CASE AUTH/3638/4/22

COMPLAINANT v NOVARTIS

Promotional claims for Xolair on a Novartis website

CASE SUMMARY

This case was in relation to the promotional messaging for Xolair on the Novartis-owned respiratory webpage for Severe Allergic Asthma (SAA) and dermatology webpage for Chronic Spontaneous Urticaria (CSU).

The Panel ruled a breach of the following Clauses of the 2021 Code in relation to use of the claim 'Think Symptom Free' in CSU on the Xolair dermatology webpage which misleadingly implied that Xolair would lead to all patients being symptom free and having achieved complete response, which was not so:

Breach of Clause 6.1	**Making a misleading claim**
Breach of Clause 6.2	**Making an unsubstantiated claim**
Breach of Clause 5.1	**Failing to maintain high standards**

The Panel ruled no breach of the following Clause of the 2021 Code in relation to use of the claim 'Think Symptom Free' in CSU on the Xolair dermatology webpage as it did not consider, noting it was a sign of particular censure, that it was warranted in the particular circumstances:

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

The Panel ruled no breach of the following Clauses of the 2021 Code in relation to use of the claim 'Unlock Life*' and qualification of the claim with a footnote on both the Xolair respiratory webpage for SAA and the Xolair dermatology webpage for CSU because in the Panel's view in the circumstances the claim was capable of standing alone and on the evidence before it, it had not been established that the claim on each webpage was misleading or incapable of substantiation:

No Breach of Clause 6.1	**Requirement that information must be accurate, up-to-date and not misleading**
No Breach of Clause 6.2	**Requirement that claims must be capable of substantiation**
No Breach of Clause 5.1	**Requirement to maintain high standards**
No Breach of Clause 2	**Requirement that activities or material must not bring discredit upon, or reduce confidence in, the**

	pharmaceutical industry

The Panel ruled no breach of the following Clauses of the 2021 Code in relation to the reference to severe asthma within the context of the Xolair respiratory webpage for SAA because it did not consider, on balance, that within the context of the webpage readers were given the impression that Xolair was for any patient with severe asthma, outside the terms of its licence:

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

On the evidence before it, The Panel ruled no breach of the following Clause of the 2021 Code, in relation to the image of a jumping man on the Xolair respiratory webpage for SAA which allegedly implied severe asthma patients would be able to exert extra physical activity just by taking Xolair:

No Breach of Clause 5.1	**Requirement to maintain high standards**

The Panel ruled no breach of the following Clause of the 2021 Code overall as the complainant had not established that there was a lack of experience, understanding and integrity from Novartis around the importance of compliance and professional standards as alleged:

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

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

FULL CASE REPORT

COMPLAINT

A complainant who described him/herself as a healthcare professional and became non-contactable, complained about what he/she described as a large number of concerns around the promotional messages for Xolair (omalizumab).

The complainant stated that this was even more concerning as a senior medical employee at Novartis had recently done videos around how Novartis were patient centric and Novartis was the best place they had worked at, so it was baffling that Xolair messages were not within the boundaries of the compliance rules. The complainant alleged that the promotional page which

was misleading, was promoting Xolair for CSU and provided a link to a webpage (XSU20-C007, July 2020).

The complainant stated that on this page, right at the outset there was a picture of what looked like a young lady scratching along with a tagline which read, 'In chronic spontaneous urticaria, Think Symptom-free, Think IgE, Think Xolair. Block IgE, UNLOCK LIFE*'. The tagline was misleading as 'think symptom free' would indicate to a busy healthcare professional that taking Xolair would lead to no more symptoms but this was not the case as symptoms could still be present in CSU even after taking Xolair. There was no evidence that 100% of patients taking Xolair were symptom free at all times in CSU.

Secondly, UNLOCK LIFE* was allegedly inappropriate as quality of life had not been shown as a primary endpoint in the trials for Xolair in CSU and the use of a * to qualify the claim with a footnote was not sufficient. Claims had to standalone. These two claims were in breach of Clauses 6.1, 6.2, 5.1 and 2.

The complainant alleged that a separate page which was promoting Xolair for use in severe asthma was also inappropriate and provided a link to the page (XSA20-C011 July 2020). The complainant stated that at the top of this page, there was an image of a male jumping and a tag line of in 'severe asthma, THINK allergy, Think IgE, THINK Xolair. Block IgE, UNLOCK LIFE*'. The complainant alleged that the initial statement of in severe asthma was not in line with the licensed indication of Xolair which was actually very specific, Xolair was indicated as add-on therapy to improve asthma control in patients with severe persistent allergic asthma who had a positive skin test or in vitro reactivity to a perennial aeroallergen and who had reduced lung function (FEV1 <80%) as well as frequent daytime symptoms or night-time awakenings and who have had multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids, plus a long-acting inhaled beta2-agonist. The complainant alleged that a busy health professional would read this and be given an immediate impression that Xolair was for any patient with severe asthma which was not the case as the licence was far [broader]. This claim of 'severe asthma' without full qualification was in breach of Clause 11.2, 5.1 and 2 as the promotion was outside the licensed indication.

On the same webpage, the complainant alleged that the image of the male jumping was inappropriate as it implied severe asthma patients would be able to exert extra physical activity just by taking Xolair but for a severe asthmatic patient this would not be the case due to limitations on activity. The complainant alleged this was a breach of Clause 5.1.

Lastly, the complainant alleged that the claim 'Unlock life*' was inappropriate considering there was no primary endpoint looking at quality of life with Xolair in severe asthma and footnotes should not be used to qualify claims. This was a clear breach of Clauses 6.1, 6.2, 5.1 and 2.

The complainant concluded that it was very disappointing that these promotional claims for Xolair across CSU and severe asthma had been allowed to be published. There was a clear lack of experience, understanding and integrity from Novartis around the importance of compliance and professional standards. The complainant stated that it was clear Novartis were not a compliance centric company and alleged a breach of Clause 2.

The Authority noted that the items were approved in July 2020 but given the items appeared to have been live when the 2021 Code came into operation and when the complaint was

submitted, they were considered under the 2021 Code. When writing to Novartis, the Authority asked it to consider the requirements of Clauses 2, 5.1, 6.1, 6.2 and 11.2 of the 2021 Code.

RESPONSE

Novartis stated that the complaint caused it concern and it had taken its content seriously. Novartis wanted to highlight that it was committed to operating in accordance with the required standards and meeting the relevant requirements and expectations. The formal response from Novartis is below.

Background

Novartis submitted Xolair (omalizumab) binds to immunoglobulin E (IgE) and prevents binding of IgE to the high-affinity IgE receptor on basophils and mast cells, thereby reducing the amount of free IgE that was available to trigger the allergic cascade leading to symptoms in Chronic Spontaneous Urticaria (CSU) and Severe Allergic Asthma (SAA).

The webpages were on the health.novartis.co.uk website which hosted promotional information about Novartis products aimed at UK health professionals. Each time a health professional accessed the website they were asked to confirm that they were a UK healthcare professional (or relevant NHS decision maker). The website hosted dedicated sections on Xolair in each of the CSU and SAA indications. These sections contained prescribing information, licensed indications, safety and efficacy data and other resources to support health professionals prescribing Xolair.

Novartis submitted that the webpages cited in the complaint were aimed at physicians experienced in the diagnosis and treatment of CSU and SAA respectively and supporting information was readily available on linked pages such that the material was sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine. Novartis stated that it would be unlikely that professionals visiting the website would make a prescribing decision based on a single image or tagline.

Novartis submitted that the relevant webpages were published in July 2020 and were still live at the time of Novartis' response (May 2022).

A Specific complaints relating to the Novartis Dermatology webpage for the Xolair indication relating to the treatment of CSU

i) 'Think Symptom-Free' CSU

[Citation of complaint]: 'The tagline was "misleading as "think symptom free" would indicate to a busy healthcare professional that taking Xolair would lead to no more symptoms but this was not the case as symptoms can still be present in CSU even after taking Xolair. There was no evidence that 100% of patients taking Xolair were symptom free at all times in CSU" (Clauses 6.1, 6.2, 5.1 and 2)'.

According to Novartis, CSU was a mast cell-driven skin disease characterized by the recurrence of transient wheals (hives), angioedema, or both for more than 6 weeks. Autoimmunity was thought to be one of the most frequent causes of CSU. Type I and II autoimmunity (IgE to auto-

allergens and IgG autoantibodies to IgE or its receptor, respectively) had been implicated in the aetiology and pathogenesis of CSU.

Novartis submitted that the 7-day Urticaria Activity Score (UAS7) was a commonly used diary-based, patient-reported outcome measure that assessed the activity of key CSU symptoms, itch severity and hive count, over seven consecutive days. It was recommended for use by NICE guidance as a way of assessing the severity of CSU objectively. Scientific publications had said that a UAS7 score of zero indicates that the patient is 'Itch and hive free' and is 'indicative of no symptoms of CSU and considered a full treatment response', and thusly, Novartis submitted, equivalent to symptom free.

Novartis submitted the most relevant clinical guideline in CSU was the EAACI/GA²LEN/EuroGuiDerm/APAACI guideline for the definition, classification, diagnosis, and management of urticaria. Amongst other goals in this guideline, treatment should be escalated until a continuous UAS7 of zero (complete response) was reached. Xolair was recommended as step-up treatment to control symptoms assessed using patient-reported outcome measures such as the UAS7. This guideline was pivotal in the treatment and management of CSU patients and familiar to physicians experienced in the diagnosis and treatment of CSU, towards whom this material was directed.

The clinical development programme for Xolair in CSU demonstrated benefits in terms of itch severity, and urticaria activity. In particular, pooled data included in the SPC indicated that a significantly greater number of patients achieved complete response with Xolair (34-44%) ($p<0.0001$) compared to 5-9% of patients in the placebo groups. Data from clinical trials detailing Xolair response rates was clearly provided in the supporting efficacy webpage clearly linked via this homepage.

Novartis submitted the imagery and statement 'think symptom free' therefore depicted guideline-recommended treatment goals and was intended to reflect an aspiration of treatment. Think Xolair reflected the potential benefits demonstrated in patients with CSU treated with omalizumab in the development programme.

On this webpage, Novartis stated that the statement 'think symptom free' was meant to request the reader to consider if Xolair may be an appropriate treatment for some patients to achieve complete response, however, when Novartis reviewed this material with fresh eyes for the purposes of this complaint, it agreed that it could be viewed as short of what was required for complete clarity. For that reason, Novartis agreed that the material could be improved and set into more context to avoid the interpretation complained of.

In light of the above, Novartis accepted a breach of Clauses 6.1 and 6.2, however, the material was certified following a robust assessment by a final signatory. High standards had been maintained therefore there has been no breach of Clauses 5.1 or 2.

ii) 'Unlock life*' – CSU

[Citation of complaint]: 'UNLOCK LIFE* was inappropriate as quality of life had not been shown as a primary endpoint in the trials for Xolair in CSU and the use of a * to qualify the claim with a footnote was not sufficient. Claims had to standalone' (Clauses 6.1, 6.2, 5.1 and 2).

Novartis submitted that the statement 'Unlock life' reflected quality of life measures. It was widely understood that if symptoms of CSU were improved in patients, those patients had a better quality of life. Xolair had demonstrated that it improved symptoms of CSU vs placebo, and hence this was capable of standing alone as a statement.

The SPC, according to Novartis, contained robust data showing a clinically relevant, statistically significant increase in quality of life scores (Dermatology Quality of Life Index; DLQI) in patients treated with Xolair compared to placebo across three, randomized placebo-controlled trials in the development programme.

Novartis submitted, subsequent to licensing, a placebo-controlled, randomized controlled trial investigated the effect of omalizumab on quality of life as a primary objective and demonstrated that omalizumab was a highly effective treatment associated with a marked and rapid improvement in angioedema symptoms, angioedema-related QoL, symptom-related fears, and psychological well-being.

On the basis of the points above, Novartis submitted the claim 'unlock life' was not inappropriate and although a footnote was provided, this was not required to substantiate the claim. High standards had been maintained. There was no breach of Clauses 2, 5.1, 6.1 or 6.2.

B Specific complaints relating to the Novartis' Respiratory and Inflammation webpage for the Xolair indication relating to the treatment of SAA

i) 'Severe asthma' claim

[Citation of complaint]: 'The initial statement of in "severe asthma" was not in line with the licensed indication of Xolair. A busy HCP would be given the impression that Xolair is for any patient with severe asthma. (Clauses 11.2, 5.1, 2)'.

Novartis submitted on this promotional webpage, the statement severe asthma was not a claim and did not imply that Xolair was suitable for all patients with severe asthma. It was clear up front with severe asthma, 'Think Allergy' came up first, in bold, clearly indicating that if a patient had severe asthma, the reader should think of allergic asthma and then the full licensed indication was given on the webpage providing full clarity of the population for whom the product was licensed, enabling the reader to determine if Xolair was an appropriate treatment for their patient.

High standards had been maintained, according to Novartis, and Xolair had been promoted in accordance with the terms of its marketing authorisation. There had, therefore, been no breach of Clauses 11.2, 5.1 or 2 according to Novartis.

ii) 'Unlock life*' – SAA

[Citation of complaint]: 'The claim "Unlock life" was inappropriate considering there was no primary endpoint looking at quality of life with Xolair in severe asthma and footnotes should not be used to qualify claims (Clauses 6.1, 6.2, 5.1, 2)'.

Novartis submitted the statement 'Unlock life' would have been understood by the professional audience that improving symptoms of Severe Allergic Asthma would improve quality of life,

Xolair had demonstrated that it improved symptoms of severe allergic asthma, and hence the statement was capable of standing alone as regards accuracy etc in that respect.

The primary outcome in pivotal clinical trials with omalizumab in the Severe Allergic Asthma indication was exacerbation rate reduction. Exacerbation rate and Quality of life were strongly associated thus a reduction in exacerbation rate was commonly accepted to improve quality of life.

The SPC contained data showing a statistically significant increase in the number of patients achieving clinically meaningful improvement in quality of life with Xolair compared to placebo in a randomized controlled trial.

Novartis submitted the following statement in the SPC demonstrated that benefits on Quality of Life were demonstrated robustly during Xolair's development programme:

- 'Quality of life scores were measured using the Juniper Asthma-related Quality of Life (AQLQ) Questionnaire. For all six studies there was a statistically significant improvement from baseline in quality of life scores for Xolair patients versus the placebo or control group.'

Novartis submitted that of the six aforementioned studies, one was a randomised, placebo-controlled trial in which an AQLQ responder analysis was included as part of a co-primary end point. Both co-primary endpoints were met in this study.

Subsequent to licensing, a randomized controlled trial demonstrated statistically significant and clinically meaningful improvement in quality of life in patients with severe allergic asthma with Xolair as a primary objective with associated clinically meaningful improvements in the activity limitation domain of the assessment.

Real world evidence had similarly demonstrated positive effects of Xolair on Quality of Life, including a study in 258 patients in England where AQLQ improved by 1.38 (1.18 to 1.58) points at 16 weeks ($p<0.001$, maintained at 12 months).

Novartis submitted that in summary the effect of Xolair on quality of life has been robustly demonstrated and this claim was not inconsistent with the product licence. The claim 'unlock life' was not inappropriate and although a footnote is provided, this was not required to substantiate the claim. High standards had been maintained according to Novartis; there had been no breach of Clauses 2, 5.1, 6.1 or 6.2.

iii) The image of the male jumping was inappropriate

[Citation of complaint]: 'The image of the male jumping was inappropriate as it implied patients with severe allergic asthma would be able to exert extra physical activity just by taking Xolair but for patients with severe allergic asthmatic, this would not be the case due to limitations on activity (Clause 5.1)'.

Novartis submitted:

- Guidelines recommended exercise in the treatment of severe asthma.

- Quotations of patients with severe asthma on the website of Asthma + Lung UK (a major UK asthma and lung disease charitable organisation) confirmed that strenuous exercise including swimming, weight training, running marathons and netball were possible in patients with well-controlled severe asthma.
- As previously described, benefits on quality of life were demonstrated robustly during Xolair's development program using the AQLQ. The AQLQ was a validated tool which assessed quality of life across four domains, one of which was activity limitation.

Novartis submitted, on the basis of the points above, that imagery of someone jumping appropriately depicted quality of life benefits that had been demonstrated in patients with severe allergic asthma treated with omalizumab. Novartis submitted there had been no breach of Clause 5.1.

Clause 2

Novartis vigorously rejected the complainant's allegation of a breach of Clause 2 arising due to a 'clear lack of experience, understanding and integrity' on the part of Novartis. There was no substantive evidence in the nature of the complaint, which was wholly focused on the interpretation of claims, that there had been a failure by Novartis in any of these areas or that Novartis was not a compliance-centric company.

Each specific facet of the complaint was addressed to an issue where the subject matter complained about had been through a robust assessment by a final signatory.

Novartis stated it took its responsibilities under the Code incredibly seriously and invested significant resources to ensure its associates developed a deep understanding of the requirements of the ABPI Code. A robust assessment was completed before signatories were notified to the MHRA and code training was provided to associates and signatories on an ongoing basis (through Code clubs and fora etc.). The Code was subject to interpretation and judgement which Novartis relied on final signatories to provide. It was entirely expected that in judging whether material fell within the requirements of the Code, there may be some degree of variance in the approach of different final signatories.

Novartis stated it took all complaints and breaches seriously and used them for learning and improvement.

Novartis submitted, in common with all other pharmaceutical companies operating in the UK, it was reliant on the skill and experience of its final signatories to understand the requirements of the Code and its application to the material being reviewed for sign-off by the final signatory. On finely balanced matters and even adopting a conservative approach, there might be isolated incidents where material was signed off that was later, when inspected in the complaints process, found not to comply with the Code. Novartis, again in common with the industry, broadly supported the PMCPA complaint process as a means to identify such isolated incidents and correct them where appropriate.

The complaint here was directed at judgment calls made on two promotional items. It could not reasonably be extrapolated into sweeping statements that called into question the competence and integrity of Novartis associates, and implied a lack of understanding by Novartis of the

regulatory environment and high compliance standards within which the pharmaceutical sector must operate.

Conclusion

It was Novartis' opinion that there had been one breach of Clauses 6.1 and 6.2 each on one of these materials and Novartis would withdraw all promotional materials relating to the CSU indication of Xolair with the statement 'Think symptom-free'. Novartis undertook to not include this statement in future materials. As outlined above, Novartis did not accept that there had been a breach of Clauses 6.1 and 6.2 in relation to the use of the statement 'Unlock life*'.

While Novartis accepted there had been a breach, Novartis stated that high standards had been maintained, the data upon which these materials were based was robust, as was the review and approval process. The special nature of the audience to whom the information was directed had also been considered.

The actions of Novartis in relation to these materials was not considered to have brought discredit on, or reduced confidence in, the pharmaceutical industry.

It was Novartis' opinion that there had been no breaches of Clauses 2, 5.1 and 11.2 in these materials.

PANEL RULING

The Panel noted that the promotional webpages at issue for Xolair (omalizumab) related to the following indications:

> Allergic asthma
>
> Xolair is indicated in adults, adolescents and children (6 to <12 years of age). Xolair treatment should only be considered for patients with convincing IgE (immunoglobulin E) mediated asthma (see section 4.2).
>
> *Adults and adolescents (12 years of age and older)*
>
> Xolair is indicated as add-on therapy to improve asthma control in patients with severe persistent allergic asthma who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen and who have reduced lung function (FEV_1<80%) as well as frequent daytime symptoms or night-time awakenings and who have had multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids, plus a long-acting inhaled beta2-agonist.
>
> *Children (6 to <12 years of age)*
>
> Xolair is indicated as add-on therapy to improve asthma control in patients with severe persistent allergic asthma who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen and frequent daytime symptoms or night-time awakenings and who have had multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids, plus a long-acting inhaled beta2-agonist.

Chronic spontaneous urticaria (CSU)

Xolair is indicated as add-on therapy for the treatment of chronic spontaneous urticaria in adult and adolescent (12 years and above) patients with inadequate response to H1 antihistamine treatment.

The Panel, noting that Xolair had therapeutic indications in chronic spontaneous urticaria (CSU) and severe allergic asthma (SAA), noted that the two promotional webpages at issue were hosted on what appeared to be the medicines section of the health.novartis.co.uk website for their respective therapy areas dermatology and respiratory; the Panel thus set out its rulings accordingly.

1 Xolair dermatology page

The Panel noted the first promotional webpage at issue was a landing page for the Xolair CSU portal for health professionals. The feature image at the start of the page included an emotive photograph of a woman, who appeared to have CSU, scratching her back; to the left of the photograph was the stylised text:

'In chronic spontaneous urticaria,
THINK Symptom-free,
THINK IgE,
THINK Xolair
(omalizumab).'

Beneath the text, within the feature image, was the Xolair (omalizumab) logo and the claim 'Block IgE, UNLOCK LIFE*', for which the corresponding footnote referred to *post hoc* analyses that 'demonstrated clinically meaningful improvements in quality of life (measured using DLQI) in patients with CSU'.

'THINK Symptom-free' Claim

With regard to the allegation that 'think symptom free' would misleadingly indicate that Xolair would lead to no more symptoms, the Panel noted Novartis' submission that the claim was intended to depict guideline-recommended treatment goals and for the reader to consider if Xolair may be an appropriate treatment for some patients to achieve complete response.

The Panel further noted Novartis' submission that NICE guidance recommended using the Urticaria Activity Score (UAS7) as a patient outcome measure to assess CSU symptoms, for which as UAS7 score of zero, known as 'complete response', was indicative of no symptoms and thus symptom free.

In the Panel's view, the claim 'THINK Symptom-free' misleadingly implied that Xolair would lead to all patients being symptom free and having achieved complete response, which was not so; 34-44% of patients achieved complete response (UAS7) as noted in the SPC. Noting that the majority of patients did not achieve complete response, the Panel considered that the claim was misleading and incapable of substantiation. A **breach of Clauses 6.1 and 6.2** were ruled, as acknowledged by Novartis.

The Panel noted its rulings of breaches above and considered that Novartis had failed to maintain high standards in relation to the claim 'THINK Symptom-free' and **a breach of Clause 5.1** was ruled. However, the Panel 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 was reserved for such use. **No breach of Clause 2** was ruled.

'BLOCK IgE, UNLOCK LIFE*' Claim

The Panel noted the claim 'UNLOCK LIFE*', which had a corresponding footnote that referred to *post hoc* analyses on quality of life, was allegedly inappropriate as quality of life had not been shown as a primary endpoint in CSU trials and qualification of the claim with a footnote was not sufficient.

The Panel noted that the supplementary information for Clause 6.1 stated, *inter alia*, claims in promotional material must be capable of standing alone with regard to accuracy etc. In general, claims should not be qualified by the use of footnotes and the like.

The Panel considered that whilst a footnote was provided, the footnote was additional, useful information that referred to *post hoc* analyses that supported the claim but was not required to qualify the claim; in the Panel's view, in the particular circumstances of the material and this case, the claim was capable of standing alone and **no breach of Clause 6.1** was ruled.

With regard to the allegation that 'unlock life' was inappropriate, the Panel did not consider that the complainant had established why it was inappropriate to make a claim based on quality life on the basis that it had not been shown as a primary endpoint in CSU trials, nor that the claim was incapable of substantiation; Novartis submitted that the SPC showed clinically relevant statistically significant increases in quality of life scores across three randomised placebo-controlled trials.

In the Panel's view, it was not necessarily unacceptable to include claims based on secondary endpoint data in promotional material so long as such claims complied with the Code and were not otherwise misleading. In that regard, noting the complainant bore the burden of proof and on the evidence before it, the Panel ruled **no breach of Clauses 6.1 and 6.2**.

Noting its comments and rulings of no breaches above, the Panel ruled **no breach of Clauses 5.1 and 2** accordingly.

2 Xolair respiratory page

The Panel noted the second promotional webpage at issue was a landing page for the Xolair respiratory portal for health professionals. The feature image at the start of the page included a photograph of a man jumping outdoors, with what appeared to be black and yellow antibodies in the air, to the left of which was the stylised text that read:

'In severe asthma
THINK Allergy,
THINK IgE,
THINK Xolair
(omalizumab).'

Again, beneath the text, within the feature image, was the Xolair (omalizumab) logo and the claim 'Block IgE, UNLOCK LIFE*', for which the corresponding footnote stated 'Xolair provides clinically meaningful improvements in quality of life for patients with severe allergic asthma'.

Severe asthma

The Panel noted the allegation that 'in severe asthma, THINK allergy, Think IgE, THINK Xolair. Block IgE, UNLOCK LIFE*' was not in line with the licensed indication of Xolair and that the impression that Xolair was for any patient with severe asthma was not the case.

The Panel noted that the size of 'severe asthma' within the feature image was in slightly smaller font than the rest of the claim and appeared immediately before 'THINK Allergy'. The Panel further noted that the full licensed indication was stated below the feature image.

In the Panel's view, noting the prominence of the 'THINK Allergy' claim, along with the presence of illustrations of antibodies in the photograph and the claim 'Block IgE UNLOCK LIFE', the webpage promoted Xolair in patients with severe allergic asthma; the Panel did not consider, on balance, that readers were given the impression that Xolair was for any patient with severe asthma, outside the terms of its licence. The Panel, therefore, did not consider that the claim or webpage as a whole was inconsistent with the particulars listed in the Xolair SPC. Accordingly, the Panel ruled **no breach of Clause 11.2**.

Noting its rulings of no breach, the Panel ruled **no breach of Clauses 5.1 and 2** accordingly.

Image of man jumping

The Panel noted the complainant's allegation that the image of the male jumping was inappropriate as it implied severe asthma patients would be able to exert extra physical activity just by taking Xolair but for a severely asthmatic patient this would not be the case due to limitations on activity.

The Panel noted Novartis' submission that guidelines recommended exercise in the treatment of severe asthma; from the enclosures provided, it appeared that exercise was recommended as a non-pharmacological intervention in difficult-to-treat asthma according to the Global Initiative for Asthma (GINA) and advice on how to stay active was recommended in severe asthma on the Asthma + Lung UK website. The Panel did not consider, based on the evidence before it, that the inclusion image of a man with severe allergic asthma jumping outdoors meant that Novartis had failed to maintain high standards and therefore the Panel ruled **no breach of Clause 5.1**.

'BLOCK IgE, UNLOCK LIFE*' Claim

The Panel noted the claim 'UNLOCK LIFE*', which had the corresponding footnote 'Xolair provides clinically meaningful improvements in quality of life for patients with severe allergic asthma', was allegedly inappropriate as quality of life had not been shown as a primary endpoint with Xolair in severe asthma and footnotes should not be used to qualify claims.

The Panel considered that whilst a footnote was provided, the footnote referred to quality of life and was not required to qualify the claim; in the Panel's view, in the particular circumstances of

the material and this case, the claim was capable of standing alone and **no breach of Clause 6.1** was ruled.

With regard to quality of life, the Panel noted Novartis' submission that the primary outcome in pivotal clinical trials with omalizumab in the Severe Allergic Asthma (SAA) indication was exacerbation rate reduction, which was strongly associated with quality of life and thus a reduction in exacerbation rate was commonly accepted to improve quality of life.

The Panel noted Section 5.1 of the Xolair SPC stated 'Quality of life scores were measured using the Juniper Asthma-related Quality of Life (AQLQ) Questionnaire. For all six studies there was a statistically significant improvement from baseline in quality of life scores for Xolair patients versus the placebo or control group'. Novartis submitted that one of the six aforementioned studies was a randomised, placebo-controlled trial (Vignola AM *et al*., 2004) in which an AQLQ responder analysis was included as part of a co-primary end point; both co-primary endpoints were met in this study.

The Panel noted the inclusion of AQLQ as a co-primary endpoint in Vignola AM *et al*., 2004 above and did not consider that the complainant had established why it was inappropriate to make a claim based on quality life, regardless of whether it had been shown as a primary endpoint in severe allergic asthma trials; nor did the complainant establish that the claim was incapable of substantiation. Noting the complainant bore the burden of proof, the Panel, on the evidence before it, ruled **no breach of Clauses 6.1 and 6.2** in this regard.

Noting its comments and rulings of no breaches above, the Panel ruled **no breach of Clauses 5.1 and 2** accordingly.

The Panel did not consider that the complainant had established there was a clear lack of experience, understanding and integrity from Novartis around the importance of compliance and professional standards and **no breach of Clause 2** was ruled.

Complaint received **24 April 2022**

Case completed **20 April 2023**