NO BREACH OF THE CODE

CASE AUTH/3827/9/23

COMPLAINANT v ROCHE

Alleged misleading information regarding Ocrevus infusion details on a promotional website

CASE SUMMARY

This case concerned allegations that a Roche promotional website contained misleading information about the administration of Ocrevus infusion.

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 (x2)	**Requirement that information must not be misleading**

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 Roche was received from an anonymous, non-contactable complainant who described themself as a health professional.

COMPLAINT

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

> "A promotional webpage which provides details of Ocrevus infusion is rather misleading. The webpage in question is [link provided]. As you can see on the webpage, there are illustrations of Ocrevus infusion for both the shorter infusion schedule and the standard infusion schedule. On both of these schedules, there is a picture of an eye and text underneath which says that observation is for 1 hour. However, this is misleading as observation should occur during the ENTIRE infusion and for one hour after completion. The SPC for the product details the following information: Patients should be monitored during the infusion and for at least one hour after the completion of the infusion (see section 4.4). There were clear patient safety risks if a HCP only monitored for an hour as specified on this webpage. For a busy HCP, the immediate impression given by the illustration is that only one hour of

monitoring is required for the administration whereas observation is actually needed for the totality of the infusion owing to potential for serious infusion related reactions. Ocrevus should only be administered through a dedicated line but this information was not specified on the webpage, considering the page provided information on administration. For a HCP exposed this information, there was potential they could administer without a dedicated line which could lead to challenges for patient safety. The SPC was very clear on the need for a dedicated line (section 4.2 - method of administration). Breaches of clauses 6.1, 5.1 & 2 had occurred."

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

ROCHE'S RESPONSE

The response from Roche is reproduced below:

"The anonymous complainant makes a general statement that the Ocrevus promotional website is misleading and then raises specific points:

The first point raised is the allegation that the noted observation period of 1 hour depicted in the summary graphic is misleading as it doesn't specifically refer to the entire infusion period and by implication could pose a clear risk to patient safety if the patient were only monitored for an hour.

The SmPC clearly states, ***"Treatment should be initiated and supervised by specialised physicians experienced in the diagnosis and treatment of neurological conditions and who have access to appropriate medical support to manage severe reactions such as serious infusion-related reactions".***

As such, Ocrevus is <u>always</u> infused in a dedicated infusion suite in a controlled hospital setting staffed by infusion staff experienced in the administration of biologic medicines and the subsequent clinical management of adverse reactions. It is logically implausible for a patient to be infused with a biologic medicine in this setting and not be monitored. Roche fails to observe the linear causality between the apparent omission of the depiction of observation period duration during the infusion in the context of the summary graphic on a website and the clinical management of a patient on the infusion suite. The patient by the very nature of the clinical setting would be monitored for the duration of their infusion suite occupancy by default, independent of discretionary choice. This is routine clinical practice and understood as such by prescribing HCPs and infusion staff to whom the Roche promotional materials are aimed.

The precise administration and monitoring instructions in accordance with the SmPC would also have been communicated in the dedicated training of the infusion nurses. Given that Ocrevus has had a marketing authorisation since 2018, it is a well-established therapeutic in every MS treatment centre in the UK and thus the probability of an Ocrevus naive HCP seeing the summary graphic and then using that isolated graphic out of context to inform their clinical management of infusion logistics, is logically implausible and improbable.

Additionally, the context of the graphic is to provide a summary of the infusion schedule and infusion suite occupancy for the prescribing HCP so that they can rapidly assimilate the cumulative time and resource savings and patient convenience that could be achieved by the shorter infusion. The shorter infusion is a recent innovative line extension and as such the intent of the piece is to highlight this in relation to the traditional longer infusion of the original marketing authorisation.

It is not intended to be a detailed replication of the SmPC and detailed infusion instructions but rather a summary of the patient journey and infusion suite occupancy duration. Within the context of the intent of the graphic and the use of other dedicated material to educate and guide the infusion staff, Roche refutes any breach of Clause 6.1 and any risk directly or indirectly to patient safety.

The second point raised in relation to the misleading nature of the Ocrevus promotional website is the allegation that the omission of the statement that Ocrevus should be administered through a dedicated line in the context of the specific graphic, could 'lead to challenges for patient safety'.

Disease-modifying treatments in MS are always prescribed and administered as monotherapy regardless of disease subtype. This is abundantly clear and understood by all HCPs and infusion staff that treat and administer infusable medicines to MS patients. When MS patients are admitted to infusion suites for their treatment, all administered treatment for that period will consist of the administration of a monotherapy and required pre-medications as per the SmPC. Patients will only ever require one IV line which in essence is the dedicated line through which their disease modifying monotherapy is administered in accordance with the SmPC. This is in stark contrast to perhaps an oncology patient where polypharmacy and single infusion lines could result in adverse reactions. There is no reason or need in the case of monotherapy Ocrevus, to have any other infusion lines during the infusion suite session and this can be readily verified with the relevant clinical staff.

Given that during an infusion suite session, only a monotherapy is administered with the relevant pre-medication and the Ocrevus SmPC does not make a distinction between the use of the dedicated line in relation to premedication, there is no plausible mechanism by which a patient could be exposed to risk at any point of the journey based on the allegation of the complainant and additionally, the complainant has not provided a clear mechanism or evidence of how patient safety could be compromised in this regard. The complainant's observations and conclusions are not logically compatible with linear causality, routine NHS clinical practice or MS treatment and administration paradigms.

The context of the graphic is to provide a summary of the infusion schedule and infusion suite occupancy for the prescribing HCP so that they can rapidly assimilate the cumulative time and resource savings and patient convenience that could be achieved by the shorter infusion. It is not intended to be a detailed replication of the SmPC and detailed administration instructions but rather a summary of the cumulative patient journey and infusion suite occupancy duration. The dedicated line through which Ocrevus is administered is a specific detail relevant to the infusion staff who are trained as such in this regard and understood as such by prescribing MS HCPs and infusion staff.

By logical extension of the complainant's allegation, the graphic also doesn't explicitly state that the Ocrevus infusion should be administered in a hospital setting or that the infusion staff be appropriately trained in the administration of Ocrevus. This is clearly understood by all prescribing HCPs and infusion staff to be logical given much in the same way as the routine monitoring a patient would receive during their infusion by extension of their environment and the fact their infusion will be given through a dedicated line.

Roche recognises the special nature of medicines and respects the professional standing of the intended audience to whom its materials are directed and takes great care not to cause offense (or patronise) in accordance with Clause 5.2.

In summary and based on the rationale provided, Roche strongly refutes any misleading claim directly or implied in relation to patient safety as a result of this webpage and therefore any associated breach of Clause 6.1.

Furthermore, there is no evidence that high standards have not been maintained and therefore Roche refutes any breach of Clause 5.1. There is also no clear evidence that this graphic in any way brings the Industry into disrepute. There is no evidence of this material prejudicing patient safety and/or public health or any of the other associated transgressions associated with Clause 2 breaches as outlined in the supplementary information to Clause 2 and on this basis Roche refutes any breach of Clause 2."

PANEL RULING

The Panel noted Ocrevus (ocrelizumab) was indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features, and adult patients with early primary progressive multiple sclerosis (PPMS) in terms of disease duration and level of disability, and with imaging features characteristic of inflammatory activity.

The Panel noted the Ocrevus summary of product characteristics (SPC) had not been provided by either party. Roche submitted the summary of product characteristics stated that treatment should be initiated and supervised by specialised physicians experienced in the diagnosis and treatment of neurological conditions and who have access to appropriate medical support to manage severe reactions such as serious infusion-related reactions. This was consistent with the information in the Great Britain and Northern Ireland prescribing information provided by the complainant which also set out the requirements for pre-medication for infusion-related reactions to be administered prior to receiving Ocrevus and specified that an initial 600mg dose was to be administered as two separate 300mg intravenous infusions, 2 weeks apart. Subsequent doses were then to be administered as a single 600mg infusion every 6 months with the first subsequent dose of 600mg being administered six months after the first infusion of the initial dose. Subsequent doses could be given in accordance with the standard infusion schedule, or if the patient did not experience a serious infusion-related reaction with any previous ocrelizumab infusion the shortened infusion schedule.

The complaint was regarding a webpage which was part of the Ocrevus promotional website and included an illustration of the Ocrevus infusion schedules.

Below the website header, navigational elements, adverse event reporting statement and links to prescribing information, the page content was headed “OCREVUS has the most clinical trial and real-world MS experience in the anti-CD20 class, including 8+ years of safety data and 250,000+ patients treated globally”. Below this heading was a graphic with a yellow circular flash reiterating the number of patients around the world treated with Ocrevus, partially superimposed on an illustration of the Earth, and a standalone reminder about the 8 years of safety data.

Below this graphic, the claim “Empower them to spend less time feeling like a patient and more time feeling like themselves” appeared, followed by “Following the initial dose of OCREVUS, there is an option for a shorter infusion schedule in suitable patients” in smaller font. The graphic at issue (described below) appeared between these statements and the claim “A shorter infusion schedule supports the lifestyle of GEN-O” highlighted through the use of coloured text and with an upper and lower coloured border. At the bottom of the page, above the website footer elements, were definitions, the licensed indication, references, date of preparation and job code.

The graphic at issue depicted the two Ocrevus infusion schedules. These were illustrated using timelines, with a coloured block indicating each step in sequence –“Pre-medication” (with an icon of an infusion bag and two tablets), “Ocrevus infusion” (with an infusion bag icon) and “Observation” (with an eye icon). The blocks were sized and labelled to indicate the duration of each step and the total time for each schedule was given to the left of each timeline. The pre-medication and observation periods were the same for both infusion schedules, at 30–60 minutes and 1 hour, respectively. For the shorter infusion schedule, the Ocrevus infusion was given over 2 hours and for the standard infusion schedule it was 3.5 hours. The time saving resulting from the shorter infusion schedule was indicated at the end of that timeline. The statement “The shorter infusion can only be administered to patients who have not experienced a serious IRR with any previous OCREVUS infusion” appeared in a blue bar below the graphic.

The Panel noted Roche’s submission that the graphic was not intended to provide detailed administration instructions but a summary of the infusion schedule and infusion suite occupancy for the prescribing health professional so that they could rapidly assimilate the cumulative time and resource savings and patient convenience that could be achieved by the shorter infusion.

Roche also submitted that as a biologic medicine Ocrevus was always infused in a dedicated infusion suite in a controlled hospital setting staffed by infusion staff experienced in the administration of biologic medicines and the subsequent clinical management of adverse reactions. Furthermore, the nature of the clinical setting meant patients would be monitored for the duration of their time at the infusion suite; this was routine clinical practice.

The Panel considered the content, layout and overall impression created by the webpage at issue. While the Panel noted that each webpage must not be misleading when read in isolation, it considered that it was clear that the primary purpose of the webpage was to communicate the option of a shorter infusion schedule for suitable patients and that it was not intended to provide comprehensive information regarding the dosing and administration of Ocrevus. The Panel noted that the complainant’s allegations solely concerned the webpage provided, and that it had no information before it about the availability of further information regarding dosing and administration on the website.

The Panel noted the complainant's first allegation concerned the observation period sections of the graphic, which was labelled "1hr". The complainant alleged this was misleading as observation should occur during the entire infusion and for one hour after completion, due to the potential for serious infusion related reactions.

The Panel considered that it was clear, from the sequential nature of the timeline graphic at issue and the overall context of the webpage, that the one-hour observation period occurred after completion of the infusion period. Having taken account of the specialised nature of the medicine, the clinical setting within which Ocrevus was routinely administered and the expertise of the intended audience, the Panel considered the presentation of a one-hour observation period in the graphic at issue did not suggest that patients required observation only at this timepoint but rather that it emphasised the requirement for a period of ongoing observation after a patient's Ocrevus infusion finished. The Panel did not consider the graphic misleading as alleged and ruled **no breach of Clause 6.1**.

The Panel noted the complainant's second allegation concerned the omission of a statement that Ocrevus should be administered through a dedicated line. The complainant alleged this could "lead to challenges for patient safety". Noting its comments about the primary purpose of the webpage, and the conditions specified in the summary of product characteristics in relation to the specialist physicians and clinical environment required for treatment with Ocrevus, the Panel considered that it was unlikely that health professionals who treat patients with Ocrevus and viewed the webpage including the graphic would not understand that it was to be administered via a dedicated line. Accordingly, the Panel did not consider that the complainant had established that the omission of information about the use of a dedicated line within the webpage was misleading or that patient safety might be comprised as a result. Accordingly, the Panel ruled **no breach of Clause 6.1**.

While the Panel considered that a message signposting readers to the summary of product characteristics for detailed information about dosing and administration could have usefully been included on the webpage, it did not consider that the complainant had established that Roche had failed to maintain high standards. The Panel ruled **no breach of Clause 5.1.**

Clause 2 was a sign of particular censure and was reserved for such use. In the light of its comments and rulings above, the Panel ruled **no breach of Clause 2**.

Complaint received **22 September 2023**

Case completed **30 July 2024**