CASE AUTH/3777/6/23 ***NO BREACH OF THE CODE***

COMPLAINANT v ASTRAZENECA

Concerns about a patient eligibility checklist for Trixeo on a company website

CASE SUMMARY

This case was in relation to a Trixeo (formoterol fumarate dihydrate/glycopyrronium/budesonide) patient eligibility checklist. The complainant alleged that the information about narrow-angle glaucoma was incomplete because it did not include information, detailed in the summary of product characteristics, about the prescriber providing counselling information for patients around acute narrow-angle glaucoma and the importance of stopping treatment if symptoms of it developed.

There was an appeal by AstraZeneca of three of the Panel's rulings.

The outcome under the 2021 Code was:

No Breach of Clause 2 [Panel's breach ruling overturned at appeal]	**Requirement that activities or materials must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**
No Breach of Clause 5.1 [Panel's breach ruling overturned at appeal]	**Requirement to maintain high standards at all times**
No Breach of Clause 6.1 [Panel's breach ruling overturned at appeal]	**Requirement that information, claims and comparisons must not be misleading**
No Breach of Clause 6.2	**Requirement that information, claims and 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 was received from an anonymous, contactable complainant who described themself as a health professional.

COMPLAINT

The complaint wording is reproduced below:

> "A Trixeo guide titled 'patient eligibility checklist' designed for HCPs around patient eligibility for Trixeo treatment was misleading. The guide was hosted on the Trixeo website resources section. There were a series of questions within this document.

Question 11 was worded – "Does your patient suffer from symptomatic prostatic hyperplasia, urinary retention or narrow-angle glaucoma". If the answer chosen was YES, the information provided read "Due to its anticholinergic activity, this medicinal product should be used with caution in patients with symptomatic prostatic hyperplasia, urinary retention or with narrow-angle glaucoma." However, this information was not fully correct as the SPC (section 4 4) for the product gave the following critical information around narrow angle glaucoma – 'Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using this medicinal product and to contact their doctor immediately should any of these signs or symptoms develop.' The information about the prescriber providing counselling information for patients around acute narrow angle glaucoma and also the importance of stopping treatment as specified in the SPC section 4 4 was omitted by AZ within the answer to qu 11. This was a patient safety concern as a HCP would simply look at the answer to qu 11 in the document as the full prescribing consideration around narrow angle glaucoma, which clearly is not the case. It was not in line with the spirit and letter of the code, nor self-regulatory framework, to provide what was incomplete information by the originators and approvers of this patient eligibility document. Breaches of clauses 6 1, 6 2, 5 1 and 2 had occurred."

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

ASTRAZENECA'S RESPONSE

The response from AstraZeneca is reproduced below:

"You have asked AstraZeneca to bear in mind the requirements of the following Code clauses when responding to this complaint, **6.1, 6.2, 5.1 and 2.** We will therefore address each of the complainant's allegations according to the relevant clauses of the ABPI Code of Practice.

The complainant alleges: *That the information was not fully correct as the SPC (section 4 4) for the product gave the following critical information around narrow angle glaucoma – 'Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using this medicinal product and to contact their doctor immediately should any of these signs or symptoms develop'*

The information about the prescriber providing counselling information for patients around acute narrow angle glaucoma and also the importance of stopping treatment as specified in the SPC section 4 4 was omitted by AZ.

Alleged breach of 6.1 & 6.2

AstraZeneca Response: The Trixeo Eligibility Checklist, available on the Trixeo website resources page, is a resource solely designed to help health care professionals (HCPs) establish whether a patient is eligible to be considered for Trixeo aligned to the licenced indication for the medicine.

The intent of the checklist is explained under the checklist access tab – 'Use our straightforward interactive checklist to identify which of your patients are eligible for

triple protection with TRIXEO, based on their prior treatment journey and clinical presentation' [screenshot provided].

The response provided to Q11 in The Trixeo Eligibility Checklist is in line with the SPC and enables the HCP to establish that patients with narrow angle glaucoma are eligible for Trixeo, but with caution due to its anticholinergic activity. The prescribing information for Trixeo states: 'Due to its anticholinergic activity, this medicinal product should be used with caution in patients with symptomatic prostatic hyperplasia, urinary retention or with narrow-angle glaucoma'.

The material was not designed to provide information to HCPs about how to counsel patients before initiation or to monitor patients following initiation of medicine. Counselling patients about the signs and symptoms of acute narrow-angle glaucoma following initiation of the medicine falls outside of the initial consideration for eligibility and therefore outside the scope and intent of the material in question.

The material also refers HCPs to additional information relevant to the prescribing of the medicine including: Prescribing Information on the first and last page of the document, SPC, safety and efficacy information, dosage information, and NICE guidance.

AstraZeneca maintains that all relevant information to help HCPs establish eligibility of a patient for consideration of Trixeo were included in the material and therefore refute a breach of clauses 6.1 & 6.2.

The complainant alleges: '*This was a patient safety concern as a HCP would simply look at the answer to qu 11 in the document as the full prescribing consideration around narrow angle glaucoma, which clearly is not the case It was not in line with the spirit and letter of the code, nor self-regulatory framework, to provide what was incomplete information by the originators and approvers of this patient eligibility document*'

Alleged breach of 2 & 5.1

AstraZeneca Response: AstraZeneca takes its responsibility to patient safety very seriously. As discussed above, additional counselling and monitoring information regarding narrow angle glaucoma falls outside of the intended purpose of the material. In addition, the material clearly highlights the need for caution when considering Trixeo for patients with a history of narrow angle glaucoma whilst referring HCPs to additional information relevant to the prescribing of Trixeo including the SPC, Prescribing Information (PI), safety and efficacy information, dosage information, and NICE guidance.

AstraZeneca refutes that the information provided was incomplete nor risk to patient safety and therefore refute a breach of clauses 2 & 5.1 of the ABPI Code of Practice."

PANEL RULING

The complaint related to a Trixeo patient eligibility checklist hosted on AstraZeneca's Trixeo website. The checklist was an interactive pdf file – each page having 'buttons' to click to jump to

another page of the file. The checklist consisted of 13 questions. The first five questions concerned the patient's COPD symptoms and current COPD treatment regimen. At the end of that section, there was a page inviting the user to find out more about the 'types of patients who can benefit' from Trixeo (via a link to the Trixeo website) or to proceed to the 'patient characteristics and comorbidities' section of the checklist to 'find out if your patient is eligible'. The 'patient characteristics and comorbidities' section consisted of eight questions related to contraindications, precautions and warnings. At the end of that section, there was a page with links to the Trixeo website inviting the user to explore the data on efficacy, safety and dosing, a note regarding coadministration, and links to prescribing information.

The complaint referred specifically to question 11: 'Does your patient suffer from symptomatic prostatic hyperplasia, urinary retention or narrow-angle glaucoma?'. The user was presented with two possible answers: yes and no. If the user clicked 'no', they proceeded to the next question. If the user clicked 'yes', they were taken to a page with the message 'Due to its anticholinergic activity, TRIXEO should be used with caution in patients with symptomatic prostatic hyperplasia, urinary retention or narrow-angle glaucoma.' and an arrow to click to proceed to the next question.

The complainant alleged that the information about narrow-angle glaucoma was incomplete because it did not include information, detailed in the summary of product characteristics for Trixeo, about the prescriber providing counselling information for patients around acute narrow-angle glaucoma and the importance of stopping treatment if symptoms of it developed. The complainant further alleged that the health professional would view the answer to question 11 in the checklist as the full prescribing consideration around narrow-angle glaucoma.

The Panel noted that section 4.4 of the summary of product characteristics (special warnings and precautions for use) included a section entitled "Anticholinergic activity" which stated: "Due to its anticholinergic activity, this medicinal product should be used with caution in patients with symptomatic prostatic hyperplasia, urinary retention or with narrow-angle glaucoma. Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using this medicinal product and to contact their doctor immediately should any of these signs or symptoms develop. Co-administration of this medicinal product with other anticholinergic containing medicinal products is not recommended (see section 4.5)."

The Panel noted that the first sentence was presented to users of the checklist who selected 'yes' to question 11 – i.e. when considering a patient for whom caution was advised based on this section of the summary of product characteristics. The second and third sentences were not included explicitly within the checklist. The Panel noted there was a statement on the final page of the checklist that advised the reader that the co-administration of Trixeo alongside some other treatments required further consideration and to see the summary of product characteristics for full details. The Panel noted strong CYP3A4 inhibitors were cited as an example in this regard but the recommendation against co-administration with other anticholinergic containing medicines was not highlighted.

The second sentence ("Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using this medicinal product and to contact their doctor immediately should any of these signs or symptoms develop.") was not included within the checklist at all and was the subject of this complaint.

The Panel noted AstraZeneca's submission that the checklist was designed to help health professionals establish whether a patient was eligible to be considered for Trixeo – it was not designed to provide information about how to counsel patients before initiation or how to monitor patients following initiation. AstraZeneca submitted that counselling patients about the signs and symptoms of acute narrow-angle glaucoma following initiation of the medicine fell outside of the initial consideration for eligibility and so fell outside of the scope and intent of the checklist. AstraZeneca submitted that the checklist referred the reader to additional information relevant to the prescribing of Trixeo, including the prescribing information and the summary of product characteristics.

The Panel considered the screenshot of the 'checklist access tab', provided by AstraZeneca, and the first page of the checklist. These were both titled "Can your patient receive triple protection with TRIXEO (formoterol fumarate dihydrate/glycopyrronium/budesonide)?" Beneath the title on both items, it read "Find out which of the patients in your practice **are eligible** for TRIXEO, and **which of those are not** (emphasis added by the Panel)." At the bottom of the 'checklist access tab', the following wording was presented in a large, prominent font: "Use our straightforward interactive checklist to identify which of your patients **are eligible** for triple protection with TRIXEO, based on their prior treatment journey and clinical presentation." (emphasis added by the Panel). There was additional information present in a small font that was not legible in the screenshot submitted to the Panel. The first page of the checklist included the indications for Trixeo Aerosphere, Bevespi Aerosphere and Symbicort Turbohaler, and a link to prescribing information and adverse reporting.

In the Panel's view, it could have been made clearer from the outset that the checklist was intended only to provide an overview of patient eligibility and that prescribers would need to refer to the summary of product characteristics for important information before prescribing. The Panel considered that "are eligible" (rather than, for example, "may be eligible") was a definitive statement that compounded the impression that there was no other information that would need to be considered.

The Panel considered the content of the page at the end of section 1 of the checklist, which the reader would reach if their patient might be eligible for Trixeo based on their prior treatment journey and clinical presentation, determined in the first five questions. This page was titled "Your patient may be eligible for TRIXEO." It included a link to the Trixeo website ("to discover the different types of patients who can benefit") and a button to click to progress through the rest of the checklist ("to find out if your patient is eligible, proceed to the patient characteristics and comorbidities section"). The Panel noted that there was no information on this page regarding safety or directing the reader to refer to the summary of product characteristics for further information. The Panel also noted the use of the definitive wording "if your patient **is** eligible" (emphasis added by the Panel), which, in the Panel's view, again implied that, having completed the full checklist, there would be no further information required.

The Panel considered the content of the final page of the checklist, which the reader would reach after answering all of the questions about patient characteristics and comorbidities. The page was titled "Your patient **is** eligible for triple protection with TRIXEO." (emphasis added by the Panel), and the Panel noted the use of definitive wording on this page. It included, among other things, a link to the Trixeo website inviting the user to explore the data on safety, links to prescribing information, and a statement that read "Note that coadministration of TRIXEO alongside some other treatments, such as strong CYP3A4 inhibitors, requires further consideration. Please see SmPC for full details." The Panel noted that, while the summary of

product characteristics was mentioned in the context of coadministration, there was no general statement to direct the reader to refer to the summary of product characteristics for the full information before prescribing, nor was there a link to the summary of product characteristics.

Whilst the Panel noted AstraZeneca's submission that the checklist was primarily intended to be used to identify which patients might be eligible for Trixeo, the Panel considered that it might not be immediately clear to a busy health professional that the summary of product characteristics contained additional important information on the use of the medicine that was not in the checklist, specifically regarding the need to immediately stop the use of Trixeo should signs and symptoms of acute narrow-angle glaucoma develop. The Panel considered that material had to be capable of standing alone with regard to the requirements of the Code and could not rely on qualification in the linked prescribing information or other linked material/webpages.

The Panel considered the immediate and overall impression of the checklist to a busy health professional. In the Panel's view, the omission of the statement "Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using this medicinal product and to contact their doctor immediately should any of these signs or symptoms develop.", compounded by the lack of any direction to refer to the summary of product characteristics for further information, meant that the checklist was misleading. The Panel, therefore, ruled a **breach of Clause 6.1**.

The Panel noted a button on the final page of the checklist invited the reader to explore the safety data. The Panel did not have this page before it.

The Panel noted the complainant had raised Clause 6.2 which stated, among other things, that any information, claim or comparison must be capable of substantiation. In the Panel's view there was no allegation that information was not capable of substantiation. The Panel therefore ruled **no breach of Clause 6.2**.

The Panel considered the omitted statement concerned important safety information about acute narrow-angle glaucoma, a potential medical emergency which required patients to stop treatment and contact their doctor immediately and, therefore in the context of patient safety it was particularly important that health professionals were made aware of this. The omission of this important information from the checklist meant that AstraZeneca had failed to maintain high standards and the Panel ruled a **breach of Clause 5.1** in that regard.

Clause 2 was a sign of particular censure and was reserved for such use. Prejudicing patient safety was an example of an activity likely to lead to a breach of this clause. Companies needed to take the utmost care when producing materials for health professionals to ensure that readers could not be misled as to the safety profile of the medicine. The Panel considered that the misleading impression created by the checklist, which was not sufficiently clear that it did not contain all the important safety information, meant that AstraZeneca had reduced confidence in and brought discredit upon the industry. The Panel ruled a **breach of Clause 2**.

APPEAL BY ASTRAZENECA

AstraZeneca's written basis for appealing is reproduced below.

> "Further to our email on 12th July 2024, please find below AstraZeneca's reasons for appealing the Panel's ruling of breaches 6.1, 5.1 and 2 of the ABPI Code of Practice

("the Code") in the above Case.

AstraZeneca strongly disagrees with the Panel's rulings in this case, and we have set out detailed reasons for this appeal below.

Background

The Complaint

The Trixeo product website is a promotional website intended for UK HCPs. It includes information about Trixeo, COPD, Aerosphere technology and hosts resources for HCPs and their patients. The eligibility checklist was accessible on the resources page. Anyone accessing the website has to declare that they are a UK HCP before they see any promotional content. The complainant alleged that the information provided around narrow angle glaucoma was incomplete, as the following information was missing *"Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using this medicinal product and to contact their doctor immediately should any of these signs or symptoms develop"*. The complainant alleged that an HCP would assume that question 11 encompassed full prescribing considerations for narrow angle glaucoma, and therefore patient safety had been jeopardised.

AstraZeneca were forwarded the complaint on 19th June 2023, and asked to consider requirements of clauses 6.1, 6.2, 5.1 and 2 of the Code.

AstraZeneca's Response and Panel Ruling

AstraZeneca responded to the PMCPA on 4th July 2023. The response letter advised the Panel that the eligibility checklist was solely designed to help HCPs establish whether a patient is eligible to be considered for Trixeo, aligned to the licenced indication. The material was not designed to provide information to HCPs about how to counsel patients before initiation or monitor patients following initiation of the medicine. The response provided to Q11 is consistent with the Summary of Product Characteristics (SPC) and clearly enables the HCP to establish that patients with narrow angle glaucoma are **eligible** to use Trixeo.

Counselling patients about the signs and symptoms of acute narrow-angle glaucoma following initiation of the medicine clearly falls outside of the initial consideration for eligibility and therefore outside the scope and intent of the material in question. The material also clearly refers HCPs to additional information relevant to the prescribing of the medicine including the SPC, Prescribing Information (PI), safety and efficacy information, dosage information, and NICE guidance.

The Panel's decision which was sent to AZ on 5th July 2024, considered the immediate and overall impression of the checklist to a busy HCP, and took the view that omission of the statement *"Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using this medicinal product and to contact their doctor immediately should any of these signs or symptoms develop"* in addition to lack of clear direction to refer to the Summary of Product Characteristics (SPC) before prescribing meant the checklist was misleading. The

omission of important patient safety information meant AstraZeneca had failed to maintain high standards, and ultimately AZ had misled HCPs on the safety profile of Trixeo bringing reduced confidence and discredit upon the industry.

The Panel ruled that AstraZeneca was in breach of clauses 6.1, 5.1 and 2 of the Code.

AstraZeneca's (AZ) Appeal

AstraZeneca strongly disagrees with the Panel's conclusion that the eligibility checklist was misleading and jeopardises patient safety and therefore, we are appealing the findings of breaches of clauses 5.1, 6.1 and 2 of the Code.

Structure and content of the eligibility checklist

The eligibility checklist is split into 2 sections:

- Section 1 includes questions 1–5, which ensure the patient meets the licensed indication for Trixeo. At the end of the first section, if the patient fits the licensed indication, the HCP is informed that 'your patient **may** be eligible', and signposted to information about COPD exacerbations on the Trixeo website, or invited to continue answering questions of the eligibility checklist. If the HCP clicked through to the website, they could navigate to information about Trixeo via option tab in the website wireframe and Trixeo prescribing information.
- Section 2 includes questions 6–13, which covers the relevant safety considerations prior to prescribing Trixeo.

Please refer to Table 1 in Appendix 1 [table provided to Appeal Board], for all safety precautions and contraindications for Trixeo as per the SPC, and whether they are relevant for an HCP pre- or post-prescription. Those that need to be considered by an HCP pre-prescription, were included in the eligibility checklist questions.

AstraZeneca's Response to Panel Ruling

We respond below to the reasons given by the Panel for concluding that the eligibility checklist was misleading, and that AZ had not maintained high standards and had reduced confidence in and brought discredit upon the industry:

Panel's Comments

- *"In the Panel's view, it could have been made clearer from the outset that the checklist was intended only to provide an overview of patient eligibility and that prescribers would need to refer to the summary of product characteristics for important information before prescribing."*
- *"There was no general statement to direct the reader to refer to the summary of product characteristics for the full information before prescribing, nor was there a link to the summary of product characteristics."*
- *"The Panel noted a button on the final page of the checklist invited the reader to explore the safety data. The Panel did not have this page before it."*

- *"The Panel considered that 'are eligible' (rather than, for example, "may be eligible") was a definitive statement that compounded the impression that there was no other information that would need to be considered."*
- *"Whilst the Panel noted AstraZeneca's submission that the checklist was primarily intended to be used to identify which patients might be eligible for Trixeo, the Panel considered that it might not be immediately clear to a busy health professional that the summary of product characteristics contained additional important information on the use of the medicine that was not in the checklist, specifically regarding the need to immediately stop the use of Trixeo should signs and symptoms of acute narrow-angle glaucoma develop. The Panel considered that material had to be capable of standing alone with regard to the requirements of the Code and could not rely on qualification in the linked prescribing information or other linked material/webpages."*

Panel's Ruling

- *"The Panel considered the immediate and overall impression of the checklist to a busy health professional. In the Panel's view, the omission of the statement "Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using this medicinal product and to contact their doctor immediately should any of these signs or symptoms develop.", compounded by the lack of any direction to refer to the summary of product characteristics for further information, meant that the checklist was misleading. The Panel, therefore,* ***ruled a breach of Clause 6.1****."*

AstraZeneca's Appeal

It was made clear at the outset that this was an eligibility checklist; this does not infer that HCPs would not need to refer to the SPC. The title of the eligibility checklist appearing on the front page **"Can your patient receive triple protection with TRIXEO? Find out which of the patients in your practice are eligible for TRIXEO, and which of those are not"** makes it sufficiently clear to HCPs that the intention of this material is to review eligibility for Trixeo treatment based on its indication and that it is not a comprehensive prescribing guide. The purpose of the checklist is to ensure the prescribing clinician considers important safety information before deciding whether Trixeo may be appropriate for their patient. The important safety considerations pre-prescription to assess eligibility are outlined in *Table 1*.

The omitted text which is the subject of the complaint *"Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using this medicinal product and to contact their doctor immediately should any of these signs or symptoms develop"* is related to HCP instructions for use and monitoring of a patient following prescription, and so this does not impact if the patient is eligible for treatment or not. No post-prescription monitoring requirements or considerations were included in the checklist for this reason. Therefore, we consider that it is reasonable to use 'definitive wording' using 'is' or 'are' in the instance that all eligibility criteria are met.

As the Panel points out, *"At the end of that section [section 2], there was a page with links to the Trixeo website inviting the user to explore the data on efficacy, safety and*

dosing, a note regarding coadministration, and links to prescribing information." HCPs are well used to making balanced prescribing decisions taking into account factors about the patient and the medicine. We submit that the eligibility checklist provided ample opportunity for HCPs to access additional information about the medicine; including at the end of the checklist (and if "your patient is eligible"), the HCP was presented with direct links to information on the Trixeo website and to its prescribing information pointing HCPs to seek further information before prescribing Trixeo.

Clause 12 of the Code requires that promotional materials have a link to the Prescribing Information. There is no requirement to also include the link to the full SPC as mentioned in the Panel's ruling. The link to Prescribing Information was available on the first and last page of the eligibility checklist, and includes the safety information related to anticholinergic activity from Section 4.4 of SPC:

"Anticholinergic activity: Due to anticholinergic activity, use with caution in patients with symptomatic prostatic hyperplasia, urinary retention or with narrow-angle glaucoma. Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using this medicinal product and to contact their doctor immediately should any of these signs or symptoms develop. Co-administration of this medicinal product with other anticholinergic containing medicinal products is not recommended."

In addition, the material included adequate opportunity for the HCP to access the full safety information for the product. This included:

1. Direct link to the prescribing information on the first and last page of the checklist. At the top of the Trixeo prescribing information, there is the prominent statement: **"Please refer to the Summary of Product Characteristics before prescribing".**
2. At the end of the checklist, if the patient is eligible for treatment with Trixeo, links were included to further information on the Trixeo website (including efficacy data, safety data, and dosing information) and to the prescribing information, providing the HCP an opportunity to seek further information about the medicine.
3. On the Trixeo safety page as shown below [screenshot provided], there is a section titled "Trixeo safety precautions". Overdose, missed doses and discontinuation are included here, with the following statement directly underneath: **"This is not an exhaustive list. Please consult the Summary of Product Characteristics for a full list of precautions and contraindications before prescribing."**

In summary, there were several opportunities flagged for HCPs to refer to prescribing information and the SPC before prescribing and the statement in question was relevant as a post-prescription consideration and therefore did not form part of the eligibility checklist; consequently, its omission was not misleading. We, therefore, refute the breach of Clause 6.1 of the Code.

Panel's Comments

- *"The Panel considered the omitted statement concerned important safety information about acute narrow-angle glaucoma, a potential medical emergency which required patients to stop treatment and contact their doctor immediately and, therefore in the context of patient safety it was particularly important that health professionals were made aware of this. The omission of this important information from the checklist meant that AstraZeneca had failed to maintain high standards".*
- *"Clause 2 was a sign of particular censure and was reserved for such use. Prejudicing patient safety was an example of an activity likely to lead to a breach of this clause."*
- *"Companies needed to take the utmost care when producing materials for health professionals to ensure that readers could not be misled as to the safety profile of the medicine."*

Panel's Ruling

- *The omission of this important information from the checklist meant that AstraZeneca had failed to maintain high standards and the Panel ruled a* ***breach of Clause 5.1*** *in that regard.*
- *"The Panel considered that the misleading impression created by the checklist, which was not sufficiently clear that it did not contain all the important safety information, meant that AstraZeneca had reduced confidence in and brought discredit upon the industry. The Panel ruled a* ***breach of Clause 2****."*

AstraZeneca's Appeal

Regarding question 11 of the checklist, subject of the complaint: "*Does your patient suffer from symptomatic prostatic hyperplasia, urinary retention or narrow-angle glaucoma?*" If the answer is 'Yes', the following message appears "*Due to its anticholinergic activity, TRIXEO should be used with caution in patients with symptomatic prostatic hyperplasia, urinary retention or with narrow-angle glaucoma.*" By including this precaution in the checklist as part of pre-prescription considerations, AstraZeneca has maintained high standards.

We completely agree that utmost care must be taken when producing materials for HCPs to ensure that readers are not misled. In this instance, AstraZeneca has not misled HCPs or prejudiced patient safety and instead, the patient eligibility checklist was designed to ensure that HCPs considered the relevant key safety information prior to prescribing the medicine. Therefore, we refute any breach of clauses 5.1 and 2 of the Code.

<u>Summary of AstraZeneca's Position</u>

- The eligibility checklist was designed as a resource to assist HCPs in assessment of patient eligibility for Trixeo, which was made explicitly clear in the checklist title and throughout the material. The checklist included key pre-prescription safety considerations as outlined in the SPC (see Table 1 in Appendix 1 [table provided to Appeal Board]). Symptoms that may develop after

treatment has started, like acute narrow-angle glaucoma, will not impact if the patient is eligible for treatment or not, and therefore was not deemed relevant for the purpose of this material.

- The checklist was intended to help HCPs better understand the safety considerations before prescribing Trixeo. Contrary to the Panel's concerns, a 'busy HCP' is likely to be in a much better position to understand potential safety considerations before prescribing Trixeo after engaging with the checklist versus one who has not.
- HCPs were signposted to information on the Trixeo website (including safety information) and Trixeo prescribing information at the end of the checklist, directing the HCP to seek further information prior to prescribing. This section in the PI regarding narrow-angle glaucoma is clearly bolded under ***"Anticholinergic activity"*** so this will not be missed by HCPs.
- 'Consult the SPC before prescribing' was included on the Trixeo website safety page and at the top of the prescribing information (links to both included in the checklist).

AstraZeneca places the highest importance upon patient safety. This is why even though this tool was focused on eligibility criteria we nonetheless included the specific warning message at question 11, referred to above. There was no attempt to hide this warning or mislead HCPs that were using the checklist. Whilst we note the Panel's comments around the need to consider the impact on busy HCPs, even the busiest HCPs are aware that there is a great deal of other important information contained with the Prescribing Information and AstraZeneca submits that the warning provided was sufficient to alert HCPs of the need to take caution and that HCPs would then be likely to refer to other materials like the Prescribing Information when moving forward with future treatment decisions.

To reiterate, AstraZeneca's view is that a warning message such as that included by AstraZeneca is a sufficient flag to HCPs of the issues of which they need to be aware and HCPs will know that further information will be available to them. However, even if the Panel is correct that this warning should have given further information, we do not believe that there is any evidence to support a finding that AstraZeneca had not maintained high standards or brought the industry into disrepute. In particular, we would submit that efforts had been made to provide a warning and that the overall tool had been created carefully and diligently: we do not think that it follows that any case in which the Panel believes that additional information should have been provided must automatically be a breach of clause 2 and/or 5.1.

AstraZeneca strongly believes that Clause 2 should be reserved for such serious circumstances where a company has genuinely brought discredit upon the industry. Ruling a breach of Clause 2 in this case is disproportionate being neither justified nor warranted.

In summary, we disagree with the Panel's Ruling that the checklist was misleading, AstraZeneca failed to maintain high standards and brought the industry into disrepute, for the reasons outlined above."

RESPONSE FROM THE COMPLAINANT

There was no response from the complainant.

APPEAL BOARD RULING

The Appeal Board observed that question 11 of the checklist at issue stated, “Does your patient suffer from symptomatic prostatic hyperplasia, urinary retention or narrow-angle glaucoma?” If the answer was “Yes”, a boxed message appeared stating “Due to its anticholinergic activity, TRIXEO should be used with caution in patients with symptomatic prostatic hyperplasia, urinary retention or with narrow-angle glaucoma.” The Appeal Board was advised by the representatives of AstraZeneca that the answer to question 11 had no effect on the outcome of the checklist. Whether the answer to question 11 was yes or no, the checklist user would proceed to question 12.

The Appeal Board confined its determination to question 11 of the checklist and the omission of the SPC statement “Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using this medicinal product and to contact their doctor immediately should any of these signs or symptoms develop”.

The Appeal Board recognised that acute narrow-angle glaucoma was a medical emergency but considered context and the intended purpose of the material at issue was important.

The Appeal Board accepted AstraZeneca’s submission that the checklist was intended to assist health professionals in assessment of patient eligibility for Trixeo.

The Appeal Board considered that the SPC text in question that was omitted from question 11 of the checklist was in relation to the health professional informing the patient about the signs and symptoms of acute narrow-angle glaucoma and to stop using the product and contact their doctor immediately, which would likely be an action that a health professional would take after assessing patient eligibility and once the prescribing decision had been made.

In the particular circumstances of this case the Appeal Board did not consider that the eligibility checklist was likely to be viewed by health professionals as a comprehensive prescribing guide. The Appeal Board observed that the first page and last page of the checklist included a prominent link to prescribing information.

The Appeal Board did not consider that question 11 of the checklist was misleading as alleged and it ruled **no breach of Clause 6.1**. The appeal on this point was successful.

The Appeal Board agreed that companies needed to take the utmost care when producing materials for health professionals to ensure that readers could not be misled as to the safety profile of the medicine. This was particularly important with the widening remit of who could be a prescriber and their differing levels of training.

Nonetheless, taking into account its ruling of no breach of Clause 6.1, the Appeal Board considered, on the narrow grounds of the appeal regarding question 11 of the checklist, that high standards had been maintained in this regard and ruled **no breach of Clause 5.1**. The appeal on this point was successful. The Appeal Board consequently ruled **no breach of Clause 2** which was reserved for particular censure. The appeal on this point was successful.

Complaint received	**12 June 2023**
Case completed	**19 September 2024**