CASE/0228/07/24 ***NO BREACH OF THE CODE***

COMPLAINANT v GSK

Allegations about patient safety data on GSK product website

CASE SUMMARY

This case was in relation to an allegation that the Great Britain and Northern Ireland prescribing information for GSK's product Jemperli (dostarlimab) included adverse reactions information that was inconsistent with the Summary of Product Characteristics.

The outcome under the 2021 Code was:

No Breach of Clause 2	**Requirement that activities or materials must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**
No Breach of Clause 5.1	**Requirement to maintain high standards at all times**
No Breach of Clause 6.1	**Requirement that information must be accurate, up-to-date and not misleading**
No Breach of Clause 12.2	**Requirement that the prescribing information must include a succinct statement of common and serious adverse reactions likely to be encountered in clinical practice**

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

FULL CASE REPORT

A complaint about GSK UK Limited was received from an anonymous, non-contactable complainant who described themselves as a health professional.

COMPLAINT

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

> "I have noticed concerning inconsistencies with the patient safety data in the PI and SPC for Jemperli, for both GB [Great Britain] and NI [Northern Ireland] professionals. This suggests that at least 2 of these documents are incorrect; that being either both PIs or both SPCs. It is highly worrying that such basic consistency checks on items/statements concerning patient safety appear not to have been conducted during the production of these documents that GSK directs healthcare professionals to on their promotional website (and will be directing healthcare professionals to in other promotional files). Inconsistency is observed in 'undesirable effects' in the PI for Jemperli. This says 'JEMPERLI monotherapy: Most common ADRs in patients with advanced or recurrent

solid tumours (>10%) were …… aspartate aminotransferase increased ……'. But SPC table 4 says this should be transaminase increased that 'includes transaminases increased, alanine aminotransferases increased, aspartate aminotransferases increased and hypertransaminasaemia'. As a result, in the first mention of common ADRs in the GB and NI PIs, safety information is inaccurate and misleading. ADRs are being excluded. Later in PI, transaminase increased is down as common after 'JEMPERLI in combination therapy AND JEMPERLI monotherapy:……', however at this point the reader has already been alerted to AST only for monotherapy administration. Do GSK believe the reader should be required to continue searching for most common ADRs after the first section of this section. The readers should be able to take all statements within the PI as true and accurate. If the reader decides to continue to the later point, the extra inconsistent information only adds confusion and does not counteract the previous incorrect and misleading ADR statement. Please consider a breach of clause 2, 5.1, 12.2. The documents are still found and linked on the company website: [URL], more targetably:
[URL to GB PI]
[URL to NI PI]
[URL GB SPC]
[URL to NI SPC]."

When writing to GSK, the PMCPA asked it to consider the requirements of Clauses 2, 5.1, 6.1 and 12.2 of the 2021 Code.

GSK'S RESPONSE

The response from GSK is reproduced below:

"GSK was extremely disappointed to have received a letter dated 16th July 2024 from the PMCPA informing us of a complaint from an anonymous, non-contactable complainant who described themselves as a health professional.

The complainant stated that they 'noticed (sic) concerning inconsistencies' between patient safety data within the Great Britain (GB) & Northern Ireland (NI) Summary of Product Characteristics (SmPC) for Jemperli▼(dostarlimab) and the safety data in the abridged Prescribing Information (PI), which is derived from those SmPCs, on the GB GSKPro website page and the NI GSKPro website page. Furthermore, the complainant believed it to be, 'highly worrying that such basic consistency checks on items/statements concerning patient safety appear not to have been conducted during the production of these documents'. The complainant considered that GSK had breached Clauses 5.1, 12.2 and Clause 2 of the Code. The complainant did not elaborate on which specific element or elements of Clause 12.2 they considered to have been breached. Additionally, the PMCPA asked GSK to bear in mind clause 6.1 when responding to the complaint.

GSK takes its responsibilities of abiding by the letter and the spirit of the Code and all other relevant UK rules and regulations very seriously. Consequently, following receipt of the complaint, we withdrew the PI and all materials containing the PI pending a thorough investigation. GSK subsequently undertook a detailed comparison of the materials in question and determined that the PIs on the aforementioned materials were not

inconsistent with the respective Jemperli SmPCs and were of the quality and high standards required by GSK and the Code.

Additionally, GSK undertook a careful critique of the in-depth reviews that the GB Jemperli PI had undergone (GB PI (PI-11976) between 17th August 2023 and 3rd October 2023 during its revision. Similar reviews of the NI PI (PI-12428) revised between 29th November 2023 and 15th December 2023) were also undertaken. Following these detailed reviews, GSK remain comfortable that the process for updating the PI for Jemperli was thorough, detailed and in line with GSK's requirements/SOP for updating PI. The PIs in question were confirmed to be fully in line with the requirements of Clause 12.2 of the Code. In particular, we found nothing during those reviews that, objectively, could be construed as inaccurate, misleading, give cause for concern with regard to patient safety, 'incorrect' (as claimed by the complainant), inconsistent with Jemperli's SmPCs, or that might otherwise constitute a breach of Clause 12.2 or 6.1. Consequently, given the rigour, diligence and thoroughness of the Jemperli PI revision process, GSK is firmly of the view that there have not been any breaches of Clauses 6.1, 12.2, 5.1 or, indeed, Clause 2 of the Code. Furthermore, at this juncture GSK would like to inform the PMCPA that one of the contributors to the comprehensive Jemperli PI review process was a former [senior health professional] at [named UK hospital] with 10 years clinical experience in the NHS of which 6 of those years were in Oncology.

GSK has laid out the specific responses to the individual clauses the PMCPA has asked us to consider in detail below.

Website background

The Jemperli webpages referred to in the complaint are part of a more extensive promotional website called GSKPro, for UK Healthcare Professionals (HCPs) only. The website contains promotional information about all GSK products currently marketed in the UK. Within the website there is a section dedicated entirely to the product Jemperli.

The Jemperli website can be accessed by three methods:

- Direct access by HCPs via a search engine, such as Google, that requires confirmation via a pop up that they are an HCP, as opposed to a member of the public for whom there is a link to a separate part of the website with relevant content.
- Via third party emails sent by [third party agency] who send emails to HCPs who have given their prior consent to receive emails from pharmaceutical companies via the [third party agency] platform.
- Direct promotion from GSK via email, sending promotional emails to HCPs who have given their consent to receive these.

The complainant's allegation relates only to the PI pages of the NI and GB GSKPro website. The PI can be accessed by HCPs from digital materials, including the GSKPro website, via a clear, prominent, direct, single click link. PI is required *inter alia,* to consist of *'a succinct statement of the information in the summary of product characteristics relating to the dosage and method of use relevant to the indications quoted in the advertisement and where not otherwise obvious the route of administration'.* Furthermore, the PI is required to contain, '*a succinct statement of the common adverse*

reactions likely to be encountered in clinical practice, serious adverse reactions and precautions and contra-indications relevant to the indications in the advertisement'.

The Code is clear that the aim of the PI is to give*, 'in an abbreviated form, the substance of the relevant information in the summary of the product characteristics'.* Of particular note is the requirement to include a statement that*, 'prescribers should consult the summary of product characteristics in relation to other adverse reactions'.*

GSK processes and structure

GSK has robust processes and structures for material approval to ensure compliance with the Code, GSK's own code, and UK regulations. All employees involved in copy approval must complete mandatory GSK copy approval SOP training. Each brand team holds a regular forum for discussion and approval (FDA), involving medical and commercial teams, to discuss and align on materials requiring copy approval, and to ensure all materials and content generated are fully compliant with the Code. Should views differ, for example over specific claims, there is a clear and well-established route of escalation for resolution.

To maintain ongoing Code knowledge, GSK conducts a monthly Code Forum meeting in which Code cases are presented and discussed as well as any other compliance/governance issues which merit awareness. While the meeting is intended principally for all medical signatories, commercial reviewers, and content owners, other staff interested to attend for their own learning and development may do so. Attendance is consistently strong, and materials discussed are stored on GSK's internal governance platform, accessible to all UK employees.

Additionally, GSK holds Governance meetings once a month for medical signatories and medical reviewers. Attendees raise Code-related agenda items for discussion, with a view to reaching consensus within the group, under the guidance of experienced senior signatories.

Furthermore, GSK has a fair and objective process for assessing and validating not only medical signatories, but also commercial reviewers. The role of the commercial reviewer is to provide commercial overview of all promotional and relevant non-promotional materials for appropriateness, including fundamental aspects and principles of the Code, as well as content suitability and strategic alignment. These assessments involve one, or more often two assessors, objectively questioning the candidate on case examples, covering multiple aspects of the Code. In addition, the appraisee must have completed a set of mandatory training requirements. In the case of medical signatories, the appraisee must have been mentored for a period by another experienced medical signatory, until the mentor deems the appraisee ready to take the assessment to become a final medical signatory.

Of particular relevance to this specific complaint, GSK has the following process in place to update PI following relevant changes to a product's SmPC:

- The regulatory team notifies the medical team of a change in SmPC with the timelines for approval from the regulatory authority.

- Following approval of the SmPC, the medical team carefully evaluates the updated SmPC to determine whether any changes to the PI are needed.
- If changes to the PI are required, the material is uploaded for review and amended in line with the updated SmPC.
- The approved, revised PI is then certified in line with the requirements of the Code.
- Materials containing the previously approved PI are withdrawn.
- Relevant existing and any subsequent new materials are reviewed and certified with the updated PI.

The PIs in question were updated in line with GSK's SOP. The need for a GB PI update was triggered on the 3rd October 2023 as a result of updates to the Jemperli GB SmPC following a licence extension for Jemperli. The updated SmPC included an indication for combination platinum-containing chemotherapy for the treatment of adult patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer (pA/r EC) and who are candidates for systemic therapy. Subsequently, an NI SmPC update triggered a similar update to the PI for HCPs in Northern Ireland on 14th December 2023 consequent upon the same licence extension.

As a result of the SmPC updates, the following required changes were made to the PI for Jemperli:

1. Therapeutic indications updated to reflect the patient population for RUBY* Part 1 dMMR/MSI-H pA/r EC.
2. Posology and method of administration updated with addition of dosing of Jemperli in combination with chemotherapy.
3. Undesirable effects updated with the addition of adverse events (AEs) aligned to Jemperli in combination with chemotherapy and Jemperli monotherapy.

* RUBY is a two-part global, randomised, double-blind, multicentre phase III trial of patients with primary advanced or recurrent endometrial cancer. Part 1 is evaluating dostarlimab plus carboplatin-paclitaxel followed by dostarlimab versus carboplatin-paclitaxel plus placebo followed by placebo. In Part 1, the dual-primary endpoints are investigator-assessed PFS based on the Response Evaluation Criteria in Solid Tumours v1.1 and OS. Safety profile is a secondary endpoint.

Jemperli and disease background

Jemperli is a programmed death receptor-1 (PD-1)-blocking antibody. Jemperli binds to PD-1 receptors, blocking the interaction with its ligands PD-L1 and PD-L2. Inhibition of the PD-L1/PD-1 pathway results in reactivation of T-cell function resulting in proliferation, cytokine production, and cytotoxic activity. Jemperli therefore potentiates T-cell responses, including anti-tumour immune responses. Jemperli is indicated:

- in combination with platinum-containing chemotherapy for the treatment of adult patients with dMMR/MSI-H pA/r EC and who are candidates for systemic therapy

- as monotherapy for the treatment of adult patients with dMMR/ MSI-H recurrent or advanced EC that has progressed on or following prior treatment with a platinum-containing regimen

Treatment with Jemperli must be initiated and supervised by specialist physicians who are experienced in the treatment of cancer and who, consequently, are well versed in the benefit:risk profiles of oncology treatments and managing adverse events arising during therapy.

Clause 12.2

As discussed earlier, the complainant 'noticed concerning inconsistencies with the patient safety data in the PI and SPC for Jemperli, for both GB and NI professionals'. GSK holds itself to the highest standards possible, particularly in matters related to the safety of patients prescribed its medicinal products. Accordingly, we disagree in the strongest possible terms with the complainant and their incorrect assertion that ADRs are excluded and safety information is inaccurate and misleading. The PI scrutinised by the complainant would not prejudice patient safety in any way whatsoever.

The GB & NI SmPCs for Jemperli contain the most up-to-date and robust information on the product. All SmPC product information, including the safety information challenged by the complainant, has been reviewed and approved by the relevant competent Regulatory Authorities. Section 4.8 (Undesirable effects) details the occurrence of AEs relating to transaminases and increases in ALT and AST. Specifically, the complainant asserts that '*Inconsistency is observed in 'undesirable effects' in the PI for Jemperli. This say (sic) 'JEMPERLI monotherapy: Most common ADRs in patients with advanced or recurrent solid tumours (>10%) were …… aspartate aminotransferase increased ……'. But SPC table 4 says this should be transaminase increases that 'includes transaminases increased, alanine aminotransferases increased, aspartate aminotransferases increased and hypertransaminasaemia'.*
As a result, in the first mention of common ADRs in the GB and NI PIs, safety information is inaccurate and misleading. ADRs are being excluded. Later in PI, transaminase increases is down as common after 'JEMPERLI in combination therapy AND JEMPERLI monotherapy:……', however at this point the reader has already been alerted to AST only for monotherapy administration.' The list of most common (>10%) AEs for Jemperli monotherapy from section 4.8 of the SmPC was presented, verbatim, in the PI. The SmPC states: 'In patients with advanced or recurrent solid tumours (N = 605), the most common adverse reactions (> 10 %) were anaemia (28.6 %), diarrhoea (26.0 %), nausea (25.8 %), vomiting (19.0 %), arthralgia (17.0 %), pruritus (14.2 %), rash (13.2 %), pyrexia (12.4 %), aspartate aminotransferase increased (11.2 %) and hypothyroidism (11.2 %). Similarly, and consistently, the PI states: 'JEMPERLI monotherapy: Most common ADRs in patients with advanced or recurrent solid tumours (>10%) were anaemia, nausea, diarrhoea, vomiting, arthralgia, pruritus, rash, pyrexia, aspartate aminotransferase increased and hypothyroidism.'

Table 4 of the SmPC lists 'Transaminases increased' as a very common (>10%) adverse reactions for Jemperli monotherapy, this is listed under the category 'Jemperli in combination therapy AND Jemperli monotherapy' in the PI. The term 'Transaminases increased' is defined in the footnote for table 4 as including 'transaminases increased, alanine aminotransferases (ALT) increased, aspartate aminotransferase (AST)

increased, and hypertransaminasaemia'. Of the four International Conference on Harmonisation (ICH) MedDRA terms, (transaminases increased, ALT increased, AST increased and hypertransaminasaemia), only AST was reported at a rate of >10%. In summary, ADRs were not excluded and the complainant is not correct in alleging that they were.

The grouping of ALT, AST and hypertransaminasaemia is supported by routine medical understanding that ALT and AST (also known as aminotransferases) are both transaminases. Aminotransferases or transaminases are a group of enzymes that catalyse the interconversion of amino acids and oxoacids by transfer of amino groups. ALT and AST are the two aminotransferases of greatest clinical significance.

GSK maintain that the PI is entirely consistent with the requirement of Clause 12.2 of the Code to provide the required elements of the SmPC succinctly. Furthermore, the complainant is wholly incorrect in alleging that 'ADRs are being excluded'. Increases in both transaminases are commonplace in medical therapeutics. Practising HCPs, in general and the specialist oncologists in particular prescribing Jemperli would fully appreciate the terminology used and, importantly, recognise its consistency with the SmPC to which they are referred. In short, HCPs would not, as alleged by the complainant, find the PI misleading or inaccurate.

Jemperli must be initiated and supervised by specialist oncology physicians. Oncologists who prescribe Jemperli and who may therefore be presented with the Jemperli PI in materials from GSK are well versed in the assessment and management of liver function and its biochemical evaluation. Measuring the blood levels of transaminases is one element of liver function testing. Haematological and clinical chemistries, including liver, kidney and thyroid function, should be evaluated at baseline and periodically during treatment. This is specified clearly in Section 4.4 of Jemperli's SmPC. As required by Clause 12.2 (part v.) of the Code this precaution for use is fully reflected in the PI for Jemperli. The complainant, however, failed to acknowledge this salient inclusion whilst alleging 'concerning inconsistencies' between the SmPC and the PI.

Additionally, GSK is mindful of a previous Code case of an anonymous oncologist v Pierre Fabre (AUTH/2799/10/15), where the panel '*...noted the highly specialised therapy area … In the Panel's view the audience would be familiar with the side effect profile of cytotoxic medicines generally*.' While Jemperli has been licensed since 2021, anti-PD-1 treatments have been available for over a decade. Oncologists who prescribe them, separately or in combination with other chemotherapeutic medicines, have extensive experience of their use and side effect profiles including liver function disturbances.

Consequently, GSK refute that there was a breach of Clause 12.2 resulting from alleged inconsistencies between the PIs for Jemperli and the Jemperli SmPCs. The PI included the necessary information on liver function test (LFT) transaminase abnormalities and was not inconsistent with the SmPC.

To conclude, GSK processes to update PI following SmPC changes were and remain robust. No change to those processes is being considered as a consequence of this anonymous complaint. A breach of Clause 12.2 is firmly denied.

Clause 6.1

The complainant alleges *inter alia* that '…safety information is inaccurate and misleading' and, further, that 'readers should be able to take all statements within the PI as true and accurate.' Therefore, the PMCPA asked GSK to consider Clause 6.1 when responding. The information contained in the referenced Jemperli PIs, subject of the complaint, was contemporaneously accurate, based on an up-to-date evaluation of all of the evidence and reflected that evidence clearly. The information did not mislead either directly or by implication, by distortion, exaggeration or undue emphasis.

While the Jemperli PI is considered sufficiently complete in itself to enable recipients to form their own opinion of the therapeutic value of the medicine, the material, as required by the Code, referred prescribers to the Jemperli SmPC. The Jemperli PI was not inconsistent with the SmPC. Consequently, GSK does not believe Clause 6.1 was breached.

Clause 5.1

The complaint alleges that 'It is highly worrying that such basic consistency checks on items/statements concerning patient safety appear not to have been conducted during the production of these documents that GSK directs healthcare professionals to on their promotional website'.

As discussed earlier, GSK processes, training, governance and management monitoring have all been designed and implemented to embed the spirit as well as the letter of the Code. GSK's standards promote rigour when creating, reviewing, approving and certifying promotional materials. We remain confident that the certification process and the quality of the cited materials are robust. The alleged PI safety considerations and the related GSK processes ensuring consistency between the materials that have been brought into question by the complainant have been critically appraised, confirmed as suitable and correct.

GSK asserts that high standards were maintained throughout the revisions to the Jemperli PIs and that the required revisions were not inconsistent with the updated changes to the Jemperli SmPCs. Consequently, GSK is confident there was not a breach of Clause 5.1.

Clause 2

The complainant asked the PMCPA to consider a breach of Clause 2 in addition to Clauses 5.1 and 12.2 of the Code. GSK notes that a ruling of a breach of Clause 2 is a sign of censure, reserved for circumstances that include prejudicing patient safety and/or public health. It is ruled when significant failings have been identified, that include *inter alia* a risk to patient safety.

In responding to the breaches alleged by the complainant, GSK has put forward strong arguments to show there was no evidence of a risk to patient safety, or a failure in the Company's systems and processes. The PI in question was fully reviewed and updated in line with the revised SmPCs.

It was neither misleading nor inaccurate and consequently was certified and the final form examined in the manner required and to the standards mandated by the Code and by GSK's own SOP. Furthermore, GSK has argued closely that the safety information at issue contained within the prescribing information was accurate and not inconsistent with the product's SmPC. The inclusion of information on increases in ALT and AST and the statements on monitoring of LFTs were also correct and in line with the SmPC. As written, the Jemperli PI did not add or create confusion. GSK takes patient safety very seriously. We believe strongly that patient safety has not been nor would be prejudiced by the prescribing information in question.

For these reasons, and all others detailed above, GSK's activities and materials do not risk bringing discredit upon or reducing confidence in the pharmaceutical industry. Consequently, GSK does not recognise that there has been a possible breach of Clause 2.

In summary, GSK has argued cogently and fully why we are confident that there have not been any breaches of Clauses 6.1, 12.2, 5.1 or Clause 2 of the 2021 ABPI Code of Practice.

Additional information

The signatories who reviewed, approved, and certified the material at issue in **AUTH/0228/07/24** are as follows:

For the GB PI (PI-11976), the final form reviewer is a registered UK [medical professional] of [XX] years with 6 years' signatory experience.

For the NI PI (PI-12428), the final form reviewer is a registered UK [medical professional] of [XX] years with 6 years' signatory experience.

Furthermore, as mentioned above, an additional reviewer involved in the process was a former [senior health professional] at [named] NHS Trust with 10 years clinical experience in the NHS of which 6 of those years were in Oncology."

PANEL RULING

This case was in relation to an allegation that the Great Britain and Northern Ireland prescribing information (PI) for GSK's product Jemperli (dostarlimab) included adverse reactions (ADR) information that was inconsistent with the Summary of Product Characteristics (SPC).

The complainant alleged that the inconsistency between the two PIs, and their respective SPCs, arose from the following extract of the two PIs which appeared under the heading "*Undesirable effects*":

"*JEMPERLI monotherapy: Most common ADRs in patients with advanced or recurrent solid tumours (> 10 %) were anaemia, nausea, diarrhoea, vomiting, arthralgia, pruritus, rash, pyrexia, aspartate aminotransferase increased and hypothyroidism.*"

The complainant highlighted specifically the reference to "*aspartate aminotransferase increased*" in this section of the PI and alleged that this was inconsistent with Table 4 in the SPC. Table 4 was under the SPC heading "*4.8 Undesirable effects*", the relevant section of which stated:

"*Table 4: Adverse reactions in patients treated with dostarlimab*

System Organ Class	***Dostarlimab monotherapy***	***Dostarlimab in combination therapy***
…	…	…
Investigations	***Very common*** *Transaminases increased(r)*	***Very common*** *Alanine aminotransferase increased,* *aspartate aminotransferase increased*

"

In relation to the wording "*Transaminases increased*" in the bottom row of the middle column above, footnote "r" (which followed the table) stated:

"*Includes transaminases increased, alanine aminotransferases increased, aspartate aminotransferases increased and hypertransaminasaemia*"

The Panel interpreted the complainant's allegation to be that because footnote "r" clarified that the wording "*transaminases increased*" included:

(i) transaminases increased,
(ii) alanine aminotransferases (ALT) increased,
(iii) aspartate aminotransferases (AST) increased, and
(iv) hypertransaminasaemia,

the PI was inaccurate and misleading because it only referred to (iii): AST increased.

The complainant further alleged that, later in the PI, "*transaminase increased is down as common after 'JEMPERLI in combination therapy AND JEMPERLI monotherapy'", however at this point the reader has already been alerted to AST only for monotherapy administration.*" However, the Panel concluded that the complainant was incorrect alleging that "*transaminases increased*" *was* listed as a common adverse event as it was listed as a "*very common*" adverse event in the SPC.

The Panel took account of the requirements of Clause 12.2:

"a succinct statement of common adverse reactions likely to be encountered in clinical practice, serious adverse reactions and precautions and contra-indications relevant to the indications in the advertisement, giving, in an abbreviated form, the substance of the relevant information in the summary of product characteristics, together with a statement that prescribers should consult the summary of product characteristics in relation to other adverse reactions".

The Panel noted that the SPC, Section 4.8 Undesirable Effects, Dostarlimab in Monotherapy stated:

> "*In patients with advanced or recurrent solid tumours (N = 605), the most common adverse reactions (> 10 %) were anaemia (28.6 %), diarrhoea (26.0 %), nausea (25.8 %), vomiting (19.0 %), arthralgia (17.0 %), pruritus (14.2 %), rash (13.2 %), pyrexia (12.4 %),* ***aspartate aminotransferase increased*** *(11.2 %) and hypothyroidism (11.2 %)*" (Panel's emphasis).

The Panel noted that the SPC, Section 4.8 Undesirable Effects, Dostarlimab in combination with chemotherapy stated:

> "*In patients with primary advanced or recurrent EC (N = 241), the most common adverse reactions (> 10 %) were rash (22.8 %), rash maculopapular (14.1%), hypothyroidism (14.1 %),* ***alanine aminotransferase increased*** *(12.9 %),* ***aspartate aminotransferase increased*** *(12.0 %), pyrexia (12.0 %) and dry skin (10.4 %)*" (Panel's emphasis).

The Panel accepted GSK's submission that the decision to group ALT, AST and hypertransaminasaemia is supported by routine medical understanding because ALT and AST are both transaminases. The Panel also took account of the fact that Vroon *et al* stated that AST and ALT are the two aminotransferases of greatest clinical significance.

It was clear to the Panel that the list of the most common ADRs (i.e. those that were >10%) for monotherapy and combination therapy within Section 4.8 of the SPC, was the basis for the PI wording referred to by the complainant.

In addition, the Panel accepted GSK's submission that, of the four International Conference on Harmonisation MedDRA terms:

(i) transaminases increased,
(ii) ALT increased,
(iii) AST increased, and
(iv) hypertransaminasaemia,

only AST increased was reported at a rate of >10% in monotherapy. Given that:

(a) AST was the only one of the four terms that was >10% in monotherapy, and also part of the individualised list of the most common ADRs in Section 4.8 of the SPC, and

(b) grouping AST and ALT together as "*transaminases*" was routine medical practise,

the Panel did not consider that the complainant had established that the PIs for Great Britain and Northern Ireland were inaccurate or misleading as alleged. The Panel therefore ruled **no breaches of Clauses 6.1 and 12.2**.

Given the above rulings and, in the absence of any other allegations from the complainant to suggest that there had been a failure to maintain high standards or that GSK had brought discredit upon, or reduced confidence in, the pharmaceutical industry, the Panel ruled **no breaches of Clauses 5.1 and Clause 2**.

Complaint received **7 July 2024**

Case completed **31 July 2025**