CASE AUTH/3488/3/21

COMPLAINANT v ASTRAZENECA

Trixeo Website

An anonymous, contactable complainant complained about the promotion of Trixeo Aerosphere (formoterol/glycopyrronium/budesonide) on AstraZeneca UK Limited's website (www.trixeo.co.uk). Trixeo Aerosphere was indicated as a maintenance treatment in adults with moderate to severe chronic obstructive pulmonary disease (COPD).

The complainant alleged that the Trixeo website did not meet the high standards within the Code. The homepage did not have different sections for health professionals, patients or members of the public. All content was accessible to anyone and so was promotion to the public and this would lead to members of the public requesting Trixeo.

The complainant alleged that the homepage had the brand name with the generic name underneath which was too small to read and this was so on every page of the website.

The complainant alleged that a claim on the homepage, 'Unleash protection from exacerbations with Trixeo[1,2*]', was not appropriate as the claim was qualified with a footnote and did not standalone. In tiny text further down the page, clarification was provided; the complainant alleged that the relative risk reduction was provided but not the actual risk reduction for the percentage reduction in exacerbations, which was misleading.

The complainant noted text on the homepage that 'In the clinical trial programme for Trixeo, LAMA/LABA refers to glycopyrronium/formoterol fumarate and ICS/LABA refers to budesonide/formoterol fumarate' which were AstraZeneca medicines and so the prescribing information should have been provided for Symbicort Turbohaler and Bevespi Aerosphere. Only prescribing information for Trixeo was provided.

The complainant alleged that a photograph of a dragon on the homepage implied that Trixeo had special properties which was in breach of the Code.

The complainant stated that on the efficacy page there were several claims about exacerbation reduction from the KRONOS and ETHOS studies. However, these claims only presented relative risk reduction and not absolute risk reduction. The complainant alleged four breaches of the Code. The complainant alleged that the claims were misleading as they exaggerated the actual exacerbation reductions for health professionals.

The complainant alleged that the headline claim on the safety page, 'Protection you can count on', was misleading and ambiguous as it implied there were no side-effects. The

big font size gave a misleading impression. The complainant also noted another prominent claim, 'A well-established safety profile'.

The complainant alleged that the prominent claim on the 'Learn More' section of the website 'You can prevent exacerbations' was misleading as it implied any patient taking Trixeo for COPD would always be prevented from having an exacerbation. However, that was not so as a COPD patient could exacerbate even when on stabilised therapy due to cold weather, adherence issues, not having follow-ups or even not using an inhaler properly which could be the case with Trixeo.

The complainant noted that the Trixeo formulary pack, available from the 'Learn More' section page, also only had relative risk reduction of exacerbations but not absolute risk reductions. It also did not provide the prescribing information for Symbicort or Bevespi Aerosphere, although there was implied mention of these two medicines throughout.

The complainant alleged that using capital letters for misleading claims was in poor taste.

The complainant alleged that the entire website was misleading, did not meet mandatory requirements of the Code and provided inaccurate and misleading claims throughout. The complainant queried the competency level of the signatory who approved the website and alleged a breach of Clause 2 on several fronts. The mobile view of this website was also a different final form to the website in that the prescribing information was not readily available as a single click away.

The detailed response from AstraZeneca is given below.

1 Access to the website

The Panel noted AstraZeneca's submission that the website was intended to be accessed by, and therefore was designed solely for, UK health professionals; a health professional declaration pop-up would have been displayed which required all users to confirm that they were health professionals before they could access any materials. The Panel noted AstraZeneca's submission that anyone not declaring themselves to be a health professional would be directed to the public AstraZeneca UK website.

The Panel noted that, according to AstraZeneca, visitors would have seen the health professional pop-up the first time they accessed the website; however, certain individuals, who allowed the use of cookies on specific browsers, might not have seen the pop-up on later visits if they used the same device and they had confirmed that they were a health professional on their first visit. The Panel noted AstraZeneca's submission that the link to the website was not publicised or sent to any patient or member of the public.

The Panel considered that the complainant had not provided any details as to how he/she had accessed the website; it was impossible to know whether he/she had accessed it initially and responded to the pop-up and then not been presented with the pop-up at subsequent visits to the website or whether he/she had freely accessed the website on the first instance on a device not previously used by a health professional who had responded to the pop-up.

The Panel noted that the complainant bore the burden of proof and did not consider that he/she had established his/her case that, on the balance of probabilities, that the website constituted promotion to the public. The Panel, therefore, ruled no breaches of the Code including no breach of Clause 2.

2 Non-proprietary name

The Panel noted AstraZeneca's submission that the website was built and certified for desktop view and, in that view, the generic name occupied a total area of no less than that taken up by the brand name and was easily readable on all pages of the website when viewed on a desktop, laptop and iPad. The Panel did not agree about the size of the non-proprietary name; in the Panel's view, the area occupied by the non-proprietary name was less than that occupied by the brand name. Nonetheless, the Panel considered that the non-proprietary name was readily readable and thus ruled no breach of the Code with regard to the desktop view of the website.

The Panel further noted that the brand logo image was not tested on mobile devices during certification by AstraZeneca and that AstraZeneca acknowledged that the generic name was small and difficult to read when viewed on mobile devices. A breach of the Code was ruled.

3 Accessibility of prescribing information

The Panel noted AstraZeneca's submission that whilst the prescribing information remained accessible on a mobile device, it required one click to reveal the full option menu and a further click to then access the prescribing information which was contrary to AstraZeneca's procedures, which required that prescribing information on promotional websites should be available via a single click link.

The Panel considered that the accessibility of prescribing information through a two click link, rather than a single click link, when viewed on a mobile device, did not fulfil the requirements of the Code and ruled a breach as acknowledged by AstraZeneca. The Panel considered that as the prescribing information was still accessible when viewed on a mobile device, albeit via two clicks, that did not constitute a breach of the Code including Clause 2.

The Panel considered that the website should have been reviewed and certified to ensure that it displayed correctly across different devices and that if it was designed for only desktop view, that this should have been made clear to readers. As the website had not been certified for viewing on mobile devices, the Panel ruled a breach of the Code and a further breach as high standards had not been maintained.

The Panel considered that a robust certification procedure underpinned self-regulation and although noting its comments and ruling above, it did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2, which was a sign of particular censure and was reserved for such use; no breach was ruled.

4 Alleged misleading claims and images

a) Claim 'Unleash protection from exacerbations with Trixeo'

The Panel noted the complainant's allegation that the claim 'Unleash protection from exacerbations with Trixeo' was not appropriate as it did not stand alone and was qualified by a footnote.

The Panel agreed with AstraZeneca's submission that the footnote in this particular context was used to provide more detailed information rather than providing a qualification and that the information in the footnote did not detract from the claim's ability to standalone. The Panel considered that the complainant had not proven his/her case and thus ruled no breach of the Code in that regard.

The Panel noted that the footnote included both the relative risk reductions and absolute rate reductions; the relative risk reduction was presented as a percentage and the absolute rate reduction was the mean number of exacerbations per patient per year.

The Panel further noted the complainant's concern that, as with the webpage, the relative risk reduction of exacerbations had been included in the Trixeo formulary pack, which was downloadable from the 'Learn More' section of the website, but there were no absolute risk reductions.

The Panel considered that both the absolute values and relative risk reduction had been provided as part of the footnote on the website and in the downloadable formulary pack, and therefore, based on the narrow allegation, no breach of the Code was ruled in each regard.

The Panel noted that the complainant had also alleged that several claims about exacerbation reduction, from the KRONOS and ETHOS studies, on the efficacy page of the website only presented relative risk reduction and not absolute risk reductions and in that regard were misleading as they exaggerated the actual exacerbation reductions for health professionals. The complainant had not specified which claims were at issue and it was not for the Panel to identify those claims on his/her behalf and rule on each one. The Panel examined the webpage at issue, and it appeared that all claims about exacerbation reduction included both the relative risk reduction and the absolute risk reductions. No breaches of the Code were ruled.

b) Claim 'You can prevent exacerbations'

The Panel noted the complainant's allegation that the claim 'You can prevent exacerbations' was misleading as it implied that any patient taking Trixeo for COPD would always be prevented from having an exacerbation despite the various triggers that could cause COPD patients on stabilised therapy to exacerbate.

The Panel considered that health professionals would be familiar with the prevalence and likelihood of exacerbations in COPD, even in patients who appeared to be well stabilised. In the Panel's view, health professionals reading the claim would not be misled into thinking that all exacerbations would be prevented with Trixeo. The Panel thus did not consider that the claim was misleading as alleged and ruled no breach of the Code.

c) Claims: 'Protection you can count on' and 'A well-established safety profile'

The Panel did not consider that the claims 'Protection you can count on' and 'A well-established safety profile' implied that Trixeo had no side-effects as alleged. In the Panel's view, it was not in itself unreasonable to refer to 'protection you can count on' in the context of a medicine and the Panel considered that reference to a well-established safety profile would be read as there being extensive information about the safety profile and that the safety profile was not unreasonable for a medicine treating COPD. Further, the three components of Trixeo had been available prior to the introduction of Trixeo. The Panel did not consider that the large font size of the claims gave a misleading impression as alleged. The Panel thus ruled no breaches of the Code.

d) Capitalisation and size of font

The Panel did not consider, with regard to the complainant's allegation that the use of upper case letters or different sizes of font was in poor taste; in the Panel's view, it might be helpful to use such features to aid readability and presentation.

The Panel noted that no reasons had been given in relation to this allegation, although the complainant had made a reference to misleading claims (point c above). Based on the evidence before it, the Panel ruled no breach of the Code.

e) Dragon image

The Panel noted that the complainant had provided no explanation as to why, in his/her view, the depiction of a dragon implied that Trixeo had special properties. The Panel did not consider that the image claimed or conveyed that Trixeo had special properties as alleged. Based on the evidence submitted by the complainant, the Panel did not consider that the image failed to maintain high standards and no breach of the Code was ruled.

5 Prescribing information for Bevespi and Symbicort Turbohaler

The Panel noted that the Trixeo formulary pack, downloadable from the website, mentioned budesonide-formoterol fumarate (Symbicort) and glycopyrrolate-formoterol fumarate (Bevespi Aerosphere) by non-proprietary names only, in relation to their inclusion in the ETHOS and KRONOS studies. The Panel noted AstraZeneca's submission that the website and formulary pack were developed to promote Trixeo and not Bevespi or Symbicort; Bevespi and Symbicort were necessary comparator arms and were thus included.

The Panel noted that clinical results for Bevespi Aerosphere and Symbicort Turbohaler were discussed, albeit only by using non-proprietary names, in the formulary pack and both products were referred to by non-proprietary name on the website. The Panel considered, however, that as both medicines were AstraZeneca products, their mention on the website and in the formulary pack meant that prescribing information should have been included in both. As no prescribing information for the two products had been provided, breaches of the Code were ruled for each medicine with regard to the website and the formulary pack. The Panel considered that high standards had not been maintained with regard to the formulary pack and the website.

The Panel did not consider that the particular circumstances warranted a ruling of a breach of Clause 2.

6 General summary allegation

The Panel noted that the complainant concluded by alleging that the entire website was misleading and did not meet the mandatory requirements of the Code.

The Panel noted AstraZeneca's submission that due to a failure to check the function of the website on mobile devices, the issue was limited to smartphones and the impact was limited.

The Panel noted its comments and rulings above however did not consider that the overall circumstances warranted further rulings of breaches of the Code, including Clause 2.

An anonymous, contactable complainant complained about the promotion of Trixeo Aerosphere (formoterol/glycopyrronium/budesonide) on AstraZeneca UK Limited's website (www.trixeo.co.uk (ref GB-25660. DOP: February 2021)). Trixeo Aerosphere was indicated as a maintenance treatment in adults with moderate to severe chronic obstructive pulmonary disease (COPD) who were not adequately treated by a combination of an inhaled corticosteroid (ICS) and a long-acting beta2-agonist (LABA) or combination of a long-acting beta2-agonist (LABA) and a long-acting muscarinic antagonist (LAMA).

COMPLAINT

The complainant alleged that the Trixeo website did not meet the high standards within the Code, was in breach of several clauses and misled users. In particular, the complainant alleged that the homepage did not have different sections for health professionals, patients or members of the public. All content was accessible to anyone and so was promotion to the public. The complainant alleged that this would lead to members of the public speaking to their health professionals to request Trixeo. This was a huge error. The complainant alleged breaches of Clauses 28.1, 28.3, 26.1, 26.2, 9.1 and 2.

The complainant further noted that the homepage had the brand name, the logo at the top and the generic name underneath. The complainant alleged that the generic name was too small to read in breach of Clause 4.3. The complainant added that the generic name was too small on every page of the website.

The complainant alleged that a claim on the homepage, 'Unleash protection from exacerbations with Trixeo[1,2]*', was not appropriate as the claim was qualified with a footnote and did not standalone in isolation. In the corresponding footnote in tiny text further down the page, clarification was provided '*Significant reductions in the rate of moderate or severe exacerbations vs LAMA [long-acting muscarinic antagonists]/LABA [long-acting β2 agonists] (24%, n=2137 vs n=2120, annual rates 1.08 vs 1.42, 95% CI 0.69–0.83; p<0.001) and ICS [inhaled corticosteroid]/LABA (13%, n=2137 vs n=2131, annual rates 1.08 vs 1.24, 95% CI 0.79–0.95; p=0.003)'. The complainant noted that the relative risk reduction was provided but not the actual risk reduction for the % reduction in exacerbations which was misleading in breach of Clause 7.2.

The complainant noted that text below the footnote on the homepage stated that 'In the clinical trial programme for Trixeo, LAMA/LABA refers to glycopyrronium/formoterol fumarate and ICS/LABA refers to budesonide/formoterol fumarate'. Both the ICS/LABA and LABA/LAMA referred to were AstraZeneca medicines and so the prescribing information should have been provided for Symbicort Turbohaler and Bevespi Aerosphere. Only prescribing information for Trixeo was provided. The complainant alleged breaches of Clause 4.1 (twice) and Clause 9.1.

The complainant noted that there was a photograph of a dragon on the homepage which implied that Trixeo had special properties and in that regard he/she alleged breaches of Clauses 7.10 and 9.1.

The complainant stated that on the efficacy page there were several claims about exacerbation reduction from the KRONOS and ETHOS studies. However, these claims only presented relative risk reduction and not absolute risk reduction. The complainant alleged four breaches of Clauses 7.2 and 9.1. The complainant alleged that the claims were misleading as they exaggerated the actual exacerbation reductions for health professionals.

The complainant alleged that the headline claim on the safety page, 'Protection you can count on' was misleading claim and ambiguous as it implied there were no side-effects. The big font size gave a misleading impression. The complainant also noted another prominent claim, 'A well-established safety profile'. The complainant alleged breaches of Clauses 7.2, 7.4, 7.9, 9.1 and 2.

The complainant further alleged that the prominent claim on the 'Learn More' section of the website 'You can prevent exacerbations' was misleading as it implied any patient taking Trixeo for COPD would always be prevented from having an exacerbation. However, that was not so as a COPD patient could exacerbate even when on stabilised therapy due to cold weather, adherence issues, not having follow-ups or even not using an inhaler properly which could be the case with Trixeo. The complainant noted that the Trixeo formulary pack (26/01/2021 Job Number: GB23993), which was available from download on the 'Learn More' section page, also only had relative risk reduction of exacerbations but not absolute risk reductions. It also did not provide the prescribing information for Symbicort or Bevespi Aerosphere, although there was implied mention of these two medicines throughout the formulary pack. The complainant alleged breaches of Clauses 4.1, 7.2, 9.1 and 2.

The complainant alleged that using capital letters for misleading claims was in poor taste and in breach of Clause 9.7.

The complainant submitted that the entire website was misleading, did not meet mandatory requirements of the Code and provided inaccurate and misleading claims throughout. The complainant considered that one would have to query the competency level of the signatory who approved and released this website and alleged a clear breach of Clause 2 on several fronts. The mobile view of this website was also a different final form to the website in that the prescribing information was not readily available as a single click away. The complainant alleged breaches of Clauses 14.1, 4.4, 9.1 and 2.

When writing to AstraZeneca, the Authority asked it to consider the requirements of the clauses cited by the complainant with the exception of Clause 28.3. In the case preparation manager's view, the allegation of a breach of Clause 28.3 duplicated the allegation of a breach of Clause 26.2 and there was thus no need to consider both clauses.

RESPONSE

AstraZeneca submitted that it took compliance with the Code extremely seriously and was committed to maintaining high standards in relation to all information it provided about its products and in all related activities.

1 The Complaint

AstraZeneca briefly summarised the complainant's allegation about the Trixeo website as follows:

- Access to the website – the website did not have separate sections for health professionals and patients or members of the public.

- Non-proprietary name – the size of the generic name underneath the brand name was too small to read when viewed on a mobile device.

- Prescribing information was not readily accessible – prescribing information was not a single click away when viewed on a mobile device.

- Misleading claims and imagery:

    - Several relative risk reduction claims did not have corresponding absolute risk reductions
    - The claim 'Unleash protection from exacerbations with Trixeo' was inappropriately qualified with a footnote at the bottom of the homepage
    - The claim 'You can prevent exacerbations' on the 'Learn More' page implied that any patient taking Trixeo for COPD would always be prevented from having an exacerbation
    - Using an image of a dragon was misleading because it implied that Trixeo had special properties
    - The claims 'Protection you can count on' and 'A well-established safety profile' were misleading and ambiguous and implied that Trixeo had no side-effects
    - The use of capital letters for the aforementioned claims was misleading and in poor taste.

- The website should have included the prescribing information for Bevespi Aerosphere and Symbicort Turbohaler.

- General allegations:

    - The entire website was misleading, did not meet mandatory requirements of the Code and provided inaccurate and misleading claims throughout.
    - The competency of the signatory who approved and released the website was questionable.

AstraZeneca submitted that it was confident that the content of the website was appropriate and that all of the promotional claims were balanced, accurate and well-substantiated. That said, as part of AstraZeneca's investigation, it had discovered that that there was an error in the way that

the website was displayed on mobile devices which it believed had led to breaches of Clauses 4.3, 4.4 and 14.1 of the Code. It was important to note that these breaches were limited to the display of the website when viewed on a mobile device and were not present when the website was viewed on any desktop, laptop, iPad or other device. The remainder of AstraZeneca's response letter provided more information on the website and explained why it refuted all other allegations or suggestions that Clauses 2, 4.1, 7.2, 7.4, 7.9, 7.10, 9.1, 9.7, 26.1, 26.2 and 28.1 of the Code had been breached.

2 The website

AstraZeneca submitted its website, trixeo.co.uk, was designed to provide UK health professionals with information about Trixeo Aerosphere. Trixeo was a prescription only medicine indicated as a maintenance treatment in adult patients with moderate to severe COPD who were not adequately treated by a combination of an inhaled corticosteroid and a long-acting beta 2-agonist or combination of a long-acting beta 2-agonist and a long-acting muscarinic antagonist.

AstraZeneca stated that following receipt of this complaint, the website was taken down whilst it addressed the issues relating to its display on mobile devices referred to above; the website would remain offline until the company was satisfied that those issues had been resolved.

3 AstraZeneca's response to the complaint

3.1 Access to the website

AstraZeneca submitted that the complainant alleged that the website did not have separate sections for health professionals and patients or members of the public and should therefore be deemed as promoting a prescription medicine to the public.

To be clear, the website was intended to be accessed by, and therefore designed solely for, UK health professionals. In keeping with common practice in the industry, the website was constructed so that a 'HCP [health professional] declaration' pop-up would be displayed which required all users to confirm that they were health professionals before they could access any materials. Anyone not declaring themselves to be a health professional would be automatically directed to the public AstraZeneca UK website.

In addition to the pop-up itself, the website was also designed to include an extra notice in the footer of each page on the site, stating:

> '*This website is intended for doctors, nurses and pharmacists in the UK*.'

The website was certified with the pop-up and footer message.

AstraZeneca was made aware that some users could access the website without a health professional pop-up every time they visited it on the afternoon of 11 March 2021 and its IT team were notified of that at 15.54. This was immediately escalated to AstraZeneca's digital team, which carried out a rigorous review and refresh of the website. That task was completed by 16:54 the same day.

AstraZeneca's IT team was unable to identify any specific issue or fault. It was AstraZeneca's belief that everyone who accessed the website before that date would have seen the health professional pop-up the first time they accessed the website. However, certain individuals, who allowed the use of cookies on specific browsers (Chrome, Safari, Edge), might not have seen the pop-up on later visits if they used the same device and they had confirmed that they were a health professional on their first visit to it. AstraZeneca understood that many other UK pharmaceutical companies adopted this approach and it meant that the only circumstance in which a member of the public could access the website without having to make a declaration would be if they were sharing a device with a health professional who had previously visited that website.

AstraZeneca noted that the link to the website was not publicised or sent to any patient or member of the public. In the unlikely event that a member of the public navigated to the website using a device shared with a health professional, they would still have been notified that the website was only intended for health professionals, as a result of the message in the footer on each page. The fact that the website was designed to include footer notices in addition to the pop-up, was testament to the fact that AstraZeneca took extra precautions to ensure compliance with the Code.

AstraZeneca's IT team had examined the issue and had taken further steps to guard against this type of technical workaround in the future. For example, AstraZeneca was creating a pop-up button which remained on the page and allowed the notice to be re-read upon clicking the button, even after users had confirmed their health professional status.

In summary, AstraZeneca submitted that the website did not advertise Trixeo to the public at any time and it thus denied breaches of Clauses 2, 9.1, 26.1, 26.2 and 28.1 of the Code.

3.2 Non-proprietary name

The complainant alleged that the size of the generic name, appearing below the Trixeo brand name on the homepage and subsequent pages of the website, was too small to read.

AstraZeneca submitted that the website was built and certified for desktop view. In that view, the generic name occupied a total area no less than that taken up by the brand name and was easily readable on all pages of the website. The website displayed correctly on desktop, laptop and iPad. However, AstraZeneca accepted that the generic name was not easy to read when viewed on a mobile device as a result of a technical issue, that unfortunately, was not identified prior to launch.

AstraZeneca wished to highlight that its procedures required all websites to be reviewed and certified on both desktop and mobile devices. AstraZeneca's Materials Management Guidance Document referred to the review of:

> '*Screen shots of all pages (including core pages, hidden webpages, error webpages, interactive and dynamic content as well as responsive design in both desktop and mobile formats*.'

The Veeva Vaults PromoMats (VVPM) Document Owner Checklist included the following reminder:

'*Brand/non-proprietary name – check size and position requirements*.'

These procedures were reinforced by training of all relevant AstraZeneca personnel. However, in this instance, due to human error, an oversight occurred during certification of the website, with the result that the brand logo image was not tested on mobile devices. AstraZeneca therefore acknowledged that the generic name was small and difficult to read when viewed on mobile devices and that the appearance of the website did not comply with Clause 4.3. However, immediately following receipt of the complaint, specific measures were put in place to ensure that the size of the generic name would appear larger on each page of the website and would be easily readable on a mobile device when the website went live again.

3.3 Prescribing information was not readily accessible

The complainant alleged that the prescribing information for Trixeo was not available through a single click link when the website was viewed on a mobile device.

As explained above, the website was built and certified for desktop view. The website displayed correctly on desktop, laptop and iPad. When viewed on a mobile device the prescribing information remained accessible but it required one click to reveal the full option menu and a further click to then access the prescribing information. AstraZeneca accepted that, in these limited circumstances, it took two clicks to access the prescribing information rather than one . AstraZeneca noted that its procedures clearly required that the prescribing information on promotional websites should be available via a single click link. However, due to the error described in above, the website was not reviewed on a mobile device for certification purposes and therefore it was not identified that two clicks might be required to access the prescribing information in this instance.

As soon as AstraZeneca was made aware of this issue, immediate action was taken to correct the website view on mobile devices and it had now installed a prescribing information button on the webpage which was available via a single click when viewed on any device. AstraZeneca noted that the errors identified in points 3.2 and 3.3 above both arose from the same root cause, ie a fault in the display of the website on mobile devices. AstraZeneca was aware of its obligations to ensure that digital content displayed correctly across all platforms where it was likely to be accessed and it took the issues raised in this complaint very seriously. The testing of websites on all digital platforms and ensuring prescribing information was accessible via a single click was a fundamental part training for all signatories and these requirements were something the company expected its signatories to check.

Consequently, AstraZeneca accepted that the website, when viewed on a mobile device, did not comply with Clause 4.4. In circumstances where the image viewed on a mobile device was not identical to the certified view, AstraZeneca accepted that this constituted a breach of Clause 14.1. Given that the prescribing information was at all times accessible via a single link when the website was viewed via desktop, laptop or iPad and was still accessible when viewed on a mobile device, albeit via two clicks, AstraZeneca believed strongly that this did not constitute a breach of Clauses 9.1 and 2.

3.4 Misleading claims and images

The complainant alleged that several claims were ambiguous and misleading and that the imagery was misleading on account that it implied Trixeo exhibited special properties.

AstraZeneca noted that it took extreme care to ensure that the claims on the website complied with the Code and all other relevant guidance and legislation. That included actively reaching out to The Medicines and Healthcare products Regulatory Agency (MHRA) for pre-vetting and approval of the majority of images and claims included on the website. Whilst AstraZeneca understood that the MHRA was not responsible for enforcing compliance with the Code, the issues raised by the complainant (the accuracy and balance of the information and whether that was misleading) were not materially different when considered under either the Human Medicines Regulations 2012 or under the Code. In these circumstances, the MHRA's robust and objective assessment of the suitability of presented data, images and claims provided an important defence against the complainant's allegations.

Claim 'Unleash protection from exacerbations with Trixeo'

AstraZeneca noted that the complainant had alleged that this was not appropriate as it was qualified with a footnote and did not stand alone in isolation. The footnote in question stated:

> 'Significant reductions in the rate of moderate or severe exacerbations vs LAMA/LABA (24%, n=2137 vs n=2120, annual rates 1.08 vs 1.42, 95% CI 0.69–0.83; p<0.001) and ICS/LABA (13%, n=2137 vs n=2131, annual rates 1.08 vs 1.24, 95% CI 0.79–0.95; p=0.003).'

AstraZeneca was aware that the Code provided that claims should be 'capable of standing alone' and that 'in general' they should not be qualified with a footnote. However, AstraZeneca maintained that the use of a footnote in this particular context was appropriate because it was used to provide more detailed information substantiating the claim rather than providing a substantive qualification. The information in the footnote did not detract from the claim's ability to standalone. Consequently, AstraZeneca did not accept the complainant's allegation that this was in breach of Clause 7.

Risk reduction

The complainant alleged that the way data was presented in the footnote on the homepage was misleading because it provided information on relative risk reduction for percentage reduction in exacerbations but did not state the absolute risk reduction. The complainant alleged this was in breach of Clause 7.2 of the Code, which required that 'relative risk should never be referred to without also referring to the absolute risk'.

AstraZeneca submitted that the allegation was factually incorrect. The footnote included both relative rate reductions and absolute rate reductions as stated below:

> 'Significant reductions in the rate of moderate or severe exacerbations vs LAMA/LABA (24%, n=2137 vs n=2120, annual rates 1.08 vs 1.42, 95% CI 0.69–0.83; p<0.001) and ICS/LABA (13%, n=2137 vs n=2131, annual rates 1.08 vs 1.24, 95% CI 0.79–0.95; p=0.003).'

The absolute annual rates in terms of the number of patients affected were clearly provided after each relative risk data point. Moreover, the MHRA explicitly recommended prominently stating the absolute rates wherever a claim was made relating to relative reductions . This met the requirement of the Code and there was no requirement to provide absolute numbers as percentages or in any format other than that provided in the footnote.

The same omission was alleged by the complainant in relation to the same data which appeared on the efficacy page and in the formulary pack. Again, the absolute annual rates were clearly referenced in exactly the same way stated above.

Consequently, AstraZeneca denied a breach of Clause 7.2.

Claim 'You can prevent exacerbations'

AstraZeneca noted that the complainant had alleged that this claim on the 'Learn More' page was misleading because it implied any patient taking Trixeo for COPD would always be prevented from having an exacerbation' and even patients on stabilised therapy could exacerbate due to cold weather, adherence issues, not having follow ups or even not using an inhaler properly which could be the case with Trixeo.

AstraZeneca submitted that the 'Learn More' page was designed to house broader disease education content related to the holistic care for COPD patients in order to prevent exacerbations. The header referenced by the complainant was a general call to action for health professionals to think about how to prevent exacerbations of COPD. The statement was not a claim about Trixeo – it was not worded 'You can prevent exacerbations with Trixeo'. It was clear from the information on the page that the content was not solely focussed on Trixeo. The references to the various webinars referred to the management of COPD, including through 'local healthcare systems' and a 'holistic approach' and not the use of Trixeo. There was no reference or implication that exacerbations could be prevented in every patient who was prescribed Trixeo.

AstraZeneca noted that the complainant did not identify any particular clause in relation to this allegation. Nonetheless, the company did not accept that the claim was misleading or in breach of any clause of the Code.

Claims 'Protection you can count on' and '*A well-established safety profile'*

AstraZeneca noted that the complainant alleged that these claims were misleading and ambiguous because they implied that Trixeo had no side-effects; breaches of Clauses 7.2, 7.4, 7.9, 9.1 and 2 had been alleged.

AstraZeneca agreed that it was important to include accurate and balanced information about potential adverse events when discussing use of its medicines; it believed the website met those requirements and therefore, it strongly disputed that the claims had the meaning alleged by the complainant.

The claim 'Protection you can count on' was principally focussed on benefits of the medicine but it was accompanied by prominent statements 'A well-established safety profile' and 'the risk of pneumonia associated with Trixeo is low relative to its benefits for exacerbations'. AstraZeneca maintained that the meanings of these statements were clear and balanced. Moreover, at the top of the page under 'A well-established safety profile', all of the most commonly reported adverse events were stated. All claims were directly referenced to the summary of product characteristics (SPC) and the registrational trials (ETHOS and KRONOS) (copies provided). The website never stated nor implied that Trixeo had no side-effects. AstraZeneca did not accept the complainant's allegations that there was a breach of Clauses 7.2, 7.4, 7.9, 9.1 and 2.

Capitalisation and size of font

AstraZeneca noted that the complainant alleged that capitalisation of the claims was in poor taste and that the use of large font was misleading and constituted a breach of Clause 9.7.

Capital letters and larger font size were used consistently and repeatedly for headings throughout the website. AstraZeneca was aware that the Code required avoidance of 'extremes' in formatting but it submitted that there was nothing extreme about the consistent use of capital letters for headings to demark sections on a webpage. The Code did not suggest otherwise. The choice of font had been used to enhance clarity of the information presented not to mislead. It was a formatting choice that had been used to aid readability. Consequently, AstraZeneca denied a breach of Clause 9.7.

Dragon image

AstraZeneca noted that the complainant had provided no explanation or particular objection with regard to his/her allegation that the website's inclusion of an image of a dragon inferred that Trixeo had special qualities.

The image depicted a small dragon sitting on a human hand and exhaling three flames representing the three active pharmacotherapies of the product. The image was carefully designed to appear non-threatening and to convey a message of reassurance and protection from exacerbations within the patient's control. This image went through extensive testing as part of a unified global marketing campaign (launched in every major market in which the medicine had been approved), and in preparation for which, AstraZeneca specifically submitted marketing materials to the MHRA in the UK. The MHRA did not raise any concerns with regard to this imagery. Therefore, AstraZeneca did not accept that this image was in breach of Clauses 7.10 or 9.1.

3.5 Prescribing information for Bevespi and Symbicort Turbohaler

AstraZeneca noted that the complainant referred to the fact that Bevespi Aerosphere and Symbicort Turbohaler were mentioned on the website and in the formulary pack, which was available to download via the website. Since both were AstraZeneca medicines, the complainant considered that their prescribing information should have been included on the website and in the formulary pack.

AstraZeneca did not accept that the inclusion of prescribing information for these products was necessary or appropriate. Clause 4.1 required the provision of prescribing information in the context of promotion of a product. The website and formulary pack were clearly developed to promote Trixeo, not Bevespi or Symbicort. Bevespi and Symbicort were necessary comparator arms in the clinical trials (Trixeo registration studies ETHOS and KRONOS) and this why reference to those products was included. The Code did not suggest that prescribing information was required in relation to comparator products that were not being promoted. This was particularly true given that the products were mainly referred to by class (ie LABA/LAMA and ICS/LABA).

AstraZeneca did not accept the complainant's allegations that Clauses 4.1, 7.2, 9.1 and 2 were breached.

3.6 General summary allegation

The complainant concluded by alleging that the entire website was misleading and did not meet the mandatory requirements of the Code. Moreover, the complainant questioned the competency of the website's signatory.

For the reasons provided in detail above, AstraZeneca did not accept that the website was misleading. AstraZeneca took great care to ensure that all information, including claims and comparisons, were accurate, balanced, fair, unambiguous and capable of substantiation. The company maintained that the evidence presented was reflected objectively and did not mislead, either directly or by implication, by distortion, exaggeration or undue emphasis. Furthermore, the MHRA pre-vetted and approved claims and images the same or similar to those on the website. Whilst AstraZeneca understood that the MHRA did not make recommendations in relation to the Code, the fact that such claims and the dragon image passed its robust and objective assessment, nevertheless, provided a strong defence to the issues raised in the current complaint. It also demonstrated the AstraZeneca's commitment to ensuring that all materials that it published were in line with all relevant laws and regulations, as well as the Code.

Signatories

AstraZeneca took the competency of its signatories very seriously. AstraZeneca had dedicated training processes to ensure that material was approved following appropriate review but it was not possible to entirely eliminate the potential for human error. The training covered the requirement to check that websites display correctly across all platforms and that the prescribing information was available via a prominent, single click link. The signatory responsible for the Trixeo website was highly experienced, had obtained all relevant qualifications and had completed all necessary training requirements. AstraZeneca was very surprised and disappointed to learn that these errors had occurred. AstraZeneca accepted that despite these processes, there had been a limited breach of Clause 14.1 by failing to check the function of the website on a mobile device and that, in turn, this error resulted in breaches of Clauses 4.3 and 4.4. AstraZeneca had arranged for the individual in question to undergo further training. AstraZeneca viewed the training of its staff and their compliance with the Code extremely seriously and it would take every step necessary to ensure that its employees met the highest standards.

Analysis of the general provisions

The complainant made numerous allegations regarding breaches of Clause 9.1 and Clause 2 of the Code.

Clause 9.1 of the Code

AstraZeneca maintained that it had upheld high standards at all times. While the company accepted the breaches that occurred in relation to Clauses 4.3, 4.4 and 14.1 due to a failure to check the function of the website on mobile devices, the issue was limited to smartphones and the impact was limited. AstraZeneca submitted that this single error did not, of itself, establish that the company did not take great care to implement and follow appropriate policies and procedures. Consequently, AstraZeneca refuted the allegation that there had been a breach of Clause 9.1.

Clause 2 of the Code

AstraZeneca was comfortable that its actions in this matter had not brought discredit to, or reduced confidence in, the pharmaceutical and so did not constitute a breach of Clause 2 of the Code. There was no evidence whatsoever that AstraZeneca had jeopardised patient safety or public health, offered inducements to prescribe, or committed any other category of behaviour that would result in a breach of Clause 2. AstraZeneca took care to have relevant claims and images for this campaign pre-vetted by the MHRA before publication on the website. AstraZeneca strongly believed that it would be inappropriate if claims accepted by the MHRA were then found to constitute a breach of Clause 2 or Clause 9.1. Any allegation of a breach of Clause 2 was strongly denied.

Overall Conclusion

In conclusion, AstraZeneca stated that it took compliance with the Code extremely seriously and was committed to maintaining high standards in relation to all information it provided about its products and in complying with the Code. AstraZeneca accepted that an isolated failure to review the function of the website on mobile devices led to breaches of Clauses 4.3, 4.4 and 14.1. Although disappointing, action was taken immediately upon discovery, and at no point did AstraZeneca jeopardise patient safety or public health. AstraZeneca was confident that the content of the website was appropriate and that all of the promotional claims were balanced, accurate and well-substantiated. Finally, for the reasons provided above, AstraZeneca refuted all other allegations by the complainant, specifically breaches of Clauses 2, 4.1, 7.2, 7.4, 7.9, 7.10, 9.1, 9.7, 26.1, 26.2 and 28.1 of the Code.

PANEL RULING

1 Access to the website

The Panel noted the complainant's allegation that that the Trixeo website's homepage did not have different sections for health professionals, patients or members of the public, and as content was accessible to anyone, this constituted promotion to the public which could have led members of the public requesting Trixeo.

The Panel noted AstraZeneca's submission that the website was intended to be accessed by, and therefore was designed solely for, UK health professionals; a health professional declaration pop-up would have been displayed which required all users to confirm that they were health professionals before they could access any materials. The Panel noted AstraZeneca's submission that anyone not declaring themselves to be a health professional would be directed to the public AstraZeneca UK website.

The Panel noted that the pop-up box provided, as part of AstraZeneca's submission, stated 'The content on this website is intended for UK Healthcare Professionals only. The website contains promotional content' and had the options 'I am not a UK healthcare professional' and 'I am a UK healthcare professional'; a footer 'This website is intended for doctors, nurses and pharmacists in the UK. Other UK residents please visit astrazeneca.co.uk' was also included.

The Panel noted that, according to AstraZeneca, visitors would have seen the health professional pop-up the first time they accessed the website; however, certain individuals, who allowed the use of cookies on specific browsers, might not have seen the pop-up on later visits

if they used the same device and they had confirmed that they were a health professional on their first visit. The Panel noted AstraZeneca's submission that the link to the website was not publicised or sent to any patient or member of the public.

The Panel further noted AstraZeneca's submission that it found out on the afternoon of 11 March that some users could access the website without a health professional pop-up every time they visited it; the company's IT team was notified and within the hour it conducted a review and refresh of the website. No specific issue or fault was identified and in AstraZeneca's view, everyone who accessed the website before 11 March would have seen the health professional pop-up the first time they accessed the website. The Panel considered that the problem with the pop-up box was unfortunate but, given that it appeared to have occurred after the submission of this complaint (and before the company was notified of the complaint), it was not relevant to the consideration of the complainant's allegation. The footer identified the intended audience and directed those who were not health professionals to another website.

The Panel considered that the complainant had not provided any details as to how he/she had accessed the website; it was impossible to know whether he/she had accessed it initially and responded to the pop-up and then not been presented with the pop-up at subsequent visits to the website or whether he/she had freely accessed the website on the first instance on a device not previously used by a health professional who had responded to the pop-up.

The Panel noted that the complainant bore the burden of proof and did not consider that he/she had established his/her case that, on the balance of probabilities, that the website constituted promotion to the public. The Panel, therefore, ruled no breach of Clauses 2, 9.1, 26.1, 26.2 and 28.1 of the Code as alleged.

2 Non-proprietary name

The Panel noted that Clause 4.3 stated that, for electronic advertisements, the non-proprietary name of the medicine or the list of active ingredients must appear immediately adjacent to the brand name at its first appearance in a size such that the information was readily readable

The Panel noted AstraZeneca's submission that the website was built and certified for desktop view and, in that view, the generic name occupied a total area of no less than that taken up by the brand name and was easily readable on all pages of the website when viewed on a desktop, laptop and iPad. The Panel did not agree, however, about the size of the non-proprietary name; in the Panel's view, the area occupied by the non-proprietary name was less than that occupied by the brand name. Nonetheless, the Panel considered that the non-proprietary name was readily readable and thus ruled no breach of Clause 4.3 with regard to the desktop view of the website.

The Panel further noted AstraZeneca's submission that, as a result of a technical issue that was not identified prior to launch, the generic name was not easy to read when viewed on a mobile device. The Panel further noted that the brand logo image was not tested on mobile devices during certification by AstraZeneca and that AstraZeneca acknowledged that the generic name was small and difficult to read when viewed on mobile devices. A breach of Clause 4.3 was ruled.

3 Accessibility of prescribing information

The Panel noted the complainant's allegation that the mobile view of the website was a different final form of the website in that the prescribing information was not a single click away.

The Panel noted AstraZeneca's submission that whilst the prescribing information remained accessible on a mobile device, it required one click to reveal the full option menu and a further click to then access the prescribing information. The Panel further noted that this was contrary to AstraZeneca's procedures, which required that prescribing information on promotional websites should be available via a single click link, and that the error occurred due to the website not being reviewed on a mobile device for certification purposes.

The Panel considered that the accessibility of prescribing information through a two click link rather than a single click link, when viewed on a mobile device, did not fulfil the requirements of Clause 4.4 and the Panel ruled a breach of the Clause 4.4 as acknowledged by AstraZeneca. The Panel considered that as the prescribing information was still accessible when viewed on a mobile device, albeit via two clicks, that did not constitute a breach of Clauses 9.1 and 2 and no breaches were ruled in that regard.

The Panel considered that the website should have been reviewed and certified to ensure that it displayed correctly across different devices and that if it was designed for only desktop view, that this should have been made clear to readers. The Panel ruled a breach of Clause 14.1, as acknowledged by AstraZeneca, as the website had not been certified for viewing on mobile devices. The Panel considered that high standards had not been maintained and a breach of Clause 9.1 was ruled.

The Panel considered that a robust certification procedure underpinned self-regulation and although noting its comments and ruling above, it did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2, which was a sign of particular censure and was reserved for such use; no breach was ruled.

4 Alleged misleading claims and images

a) Claim 'Unleash protection from exacerbations with Trixeo'

The Panel noted the complainant's allegation that the claim 'Unleash protection from exacerbations with Trixeo' was not appropriate as it did not stand alone and was qualified by the footnote:

> 'Significant reductions in the rate of moderate or severe exacerbations vs LAMA/LABA (24%, n=2137 vs n=2120, annual rates 1.08 vs 1.42, 95% CI 0.69–0.83; p<0.001) and ICS/LABA (13%, n=2137 vs n=2131, annual rates 1.08 vs 1.24, 95% CI 0.79–0.95; p=0.003).'

The Panel noted AstraZeneca's submission that the footnote (referenced to the Trixeo SPC and to Rabe *et al* (2020), the ETHOS study) in this particular context was used to provide more detailed information rather than providing a substantive qualification and that the information in the footnote did not detract from the claim's ability to standalone. The Panel agreed with AstraZeneca's submission and considered that the complainant had not proven his/her case and shown otherwise. The Panel thus ruled no breach of Clause 7.2 in that regard.

The Panel noted the complainant's allegation that the absolute risk reduction was not stated in the footnote. The Panel noted that the footnote included both the relative risk reductions and absolute rate reductions; the relative risk reduction was presented as a percentage and the absolute rate reduction was the mean number of exacerbations per patient per year.

The Panel noted that the supplementary information to Clause 7.2 stated that referring only to relative risk, especially with regard to risk reduction, could make a medicine appear more effective than it actually was and that in order to assess the clinical impact of an outcome, the reader also needed to know the absolute risk involved. Absolute risk could be referred to in isolation.

The Panel further noted the complainant's concern that, as with the webpage, the relative risk reduction of exacerbations had been included in the Trixeo formulary pack, which was downloadable from the 'Learn More' section of the website, but there were no absolute risk reductions. The Panel noted that the complainant had not referred to any specific section of the formulary pack but it noted in a section which detailed the ETHOS study that absolute values had been given.

The Panel considered that both the absolute values and relative risk reduction had been provided as part of the footnote on the website and in the downloadable formulary pack, and therefore, based on the narrow allegation, no breach of Clause 7.2 was ruled in each regard.

The Panel noted that the complainant had also alleged that several claims about exacerbation reduction, from the KRONOS and ETHOS studies, on the efficacy page of the website only presented relative risk reduction and not absolute risk reductions and in that regard were misleading as they exaggerated the actual exacerbation reductions for health professionals. The complainant had not specified which claims were at issue and it was not for the Panel to identify those claims on his/her behalf and rule on each one. The Panel examined the webpage at issue, and it appeared that all claims about exacerbation reduction included both the relative risk reduction and the absolute risk reductions. No breach of Clauses 7.2 and 9.1 were ruled.

b) Claim 'You can prevent exacerbations'

The Panel noted the complainant's allegation that the claim 'You can prevent exacerbations', which appeared on the 'Learn More' page, was misleading as it implied that any patient taking Trixeo for COPD would always be prevented from having an exacerbation despite the various triggers that could cause COPD patients on stabilised therapy to exacerbate.

The Panel noted AstraZeneca's submission that the 'Learn More' page was designed to house broader disease education content related to the holistic care for COPD patients in order to prevent exacerbations and that the statement was not a claim about Trixeo but was a general call to action for health professionals to think about how to prevent exacerbations of COPD.

In the Panel's view, the 'Learn More' link, on a website promoting Trixeo, would have been seen by readers as a link to learn more about Trixeo. Nonetheless, the Panel considered that health professionals would be familiar with the prevalence and likelihood of exacerbations in COPD, even in patients who appeared to be well stabilised. In the Panel's view, health professionals reading the claim would not be misled into thinking that *all* exacerbations would be prevented with Trixeo even though Section 4.1 of the Trixeo SPC, Therapeutic indications, referred the

reader to information in Section 5.1 about the prevention of exacerbations. The Panel thus did not consider that the claim was misleading as alleged and no breach of Clause 7.2 was ruled.

c) Claims: 'Protection you can count on' and '*A well-established safety profile'*

The Panel did not consider that the claims 'Protection you can count on' and 'A well-established safety profile' implied that Trixeo had no side-effects as alleged. In the Panel's view, it was not in itself unreasonable to refer to 'protection you can count on' in the context of a medicine and the Panel considered that reference to a well-established safety profile would be read as there being extensive information about the safety profile and that the safety profile was not unreasonable for a medicine treating COPD. Further, the three components of Trixeo had been available prior to the introduction of Trixeo. The Panel did not consider that the large font size of the claims gave a misleading impression as alleged. The Panel thus ruled no breaches of Clauses 7.2, 7.4, 7.9, 9.1 and 2.

d) Capitalisation and size of font

The Panel did not consider, with regard to the complainant's general comment, that the use of upper case letters or different sizes of font was in poor taste as alleged; in the Panel's view, it might be helpful to use such features to aid readability and presentation.

The Panel noted that no reasons had been given in relation to this allegation, although the complainant had made a reference to misleading claims (point c above). Based on the evidence before it, the Panel ruled no breach of Clause 9.7.

e) Dragon image

The Panel noted that the material used an image on an outstretched human hand upon which sat a dragon exhaling three flames. The Panel noted that the complainant had provided no explanation as to why, in his/her view, the depiction of a dragon implied that Trixeo had special properties. AstraZeneca submitted that the image was intended to convey the message of reassurance and protection from exacerbations, within the patient's control; the three flames represented the three active components of Trixeo.

The Panel did not consider that the image claimed or conveyed that Trixeo had special properties as alleged. Based on the evidence submitted by the complainant, the Panel did not consider that the image failed to maintain high standards and no breach of Clauses 7.10 and 9.1 was ruled.

5 Prescribing information for Bevespi and Symbicort Turbohaler

The Panel noted that the Trixeo formulary pack which was available to download from the website, mentioned budesonide-formoterol fumarate (Symbicort) and glycopyrrolate-formoterol fumarate (Bevespi Aerosphere) by non-proprietary names only, in relation to their inclusion in the ETHOS and KRONOS studies. The Panel noted AstraZeneca's submission that the website and formulary pack were developed to promote Trixeo and not Bevespi or Symbicort; Bevespi and Symbicort were necessary comparator arms and were thus included.

The Panel noted that clinical results for Bevespi Aerosphere and Symbicort Turbohaler were discussed, albeit only by using non-proprietary names, in the formulary pack and both products

were referred to by non-proprietary name on the website. The Panel considered, however, that as both medicines were AstraZeneca products their mention on the website and in the formulary pack meant that prescribing information should have been included in both. As no prescribing information for the two products had been provided, breaches of Clause 4.1 were ruled for each medicine with regard to the website and the formulary pack. The Panel considered that high standards had not been maintained and ruled breaches of Clause 9.1 with regard to the formulary pack and the website.

The Panel noted its rulings above but did not consider that the particular circumstances in this case warranted a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such. No breach of Clause 2 was ruled.

6 General summary allegation

The Panel noted that the complainant concluded by alleging that the entire website was misleading and did not meet the mandatory requirements of the Code.

The Panel noted AstraZeneca's submission that while the company accepted the breaches that occurred in relation to Clauses 4.3, 4.4 and 14.1, due to a failure to check the function of the website on mobile devices, the issue was limited to smartphones and the impact was limited.

The Panel noted its comments and rulings above of three breaches of Clause 9.1 in relation to the lack of certification on a mobile device and the lack of prescribing information for Bevesbi and Symbicort in the Trixeo formulary pack and on the website. However, the Panel did not consider that the overall circumstances warranted a further ruling of a breach of Clause 9.1 or a ruling of a breach of Clause 2; no breaches of Clauses 9.1 and 2 were ruled.

Complaint received **10 March 2021**

Case completed **29 September 2021**