CASE/0749/09/25

ROCHE v NEURAXPHARM

Allegations regarding a Briumvi (ublituximab) promotional presentation

CASE SUMMARY

This intercompany complaint related to a promotional symposium by Neuraxpharm for Briumvi (ublituximab) at a conference in March 2025. Roche alleged that the presentation in question was misleading because it implied a clinically relevant differentiation and advantage based on glycoengineering and associated *in vitro* antibody-dependent cellular cytotoxicity (ADCC) data, which had not been established.

The outcome under the 2024 Code was:

Breach of Clause 5.1	**Failing to maintain high standards**
Breach of Clause 6.1	**Providing misleading information**

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 was received about Neuraxpharm UK Ltd from Roche Products Ltd.

COMPLAINT

The complaint wording is reproduced below:

> "Roche is seeking PMCPA adjudication to ensure appropriate resolution of concerns arising from Neuraxpharm's promotional presentation regarding ublituximab at the [named patient organisation] Meeting in March 2025. Whilst extensive intercompany dialogue (ICD) has addressed certain issues, two points of concern remain unresolved which Roche believes represent significant breaches of the ABPI Code of Practice. A copy of the correspondence exchanged between Roche and Neuraxpharm during ICD is attached, together with an executive summary below.
>
> For context, Roche Products Limited holds marketing authorisation for Ocrevus (ocrelizumab), licensed in the UK for the treatment of adult patients with relapsing forms of multiple sclerosis (RMS) and for early primary progressive multiple sclerosis (PPMS). Neuraxpharm UK Ltd markets Briumvi (ublituximab), licensed in the UK for the treatment of adult patients with relapsing forms of multiple sclerosis (RMS). For ease of reference, the relevant Summary of Product Characteristics (SPCs) for both medicines are attached. In addition, the slides presented at the [named patient organisation] Meeting, which formed the basis of the intercompany dialogue, are attached.

Executive summary of ICD

Roche's fundamental concern is that Neuraxpharm's presentation places undue emphasis on glycoengineering and associated in vitro Antibody-Dependent Cellular Cytotoxicity (ADCC) data, creating the misleading impression that these features confer a proven clinical advantage over other anti-CD20 therapies, when no such clinical relevance has been established. Roche believes this approach breaches the ABPI Code by extrapolating non-clinical findings to the clinical setting and by positioning glycoengineering as a unique differentiator without comparative clinical evidence. As such, Roche considers this a breach of Clause 6.1 of the ABPI Code of Practice and, given Neuraxpharm's stated position that such use of data is acceptable and will continue, also a breach of Clause 5.1 for failing to maintain high standards.

The presentation in question placed in vitro ADCC data alongside clinical efficacy outcomes under the heading *'The importance of glycoengineering'*, thus creating the impression that glycoengineering provides ublituximab with a unique clinical advantage. Neuraxpharm have argued that the data were clearly marked as 'in vitro,' properly referenced, and that disclaimers could be used in the future to avoid misunderstanding. Roche does not believe that such disclaimers address the fundamental issue. The fact remains that the clinical significance of glycoengineering has not been established. By continuing to highlight this feature, Neuraxpharm risks misleading healthcare professionals into believing it represents direct clinical relevance or significance where no clinical evidence supports this claim.

Roche is equally concerned that the repeated focus on glycoengineering positions ublituximab as uniquely differentiated from other anti-CD20 therapies, despite there being no comparative clinical evidence to support such a distinction. Neuraxpharm have argued that glycoengineering was presented as a legitimate topic of educational interest for healthcare professionals. Roche does not share this view. Without established clinical relevance, the emphasis placed on glycoengineering goes beyond education and amounts to promotional positioning. This creates a misleading overall impression by implying that ublituximab possesses a proven therapeutic advantage over other treatments in the same class, when that has not been demonstrated.

Despite multiple exchanges, including Roche's letters dated 12 May, 6 June, and 4 July 2025, as well as a face-to-face ICD meeting on 12 September 2025, Roche and Neuraxpharm remain in fundamental disagreement regarding the promotional use and overemphasis of glycoengineering in the presentation and its intended use in future materials.

Roche maintains that the presentation is misleading in implying a clinically relevant differentiation based on glycoengineering. In our view, this constitutes a breach of Clause 6.1 (accuracy, balance, non-misleading claims) and Clause 5.1 (failure to maintain high standards). Accordingly, Roche requests that the PMCPA provide an independent determination on whether Neuraxpharm UK Ltd's conduct in this matter breaches the Code."

When writing to Neuraxpharm, the PMCPA asked it to consider the requirements of Clauses 5.1 and 6.1 of the 2024 Code.

NEURAXPHARM'S RESPONSE

The response from Neuraxpharm is reproduced below:

> "Further to your letter of 31st October 2025, please find below the response from Neuraxpharm relating to each alleged Clause breach (5.1, 6.1). Within the enclosure of this response, you will find the following document trail: [details of intercompany dialogue correspondence provided].
>
> Further to several rounds of ICD (details attached), including a face-to-face meeting on the 12th of September 2025 please find a summary below of Neuraxpharm's position and response.
>
> Roche initially approached Neuraxpharm on 12th May 2025 and this complaint **was specific to the content of a Neuraxpharm promotional symposium at the [named patient organisation] meeting**, 23rd – 25th March 2025. Roche raised four issues:
>
> 1. Glycoengineering, Antibody-Dependent Cellular Cytotoxicity (ADCC), and B Cell Depletion
> 2. Emphasis on technical features implying unique benefit
> 3. Presentation of Confirmed Disability Progression (CDP) Data
> 4. Presentation of B Cell depletion data
>
> The first round of ICD was successful in resolving issues three and four, Roche replied on the 6th of June 2025, confirming this and stating that issues one and two remained unresolved:
>
> 1. Glycoengineering, ADCC and B cell depletion
> 2. Emphasis on technical features implying unique benefit
>
> Throughout the ICD process (three rounds of letters and a face-to-face meeting), Neuraxpharm has maintained the following:
>
> - At the meeting in question, there was never any intent on the part of Neuraxpharm or the speaker (who was briefed explicitly, verbally, prior to the meeting) to extrapolate the in vitro data to the clinical situation from either the presentation of the in vitro data or the explanation of the technical features of ublituximab and glycoengineering
>
> - The in vitro data (slide 13) was presented in a clear, factual manner with references. Neuraxpharm does not believe that in the context of this meeting, HCPs would have been misled:
>
> - Clause 6.1 – specifically talks about in vitro data not being used in a way that misleads to its significance and that the extrapolation of such data should only be made where there is data to show it is of direct relevance
>
> - The slides presented at the meeting **did not extrapolate any data to imply direct relevance**

- The [named patient organisation] meeting was an important opportunity for education and information sharing in the MS space, to a relevant audience of HCPs. Neuraxpharm maintains our stance that in view of this, discussion of the first glycoengineered disease modifying therapy for MS was of value to HCPs. There are recent publications available which support this as an area of interest. In addition to this, Neuraxpharm has received positive delegate feedback from the [named patient organisation] meeting organisers regarding the content, the value and the quality of our symposium

- Throughout the course of the ICD, Neuraxpharm has responded timely and constructively, upholding the desire to resolve all issues amicably and in the best spirit. To this end, in our response letter dated 20th June 2025, we reiterated that we do not believe that HCPs would have been misled by this presentation and nor was it our intention. In the spirit of ICD and wanting to uphold the highest standards, Neuraxpharm offered to implement the following actions (which we believe were a fair and reasonable offering), with respect to any future presentations of the in vitro data in question:

    - To further underline the data, Neuraxpharm will highlight within the immediate visual field of any presentation of this data a statement to the effect that:
        - *'The clinical significance of this in vitro data has not been established.'*

    - Neuraxpharm will not use 'The importance of glyco-engineering' as a title and will instead reflect the in vitro investigational nature of the data.

    - In the interest of providing further clarity on the in vitro data (referenced here - Steinman L, et al. N Engl J Med. 2022;387(8):704–714), we will ensure that unless the clinical relevance of this data is established, any future information presented on this (presented at symposia, presentations, and in newly created material from the date of this letter) will not be immediately preceded or followed up by data on clinical efficacy.

- During the face-to-face meeting and in their letter to the PMPCA (24th September 2025), Roche has also stated that Neuraxpharm's promotional symposium placed 'undue emphasis' and 'repeated focus' on glycoengineering. The [named patient organisation] meeting symposium consisted of 41 slides in total, of these, **only 2 slides** (slides 12 and 13) refer to glycoengineering. Therefore, with 95% of the presentation **not** discussing/mentioning/referring to glycoengineering, it is simply incorrect to state that undue emphasis was placed.

Neuraxpharm are confident that the actions proposed above demonstrate our commitment to providing education on this emerging topic in a balanced manner and reinforces that Neuraxpharm **did not, nor was there an intention to extrapolate to the clinical situation. Neuraxpharm therefore refute all allegations that relate to Clauses 5.1 and 6.1**

Neuraxpharm must also comment that the tone of the correspondence from Roche, especially with regards to the *'actions requested by Roche'* section at the end of each letter were rather aggressive and often exceeded the jurisdiction of ICD with respect to their demands."

PANEL RULING

This intercompany complaint related to a promotional symposium by Neuraxpharm for Briumvi (ublituximab) at a conference in March 2025, and, in particular, the presentation of glycoengineering and associated *in vitro* antibody-dependent cellular cytotoxicity (ADCC) data.

Intercompany dialogue (ICD) had successfully resolved Roche's concerns relating to confirmed disability progression and B-cell depletion data. However, ICD had not resolved Roche's concerns relating to the presentation of the *in vitro* ADCC and glycoengineering data. Although Roche had referred to two outstanding allegations, the Panel considered that they amounted to the same issue: that the presentation in question was misleading because it implied a clinically relevant differentiation and advantage based on glycoengineering, which had not been established.

During ICD, Neuraxpharm offered to implement changes to future presentations of the *in vitro* data at issue, including highlighting that the clinical significance of the data had not been established, amending a slide title and not presenting *in vitro* data immediately adjacent to clinical efficacy data. However, notwithstanding those proposals, there remained a fundamental disagreement between the parties about whether the March 2025 slides were a breach of the Code or not, and that had not been resolved during ICD.

The Panel did not consider the issue before it was whether the prospective changes proposed by Neuraxpharm were acceptable, nor did it make any determination as to whether glycoengineering could ever be discussed in Briumvi promotional material. The Panel considered that the matter referred to it was whether, in the context of the symposium slides at issue, reference to glycoengineering and associated *in vitro* data was misleading, together with a related allegation of a failure to maintain high standards.

At the time of the presentation, Roche had a marketing authorisation for Ocrevus (ocrelizumab) and Neuraxpharm for Briumvi, both of which were anti-CD20 therapies that had a licence for the treatment of adult patients with relapsing forms of multiple sclerosis (MS) with active disease.

<u>The presentation</u>

The presentation at issue was titled "*Briumvi – Research to Reality: Supporting Patient Outcomes*" and consisted of 41 slides. It was split into two main sections, with the glycoengineering data appearing in the first section titled "*Not all anti-CD20s are the same: Translating points of differentiation for people with MS*". There were two slides that made specific reference to glycoengineering.

The first slide appeared to the Panel to be the main introductory slide to Briumvi and was titled "*Briumvi – what is it?*" followed by a headline statement of "*An anti-CD20 therapy with glyco-engineering. What does that mean?...*". The rest of the slide consisted of the following bullet pointed statements alongside a pack shot visual of Briumvi:

- *"Compared to existing anti-CD20 DMTs [Disease Modifying Therapies], BRIUMVI has been glyco-engineered to remove fucose sugar molecules from the Fc [fragment crystallizable region] domain of the antibody*
- *This allows for closer interaction with the Fc receptor on natural killer (NK) immune effector cells*
- *In the Phase III studies, treatment with BRIUMVI resulted in a median reduction of 97% of CD19+ B cell counts from baseline values after the first infusion in both studies and remained depleted at this level for the duration of dosing"*

The following slide was titled "*The importance of glyco-engineering*" and featured a visual comparing the interference of sugar molecules in the binding affinity of non-glycoengineered anti-CD20 to that of ublituximab that has had certain sugar molecules removed through glycoengineering. The slide featured two prominent statements:

- *"BRIUMVI is modified by glyco-engineering such that certain fucose residues are removed*
- *In in vitro studies, BRIUMVI had 25-30 times the antibody-dependent cellular cytolysis potential of other anti-CD20 antibodies"*

The slides on glycoengineering were followed by a slide detailing that "*BRIUMVI demonstrated a median B cell depletion of 97% from baseline values after the first infusion in both phase III studies*" with a graphical illustration comparing Briumvi with teriflunomide from the ULTIMATE I and II clinical trials. The subsequent slide appeared to the Panel to be a key efficacy data slide for Briumvi titled "*BRIUMVI: the first anti-CD20 in MS to achieve an ARR [Annualised Relapse Rate] of <0.1 in two phase 3 clinical trials*". This was followed by slides detailing efficacy and safety data for Briumvi before moving on to another section in the presentation not specifically related to Briumvi.

Clause 6.1

Roche alleged that the emphasis on glycoengineering and associated *in vitro* ADCC data in the presentation created a misleading impression that these features in relation to ublituximab conferred a proven clinical advantage over other anti-CD20 therapies, when no such clinical relevance had been established.

Neuraxpharm submitted that:

- the discussion of the first glycoengineered disease modifying therapy for MS was of value for health professionals,
- the *in vitro* data was presented in a clear, factual manner,
- there was no intention to extrapolate the glycoengineering data to the clinical situation,
- health professionals would not have been misled by the data.

Clause 6.1 of the Code stated:

> "*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.*"

The supplementary information to Clause 6.1 further stated:

> "***data derived from in vitro studies, studies in healthy volunteers and in animals*** *must not be used in a way that misleads as to its significance. The extrapolation of such data to the clinical situation should only be made where there is data to show that it is of direct relevance and significance*" (emphasis as it appeared in the supplementary information).

The Panel took account of the fact that the Summary of Product Characteristics (SPC) for Briumvi included, in relation to its mechanism of action *('Section 5.1. Pharmacodynamic properties'*), that:

> *"The binding of ublituximab to CD20 induces lysis of CD20+ B cells primarily through antibody-dependent cell-mediated cytotoxicity (ADCC) and, to a lesser extent through complement-dependent cytotoxicity (CDC). Due to a specific glycosylation pattern of its Fc region, ublituximab displays an increased affinity for the FcγRIIIa (CD16) and antibody-dependent cellular cytolysis against B cells."*

The Panel did not consider that reference to glycoengineering, as a characteristic of Briumvi, was in and of itself unacceptable. Nor did the Panel consider that the Code prohibited discussion of *in vitro* studies. However, care was needed to ensure that clinical relevance or benefit was not misleadingly inferred or claimed in the absence of clinical evidence, especially when making comparisons with other therapies.

Roche submitted that the clinical relevance of glycoengineering and associated *in vitro* ADCC data had yet to be established, and the Panel noted that Neuraxpharm had not disputed this. Neuraxpharm, as part of ICD, had agreed to include a disclaimer to this effect in future. The Panel also took account of Cree et al 2025, provided by Neuraxpharm, which stated that "*Clinical advantages of glycoengineering can only be observed in head-to-head studies…while no head-to-head studies have been conducted in multiple sclerosis to date…*". The Panel therefore concluded, based on the evidence before it, that the clinical relevance of glycoengineering and associated *in vitro* ADCC had yet to be established.

The Panel considered the immediate and overall impression created by the material and took note of the following:

- The data at issue appeared within a section of the presentation titled "*Not all anti-CD20s are the same: Translating points of differentiation for people with MS*".
- The fact that Briumvi was glycoengineered was the first message regarding the product and the first two slides regarding the product solely discussed glycoengineering.
- The second slide was titled "*The <u>importance</u> of glyco-engineering*" (emphasis added by the Panel).
- The slides made comparisons between ublituximab and other anti-CD20 products including:
  - "*Compared to existing anti-CD20 DMTs, BRIUMVI has been glyco-engineered to remove fucose sugar molecules from the Fc domain of the antibody*", and
  - "*In in vitro studies, Briumvi had 25-30 times the antibody-dependent cellular cytolysis potential of other anti-CD20 antibodies*".
- The data on glycoengineering preceded clinical efficacy data and the claim that Briumvi was the first anti-CD20 in multiple sclerosis to achieve ARR of <0.1 in two phase 3 clinical trials.

- There was no reference to the fact that the clinical relevance of glycoengineering and its associated *in vitro* ADCC data had yet to be established.

The Panel took account of the factors above and considered that the presentation of glycoengineering, and the context in which it was presented, was intended to distinguish Neuraxpharm's Briumvi from other anti-CD20 therapies. In this regard, the Panel noted glycoengineering was referred to within a section which purported to discuss points of differentiation for patients with MS.

The Panel further considered that the location of the glycoengineering and *in vitro* ADCC data as the primary messages regarding Briumvi, prior to clinical data slides, might have implied that this was of direct clinical relevance and significance. The Panel concluded that this misleading impression was compounded by one of the subsequent slides implying special merit by stating that Briumvi was the first anti-CD20 to achieve an ARR of <0.1 in two phase 3 clinical trials.

In the circumstances of this case, the Panel considered that the presentation of glycoengineering, and the associated *in vitro* data, could not be seen as anything other than implying additional clinical benefit. The Panel did not consider that the explicit reference to "*in vitro*" in the comparative ADCC claim was sufficient to negate this misleading impression.

The Panel concluded that the glycoengineering and associated ADCC *in vitro* data were likely to be interpreted as constituting clinically relevant and meaningful differentiation compared to other anti-CD20 therapies. In the absence of such evidence, the Panel considered that the emphasis on glycoengineering during the presentation of Briumvi was likely to mislead as to the clinical significance of its data. The Panel therefore ruled a **breach of Clause 6.1**.

<u>High standards (Clause 5.1)</u>

The Panel took into account that the slides in question appeared within a section entitled "*Not all anti-CD20s are the same: Translating points of differentiation for people with MS*" and that the claims relating to glycoengineering and its associated *in vitro* ADCC data were presented as points of differentiation from other anti-CD20 therapies.

The Panel acknowledged that Neuraxpharm had offered, as part of ICD, to implement changes to future presentations in relation to *in vitro* data. However, the Panel was nonetheless concerned that Neuraxpharm had failed to recognise that the presentation placed undue importance on glycoengineering and that the presentation misleadingly attributed clinically meaningful relevance and significance which had not yet been established.

The Panel therefore concluded that Neuraxpharm had failed to maintain high standards and ruled a **breach of Clause 5.1**.

Complaint received **26 September 2025**

Case completed **6 July 2026**