fair, and that material must also be sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine. It was a well-established principle of the Code that promotional material must stand alone and not rely on qualification in the prescribing information. The Panel noted the incidences of pneumonia in each arm, as outlined in Allegation 1 above, and that it was higher in the Trixeo groups and dual therapy ICS/LABA treatment group than in those that received the LAMA–LABA combination. According to Trixeo's summary of product characteristics, pneumonia was the most reported and common adverse reaction (4.6%). Section 4.4, Special warnings and precautions for use, included:

> "*Pneumonia in patients with COPD*
>
> *An increase in the incidence of pneumonia, including pneumonia requiring hospitalisation, has been observed in patients with COPD receiving inhaled corticosteroids. There is some evidence of an increased risk of pneumonia with increasing steroid dose but this has not been demonstrated conclusively across all studies.*
>
> *There is no conclusive clinical evidence for intra-class differences in the magnitude of the pneumonia risk among inhaled corticosteroid products.*
>
> *Physicians should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of such infections overlap with the symptoms of COPD exacerbations.*
>
> *Risk factors for pneumonia in patients with COPD include current smoking, older age, low body mass index (BMI) and severe COPD."*

The Panel considered that the increased incidence of pneumonia was an important safety consideration. However, the health professional did not make any specific claim or inference regarding this. The Panel was unsure why the complainant alleged pneumonia needed to be mentioned specifically in isolation from other adverse events and cautions.

Nonetheless, the Panel took account of the overall context of the video, noting the allegation relating to the lack of safety data was broad. The Panel considered the video was promotional material for Trixeo, directed at health professionals, which only described the positive patient outcomes and merits of Trixeo, without reference to its safety profile. There was no inclusion of any adverse events or any qualification of safety outcomes. In the Panel's view, the video was

not sufficiently balanced or complete to enable recipients to form their own opinion of the therapeutic value of the medicine. The Panel therefore ruled a **breach of Clauses 6.1**.

3. Hanging comparison

The Panel considered the statement in question - *"The ETHOS data showed in patients with moderate to severe COPD, it improved lung function".* The complainant alleged that "improved lung function" was a hanging comparison, as the video did not include a reference to what the improvement in lung function was being compared.

Clause 6.1 required, among other things, comparative statements to be balanced, fair, objective, unambiguous and not misleading. The supplementary information to Clause 6.1 stated that "*hanging comparisons whereby a medicine is described as being better or stronger or suchlike without stating that with which it is compared, must not be made*".

The Panel noted that the ETHOS study was a randomised controlled trial with four arms, comparing two doses of triple therapy with two different dual therapy combinations over 52 weeks in patients with moderate-to-severe COPD. In the sub-study (which was referred to in the video):

- patients participated in a 4-hour pulmonary function test
- primary endpoints at week 24 were:
    - change from baseline in morning pre-dose trough forced expiratory volume in one second (FEV_1) of Trixeo *versus* glycopyrrolate/formoterol fumarate
    - FEV_1 area under the curve from 0 to 4 hours ($AUC_{0–4}$) of Trixeo *versus* budesonide/formoterol fumarate

In the Panel's view, the statement that the ETHOS study showed "*improved lung function*" was ambiguous as to whether the improvement was an absolute improvement in time or a comparison against an alternative treatment regimen. There was no further information included in the video to qualify this statement. In the Panel's view, the claim was not sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine and, in the absence of an explicit comparator or appropriate qualification, constituted a hanging comparison. The Panel therefore ruled a **breach of Clause 6.1**.

4. Clauses 5.1 and 2

The complainant alleged breaches of Clause 5.1 and 2 in relation to Allegations 1-3 above.

The Panel took account of its rulings in relation to the lack of completeness of information provided. The video also presented only favourable outcomes with Trixeo and lacked a balance of safety information. The Panel concluded that the undue emphasis on the positive response with Trixeo, without sufficient qualification and balance, was such that high standards had not been maintained and a **breach of Clause 5.1** was ruled in this regard.

The Panel recognised that Clause 2 was a sign of particular censure for cases where a company had brought discredit upon, or reduced confidence in, the pharmaceutical industry. While the Panel considered it essential that health professionals are able to rely on materials produced by companies to be balanced and complete, the Panel concluded that its ruling of a

breach of Clause 5.1 adequately covered this allegation. The Panel's view was that the circumstances of this allegation did not warrant an additional ruling. The Panel therefore ruled **no breach of Clause 2**.

5. Exaggerated claim

The complainant referred to the statement *"And this patient, I was very pleased to hear, had said that it actually changed their life"* and alleged that this was an exaggerated claim.

The Panel acknowledged the statement was made in relation to patient feedback that the health professional had received. However, the Panel considered it nonetheless appeared within promotional material for Trixeo, which was the only medicine mentioned. It was an established principle that individual patient cases in promotional material must not exaggerate a medicine's properties.

The Panel considered Clause 14.4 which stated:

> "*Promotion must encourage the rational use of a medicine by presenting it objectively and without exaggerating its properties. Exaggerated or all-embracing claims must not be made and superlatives must not be used except for those limited circumstances where they relate to a clear fact about a medicine. Claims should not imply that a medicine or an active ingredient has some special merit, quality or property unless this can be substantiated.*"

Although the Panel acknowledged AstraZeneca's submission that the health professional did not suggest that Trixeo will change all patients lives, the Panel did consider the statement to be a claim that Trixeo had special merit.

Without any further qualification or context, the Panel concluded that the singular case study was insufficient to satisfy the requirements of Clause 14.4. There would likely be examples of patients to whom the claim did not apply and, as a balance of information was not provided, the claim could be considered as exaggerating the benefits of Trixeo. The Panel ruled a **breach of Clauses 14.4**.

The complainant cited a breach of Clause 5.1 in relation to the exaggerated claim. The Panel considered that AstraZeneca had complete editorial control over the final video prior to certification and publication, and was responsible for its content. The Panel therefore concluded that the failure to identify and address the claim at issue in the video meant that AstraZeneca had failed to maintain high standards. The Panel therefore ruled a **breach of Clause 5.1**.

Complaint received **27 November 2024**

Case completed **4 November 2025**