CASE AUTH/3668/6/22

COMPLAINANT v GALAPAGOS

Promotion of Jyseleca

CASE SUMMARY

This case was in relation to claims made on Galapagos UK's website (strengthofbalance.co.uk) for its product Jyseleca (filgotinib).

In relation to the claim 'strength of balance', the Panel ruled a breach of the following Clause of the 2021 Code as the claim as it appeared on the homepage was ambiguous and there was insufficient additional information to allow the reader to understand what it meant:

Breach of Clause 6.1	**Making a misleading claim**

In relation to the claim 'strength of balance' The Panel ruled no breach of the following Clauses of the 2021 Code given that the meaning of the claim, as it appeared on the homepage, was unclear, it was difficult to understand how it could be said to imply a special merit and the Panel did not consider that the complainant had established that the claim in question implied a special merit that could not be substantiated as alleged:

No Breach of Clause 6.2	**Requirement that claims/information/comparisons must be capable of substantiation**
No Breach of Clause 14.4	**Requirement that claims should not imply that a medicine or an active ingredient has some special merit, quality or property unless this can be substantiated**

In relation to the claim 'delivering breakthroughs in RA and inflammation', the Panel ruled no breach of the following Clauses of the 2021 Code because although the Panel was concerned about the phrase in question, in the particular circumstances of this case, the complainant had submitted no material and had not identified any specific evidence to support his/her position and the Panel did not consider that he/she had established his/her case on the balance of probabilities and in the absence of any evidence on this point, and on this very narrow ground alone, the Panel did not consider that the claim 'delivering breakthroughs in RA and inflammation' misleadingly implied that Jyseleca had a special merit that could not be substantiated:

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/information/comparisons must be capable of substantiation**
No Breach of Clause 14.4	**Requirement that claims should not imply that a medicine or an active ingredient has some special merit, quality or property unless this can be substantiated.**

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

FULL CASE REPORT

A contactable complainant who described him/herself as a concerned health professional complained about Galapagos UK's website (strengthofbalance.co.uk) for its product Jyseleca (filgotinib).

Jyseleca is indicated, *inter alia*, for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to, one or more disease-modifying anti-rheumatic drugs (DMARDs). Jyseleca may be used as monotherapy or in combination with methotrexate (MTX).

COMPLAINT

The complainant stated that Jyseleca: was described on the website as 'Strength of Balance From Galapagos, delivering breakthroughs in RA and Inflammation'.

The terms 'strength of balance' and 'delivering breakthroughs in RA and Inflammation' both appeared to be implying special merit of this product. There were several other (Janus kinase) JAK inhibitors that were used in inflammatory diseases, and none had been demonstrated to be a 'breakthrough' in treatment – not that any references were included to justify this term. Neither of these terms were used in other Galapagos websites, ie www.glpg.com/uk/ so do not appear to be terms that were intended to be used in a general, non-specific sense; if such an excuse could be used for statements used both at the URL of a product website and repeated at the top of the website.

The complainant asked the PMCPA to investigate this inappropriate, unsubstantiated series of claims.

When writing to Galapagos, the Authority asked it to consider the requirements of Clauses 6.1, 6.2 and 14.4 of the 2021 Code.

RESPONSE

Galapagos submitted that the homepage of the website, intended for health professionals in the UK and the Republic of Ireland, featured a banner stating 'Strength of Balance' and a sub-banner stating 'From Galapagos, delivering breakthroughs in RA and Inflammation'.

Background to JAK inhibitors

Galapagos submitted that Rheumatoid arthritis ('RA') was a complex, heterogenous and progressive systemic autoimmune disease that affected the joints as well as numerous other organs of the body. Treatments for RA targeted the dysregulation of the immune system, reducing inflammation and thereby restoring balance.

Galapagos submitted that there were several classes of medicinal products routinely used to treat RA, namely: conventional synthetic Disease Modifying Anti-Rheumatic Drugs ('cDMARDs'); and advanced therapies, which encompassed both biological Disease Modifying

Anti-Rheumatic Drugs ('bDMARDs') that had been available for some time, and newer targeted synthetic Disease Modifying Anti-Rheumatic Drugs ('tsDMARDs') including JAK inhibitors ('JAKi'). There were a number of different medicines available within each of these categories, with differing mechanisms of action. However, all DMARDs exerted their therapeutic effects by targeting aspects of the immune system and required routine monitoring.

bDMARDs included tumor necrosis factor (TNF) inhibitors ('TNFi'), which were commonly used as first line advanced therapy after, or in addition to, cDMARD treatments. Rheumatologists were therefore experienced in use of TNFi treatments and more recently introduced advanced therapies were often compared to a TNFi, generally adalimumab, as the most widely used product, in head-to-head trials. Relative to TNFis, there was considerably less clinical experience with tsDMARDs, including the JAKi class of treatments (four were licensed to treat RA in the UK), and therefore clinicians were particularly interested in assessing the benefit: risk profile of newer classes of medicines in clinical practice.

Jyseleca

Jyseleca was a JAK1 preferential inhibitor indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who had responded inadequately to, or who were intolerant to, one or more DMARDs. Jyseleca might be used as monotherapy or in combination with methotrexate.

In addition, Jyseleca was indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who had had an inadequate response with, lost response to, or were tolerant to, either conventional therapy or a biologic agent.

Website structure

The website was directed towards UK and Ireland health professionals (Galapagos referred to 'Home' page. It was divided into sections, from left to right: an initial page ('At A Glance'), provided an overview of the main product benefits. Specific areas addressed the detailed efficacy, safety and mechanism of action ('MOA') and dosing information and there was a 'Resources' page which provided a detailed, downloadable, Prescribing Guide.

A clear statement in the blue flash at the very top of every page directed health professionals to the prescribing information (PI) link in the footer, where links to the PI and the summary of product characteristics (SPC) could both be found. The method of administration (MOA) and Dosing page also linked directly to the comprehensive Jyseleca Prescribing Guide, which was based on the SPC and Risk Management Measures ('RMM') and contained additional resources for prescribers.

References for the statements which were the subject of this complaint were provided and copies of the signatures certifying the website.

'Strength of balance'

Galapagos strongly disagreed that the term 'strength of balance' misrepresented the merits associated with Jyseleca. The term first appeared on the homepage of the website and was further explained on the initial page 'At a Glance' which stated:

'Jyseleca - A JAK1 preferential inhibitor for moderate to severe RA offering a balance of [1-6]: SUSTAINED EFFICACY [2-5] […. and …] ACCEPTABLE TOLERABILITY [1,7,8].'

Thus, the use of the statement 'strength of balance' reflected the fact that Jyseleca was associated with both sustained efficacy and acceptable tolerability, consistent with the identified references.

Further information was given beneath each heading, as follows:

'SUSTAINED EFFICACY [2-5]
In Phase 3 trials, JYSELECA demonstrated:

- *ACR20 response as early as Week 2 in 37% of patients (n=475) vs. 15% of patients in the MTX + placebo group (n=475; p<0.001)[2]*
- *ACR70 response in 44% of patients by Week 52 (n=475)[2]*
- *DAS28-CRP <2.6 remission achieved in 54% of patients at Week 52 (n=475)[2]*
- *Zero radiographic progression* at Week 52 in 88% of patients (n=475)[6].'*

'ACCEPTABLE TOLERABILITY [1,7,8]
In Phase 2 and 3 trials, JYSELECA demonstrated:

- *Similar observed rates of serious infections and herpes zoster compared to adalimumab[7,8]*
- *Consistently low rates of JAK inhibitor-associated adverse events up to 52 weeks:1,7†*
  - *low rates of serious infection1†*
  - *low rates of herpes zoster1†*
  - *low rates of VTE7†*

Common adverse events (≥1/100 to <1/10) include: nausea, upper respiratory tract infection, urinary tract infection, dizziness.[1]

** Defined as change from baseline in modified Total Sharp Score ≤0.6*

† Based on AE rates observed as 'Uncommon' (<1% and >0.1%) or of lower frequency in the JYSELECA clinical trials.[1,7].'

The references that supported each statement were provided in the usual superscript format and a list of references was provided on the same page. Many of the references were clinical papers that accurately portrayed the results of clinical trials. The papers had undergone peer review and had been subjected to the usual scientific scrutiny. Copies of the references were provided.

The amount of information provided on the website itself, and within the referenced papers, was sufficient to allow health professionals to properly evaluate the efficacy and tolerability profile of the product.

In addition, the provision of links to relevant reference material, including the PI, SPC, Risk Management Material (RMM), meant that users of the website were able to access sufficient information to form their own opinion of the therapeutic value of the product.

<u>'Sustained Efficacy'</u>

The next section of the website, following 'At a Glance', 'EFFICACY' delved further into the data from the Phase 3 trials that supported the claim of sustained efficacy. It stated:

*'**In Phase 3 trials, JYSELECA demonstrated:***

> *Rapid and lasting efficacy from Week 2 to Week 52, with or without MTX[2-5] ACR Data*
> *DAS28-CRP <2.6 remission in MTX-IR and biologic-IR patients[2,3] DAS28-CRP Remission >*
> *Successful inhibition of radiographic progression[2,4-6]* Radiographic Progression *>.'*

Next to each bullet point there was a click through which took the viewer to a new page with clear graphs showing the data flow at various timepoints in FINCH 1, FINCH 2 AND FINCH 3. Additional information about the studies was available via a box beneath the graphs 'Study Details'. Clicking on this box revealed the fact that all three studies were double-blind placebo-controlled trials.

Further down the 'Efficacy' page there was a heading 'Discover Strength of Balance' underneath which was the same click throughs to: ACR Data; DAS28-CRP Remission; Radiographic Progression and an additional click through to 'Head-to-head vs. Adalimumab' which set out in a table 'Efficacy outcomes at Week 12 - Exploratory analysis of the FINCH 1 trial[2,8]' and provided the study details.

As such, it was clear to health professionals visiting the website that the term 'strength of balance' referred partly to sustained efficacy and that this was supported by data from the clinical trials.

The efficacy of Jyseleca was substantiated by the following references:

JYSELECA SPC. Available at: www.medicines.org.uk / www.medicines.ie. Last accessed: June 2022.
Combe B, *et al*. Ann Rheum Dis 2021;doi:10.1136/annrheumdis-2020-219214.
Genovese MC, *et al*. JAMA 2019;322(4):315–325.
Westhovens R, *et al*. Ann Rheum Dis 2021;doi:10.1136/annrheumdis-2020-219213.
Kavanaugh A *et al*. J Rheumatol 2021;48:1230–8.
Data on file - Gilead Sciences Ltd - INF-UK-20-04.
Genovese MC, *et al*. Poster presented virtually at the European League Against Rheumatism (EULAR) 2020 E-Congress, June 3-6, 2020.
Data on file – Gilead Sciences Ltd - INF-UK-20-17.
Winthrop K, *et al*. Poster presented virtually at American College of Rheumatology Convergence; November 5–9, 2020.

'Acceptable Tolerability'

The next page across, 'SAFETY', had the sub-heading 'ACCEPTABLE TOLERABILITY'. Further down the page, in a similar format to the 'Efficacy' page, was a heading 'Discover Strength of Balance' underneath which were click throughs to pages called:

- *'Common and Serious AEs'*
- *'Clinical Trial AE Profile'*
- *'AEs VS. Adalimumab.'*

Each page provided data from Phase 2 and 3 clinical trials. There was also a click through to the SPC and RMM *'for complete information regarding the safety and use of Jyseleca'.* This was followed by the statement:

> *'**In Phase 2 and 3 trials, JYSELECA demonstrated:***
>
> > *Low rates* of JAK inhibitor-associated adverse events[1†]*
> > *Similar observed rates of serious infections, Herpes Zoster and VTE compared to adalimumab[2,3].'*
>
> *Based on AE rates observed as 'Uncommon' (<1% and >0.1%) or of lower frequency in the JYSELECA clinical trials.1,2
>
> †JAK inhibitor-associated adverse events defined as VTEs, Herpes Zoster Reactivation and Serious Infections.[4]

Health professionals visiting the website were therefore notified that the term 'strength of balance' referred partly to acceptable tolerability, which was supported by the available safety data.

The statements on acceptable tolerability were substantiated by the following references:

> JYSELECA SPC. Available at: www.medicines.org.uk / www.medicines.ie. Last accessed: June 2022.
> Genovese MC, *et al.* Poster presented virtually at the European League Against Rheumatism (EULAR) 2020 E-Congress, June 3–6, 2020.
> Data on file - Gilead Sciences Ltd - INF-UK-20-17.

'delivering breakthroughs in RA and inflammation'

The statement 'delivering breakthroughs in RA and inflammation' appeared only once on the website on the homepage. The full sentence read 'From Galapagos, delivering breakthroughs in RA and Inflammation'.

As was clear from consideration of the full sentence, the claim referred to Galapagos (rather than any specific product) and the Galapagos aim was to deliver breakthroughs in rheumatoid arthritis and inflammation, as evidenced in various sections of the Galapagos corporate website. No specific product was named, and the term 'breakthroughs' was plural, indicating that the statement related to more than one product. The disease areas, which were the focus of Galapagos' interests, included inflammation and rheumatoid arthritis, as demonstrated by the current indications for Jyseleca (rheumatoid arthritis and ulcerative colitis) and the company's pipeline, which included two further potential inflammation indications for Jyseleca and investigation of an additional five molecules as potential therapies for various inflammatory diseases. The reference to 'RA and inflammation' in the statement complained of reflected those interests. Given that the statement did not refer to Jyseleca, but rather to Galapagos' mission and dedication to inflammation (as demonstrated by Galapagos' pipeline), it was not a 'product claim' and therefore could not be considered 'a claim implying special merit'. As such, it did not require substantiation.

Clause 14.4

Clause 14.4 provided:

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

Neither of the two statements identified by the complainant constituted exaggerated or all-embracing claims or included superlatives.

- The 'strength in balance' statement referred specifically to Jyseleca and the fact that the product achieved a balance between sustained efficacy and acceptable tolerability. This balance was substantiated and appropriately referenced. The fact that the statement also appeared in the URL did not alter this analysis.
- The 'delivering breakthroughs in RA and inflammation', did not refer to any specific medicinal product, but rather to Galapagos itself and its mission statement. The complainant recognised this situation, but suggested that, because the term was not used on other Galapagos websites, it was not a term that was 'intended to be used in a general non-specific sense'. However, as explained above, and confirmed by Annex 12, the wording 'delivering breakthroughs' was a company mission statement included on the Galapagos corporate website.

In the above circumstances, Galapagos did not consider that the statements identified by the complainant breached Clause 14.4 of the Code.

Clause 6.1

Clause 6.1 provided:

'Information, claims and comparisons must be accurate, balanced, fair, objective and unambiguous and must be based on an up-to-date evaluation of all the evidence and reflect that evidence clearly. They must not mislead either directly or by implication, by distortion, exaggeration or undue emphasis.

Material must be sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine.'

Galapagos did not consider that the two statements identified by the complainant breached Clause 6.1:

- Galapagos set out the basis for the 'Strength of Balance' statement, which was further explained and referenced on the initial page on the website 'At a Glance'. The statement was consistent with the available evidence and did not mislead either directly or by implication. The references provided were sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine. As indicated in Galapagos' response to Clause 14.4, there was no exaggeration.
- The 'delivering breakthroughs in RA and inflammation' statement related to the company ('From Galapagos, delivering breakthroughs in RA and inflammation') and not to any specific product. Galapagos' response to Clause 14.4 was repeated.

Clause 6.2

Clause 6.2 provided:

> *'Any information, claim or comparison must be capable of substantiation.*
>
> *Companies must provide substantiation, following a request for it as set out in Clauses* 14.3 *and* 18.2*. In addition, when data from a clinical trial is used, companies must ensure that where necessary, that trial has been registered and the results disclosed in accordance with* Clause 4.6*.'*

Galapagos did not consider there had been any breach of Clause 6.2:

- The 'Strength of Balance' statement was substantiated by the references provided. The complainant did not suggest that he/she had previously requested this material from Galapagos and it was not aware that he/she had done so.
- The 'delivering breakthroughs in RA and inflammation' statement related to the company ('From Galapagos, delivering breakthroughs in RA and inflammation') and not to any specific product. Galapagos' response to Clause 14.4 was repeated.

Conclusion

In summary, it was Galapagos' position that the statements identified by the complainant did not breach Clauses 14.4, 6.1 or 6.2 of the Code. Galapagos hoped that this response addressed any concerns of the PMCPA in relation to the issues raised by the complainant.

PANEL RULING

The Panel noted that the complainant provided a screenshot of what appeared to be the homepage of the Jyseleca 'strengthofbalance' website which included a prominent banner at the top of the page stating 'Strength of Balance From Galapagos, delivering breakthroughs in RA and Inflammation' which appeared on the background image of a lion with the stem of a red flower in its mouth held horizontally walking through grass.

'Strength of balance'

The Panel noted that Galapagos strongly disagreed that the term 'strength of balance' misrepresented the merits associated with Jyseleca; according to Galapagos, it reflected the fact that Jyseleca was associated with both sustained efficacy and acceptable tolerability, consistent with the identified references. The Panel noted Galapagos' submission that the term first appeared on the homepage of the website and was further explained on the 'At a Glance' page which stated:

> *'Jyseleca - A JAK1 preferential inhibitor for moderate to severe RA offering a balance of [1-6]: SUSTAINED EFFICACY [2-5] […. and …] ACCEPTABLE TOLERABILITY [1,7,8].'*

The Panel noted Galapagos' reference to qualifying information elsewhere on the website and considered that each webpage should not be misleading if read in isolation. Companies had to be particularly careful that each webpage complied with the Code and did not rely on information elsewhere to ensure Code compliance. In the Panel's view, it was not immediately

obvious when reading the homepage what 'strength of balance' was meant to convey; it was not clear until readers read the subsequent webpage. In this regard, the Panel noted that some readers might not look at the 'At a Glance' webpage and certain readers might consider that the claim in question referred in part to potency. The claim in question within the banner was not qualified by text elsewhere on the homepage within its visual field. Boxes immediately beneath the banner featured images of the lion and apparent links to 'At a Glance', 'Efficacy', 'Safety' and 'Mode of Action and Dosing'.

The Panel considered that the claim 'strength of balance' as it appeared on the homepage was ambiguous and there was insufficient additional information to allow the reader to understand what it meant. A **breach of Clause 6.1** was ruled. The Panel did not consider that the claim, although ambiguous, implied a special merit for Jyseleca. In the Panel's view, given that the meaning of the claim, as it appeared on the homepage, was unclear, it was difficult to understand how it could be said to imply a special merit. The Panel did not consider that the complainant had established that the claim in question implied a special merit that could not be substantiated as alleged and **no breach of Clauses 6.2 and 14.4** were ruled.

'delivering breakthroughs in RA and inflammation'

The Panel noted Galapagos' submission that the claim referred to Galapagos rather than any specific product; no specific product was named and the term 'breakthroughs' was plural, indicating that the statement related to more than one product. The Panel further noted Galapagos' submission that its aim was to deliver breakthroughs in rheumatoid arthritis and inflammation, as evidenced in various sections of the Galapagos corporate website, and given that the statement did not refer to Jyseleca, but rather to Galapagos' mission and dedication to inflammation, it was not a 'product claim' and therefore could not be considered 'a claim implying special merit' and did not require substantiation.

The Panel considered that, in certain circumstances, a corporate mission statement might be regarded as promotional: both its content and context were relevant factors. The Panel considered that the statement, which was an integral part of a banner at the top of the homepage of the promotional website for Jyseleca, would be seen as a strong claim for Jyseleca; that it was a breakthrough in RA and inflammation that had been delivered by Galapagos. Indeed, this was the view of the complainant. The Panel noted that the complainant had the burden of proving his/her complaint on the balance of probabilities. The Panel noted the complainant's allegation that the claim implied a special merit of Jyseleca when there were several other JAK inhibitors that were used in inflammatory diseases, and none had been demonstrated to be a 'breakthrough' in treatment and there were no references to justify this term. The Panel noted its finding above that the term 'delivering breakthroughs in RA and inflammation' was a strong claim for Jyseleca and considered that the company should be cautious when using such strong claims. Nonetheless, in the particular circumstances of this case, the complainant had submitted no material and had not identified any specific evidence to support his/her position. The Panel noted that the complainant bore the burden of proof and considered that he/she had not established his/her case on the balance of probabilities. Whilst the Panel was concerned about the phrase in question, in the absence of any evidence on this point, and on this very narrow ground alone, the Panel did not consider that the claim 'delivering breakthroughs in RA and inflammation' misleadingly implied that Jyseleca had a special merit that could not be substantiated and the Panel therefore ruled **no breach of Clauses 14.4, 6.1 and 6.2**.

Complaint received **29 June 2022**

Case completed **3 July 2023**