CASE AUTH/3639/4/22

COMPLAINANT v ROCHE PRODUCTS LTD

Allegations about a Polivy promotional website

CASE SUMMARY

This case was in relation to allegations that the dosing page of the Polivy (polatuzumab vedotin) promotional website missed important administration instructions included in the Polivy summary of product characteristics (SPC) that were required to ensure patient safety.

The Panel ruled a breach of the following Clauses of the 2021 Code because the dosing webpage, which was intended to advise health professionals on the appropriate administration of the medicine, gave the misleading impression that it contained all the important information health professionals needed to administer Polivy, which was not so in respect of specific instructions about a particular infusion line and dose modifications in the event of an infusion related reaction:

Breach of Clause 6.1	**Providing misleading information**
Breach of Clause 5.1	**Failing to maintain high standards**
Breach of Clause 2	**Bringing discredit upon, and reducing confidence in, the pharmaceutical industry**

The Panel ruled no breach of the following Clauses of the 2021 Code on the basis that:

- **health professionals were unlikely to be misled about the route of administration for Polivy (i.e. that it was to be administered as IV infusion and not IV bolus or push)**
- **there were no allegations that information was not capable of substantiation**
- **dose modifications information in relation to an infusion-related reaction was provided on the safety webpage**:

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

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

FULL CASE REPORT

An anonymous contactable complainant who described themselves as a health professional complained about Roche's Polivy (polatuzumab vedotin) promotional website.

COMPLAINT

The complainant alleged that the dosing page (GB-00004744; date of preparation September 2021) missed important administration instructions included in the Polivy summary of product characteristics (SPC) which were required to ensure patient safety.

The complainant noted that in the blue sections on the webpage which listed out Day 1 and Day 2, it was stated that a dose of Polivy 1.8mg/Kg IV* was needed. The complainant stated that Polivy could only be given as intravenous infusion and by leaving it as IV* this could be misinterpreted as IV bolus or IV push. The SPC for Polivy specifically mentioned the following:

> Polivy must be reconstituted and diluted using aseptic technique under the supervision of a healthcare professional. It should be administered as an intravenous infusion through a dedicated infusion line equipped with a sterile, non-pyrogenic, low-protein binding in-line or add-on filter (0.2 or 0.22 micrometer pore size) and catheter. Polivy must not be administered as intravenous push or bolus.

The complainant alleged that it should have been made clear that Polivy should be given by intravenous infusion only, instead of leaving as IV; the immediate impression to a busy health professional was important and writing IV was allegedly misleading without full qualification. Simply stating IV risked patient safety considering it could be seen as a bolus or push. Also, it was concerning that the SPC guidance around the particular infusion line required was not included on the page. This was also, according to the complainant, a material risk to patients in breach of Clauses 6.1, 6.2, 5.1 and 2.

The complainant alleged that further important guidance in the SPC was also missing around slowing down the infusion. The following was stipulated in the SPC:

> The infusion rate of Polivy should be slowed or interrupted if the patient develops an infusion-related reaction.

The complainant alleged that this information about slowing down the infusion was not provided anywhere on this promotional webpage which meant it was not balanced or accurate around administration instructions. The complainant alleged breaches of Clauses 6.1, 6.2, 5.1 and 2.

When writing to Roche, the Authority asked it to consider the requirements of Clauses 6.1, 6.2, 5.1 and 2 of the Code as cited by the complainant.

RESPONSE

Roche submitted that it was committed to the appropriate use of medicines, protecting the safety of patients and strove to maintain high standards in the ethical promotion of its medicines. It was therefore disappointed to receive a complaint of this nature.

Roche explained that the complaint referred to a page on the Roche resources website. Each product page contained a menu with links to separate pages of detailed information on efficacy, safety, dosing, in addition to other product dependent pages.

Roche noted the complainant referred to a Roche Resources page which highlighted the dosing requirements for Polivy (polatuzumab vedotin) an antibody-drug conjugate, indicated in combination with bendamustine and rituximab for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant. Roche rejected the allegations and breaches of Clauses: 6.2, 6.1, 5.1 and 2.

Allegation 1: Polivy IV* '…. could be misinterpreted as IV bolus or IV push'.

Roche submitted that the resources page referred to by the complainant formed part of a number of pages detailing the different elements of Polivy. The page in question contained, amongst other things, a summary of the dosing schedule for Polivy across 4 blue boxes; the first two boxes contained information on the medicine, dose and route of administration, followed by two additional boxes, one detailing a wait period of 21 days and the fourth box detailing the recommended repeat cycle.

Below this were 2 red boxes, the first detailed the need for an initial 90 minute IV infusion in which the patient should be monitored for infusion related reactions during and for 90 minutes after the infusion has been completed; the second red box detailed that a 30 minute IV infusion may be administered for subsequent infusions should the initial infusion be well tolerated.

Below the red boxes was a link to a dosing guide and 3 sections of text in a font size equal to other text on the page. The first section highlighted a maximum recommended dose for Polivy, the second highlighted the need to refer to the Summary of Product Characteristics (SPC) and local hospital guidelines for further information and monitoring recommendations along with section 4.4. of the SPC on special warnings and precautions for use, and the third highlighted the meaning of any relevant acronyms. Below this was a reference section which highlighted the Polivy SPC.

To the side of the page were three links to further information, one of which was a link to further information on the safety profile of Polivy.

In response to the complaint that simply stating the term 'IV' risked patient safety considering it could be seen as a bolus or push, Roche submitted that it was evident when viewing the webpage in question that a health professional (HCP) reading the page would see the red boxes which highlighted further information on the administration including the title statements '90-minute initial IV infusion' and '30-minute subsequent infusions'. Roche therefore felt that an HCP, particularly those trained in the administration of such a product, would be aware that a 90 minute or 30 minute IV infusion would not be given via push or bolus dosing.

Furthermore, the Roche resources page in question contained two adverse event reporting statements, a link to prescribing information, a link to further information on adverse events reporting and additional monitoring, a link to the Polivy safety profile, and a section of text highlighted the need to refer to the full SPC, the local hospital administration guide and Section 4.4 of the SPC for special warnings and precautions for use. Roche submitted that all of which

were in place to ensure the promotion of Polivy was done with full consideration for the safety of patients.

Roche acknowledged and respected the high skill and expertise of the target audience in question and felt that the information given was sufficient to enable the HCP to make their own informed decision based on the information provided, including the references given.

In light of the above, Roche felt the information provided on the Polivy Roche Resources page was accurate, balanced, fair, objective and unambiguous, reflected the SPC, did not mislead the HCP and enabled them to form their own opinion of the medicine. Roche submitted that this was further evidenced by the complainant's ability to find the relevant information on the product in the SPC. Roche therefore denied a breach of Clauses 6.1 and 6.2.

On this basis Roche believed it had maintained the high standards expected of the industry and with full consideration for patient safety, and therefore Roche denied a breach of Clauses 5.1 and 2, and fully acknowledged the reservation of the aforementioned clause for situations of particular censure.

Allegation 2: Missing guidance from the SPC around the 'particular infusion line' and 'slowing down' the infusion.

Roche submitted that the Polivy Roche Resources page in question contained a number of references pointing the reader to relevant safety data and further information on the special precautions of the medicine. More specifically the page recommended the reader to refer to the SPC and hospital guidelines in order to ensure the reader was fully informed before making their own decision on the use of Polivy in a patient.

Roche acknowledged that a health professional would make their own decision before prescribing a treatment to a patient. The intent of the page was to provide information that could support rather than dictate their decision, as evidenced by a number of recommendations to consult further literature. Roche maintained that in addition to the evidence of this provided above, it was also of note that the prescribing information linked on the Polivy Roche Resources page contained, amongst other things, the statements *'Polivy must only be administered under the supervision of a healthcare professional experienced in the diagnosis and treatment of cancer patients.'* and *'Please refer to the SmPC prior to use of Polivy'*.

As such Roche felt the page in question provided a balanced top line overview of the dosing and administration of the licensed regimen of Polivy, whilst providing a number of recommendations to refer to additional data and the full SPC along with any relevant local guidance before prescribing Polivy.

In response to the allegation that information provided in the SPC regarding adaptation of the infusion rate in light of infusion related reactions was 'not present anywhere on the webpage', Roche drew attention to the first of the two red boxes on the Polivy Roche Resources page for dosing and administration, which stated '*Monitor patients for infusion related reactions during the infusion and for a minimum of 90 minutes following completion of the dose*'. Below this was a statement referring the reader to consult the SPC and their hospital's guidelines for further information and monitoring recommendations. There was also a link to the prescribing information, which included the statement *'Please refer to SmPC for dose modifications and dose adjustments'* and also a section on infusion related reactions which included the statement

'*If an infusion-related reaction occurs, the infusion should be interrupted and an appropriate medical management should be instituted*'.

Roche reiterated that there was a link to the right of the dosing page titled *'Find out about the POLIVY safety profile'*. The link took the reader to the Polivy safety page which, amongst other things, contained a section titled *'Dose modifications*'. Below this title was the statement: *'The infusion rate of POLIVY should be slowed or interrupted if a patient develops an infusion-related reaction'*. This section of the safety page continued on to detail dose modifications required in specified settings.

Roche therefore felt it was evident that the relevant information referred to by the complainant was available on the Polivy pages of Roche Resources and would therefore not be a matter for complaint. As such Roche denied breaches of any clauses implied in regard to this matter.

In light of the above, Roche concluded the information provided on the Polivy Roche Resources page was accurate, balanced, fair, objective and unambiguous, reflected the SPC, did not mislead the reader and enabled them to form their own opinion of the medicine. Roche submitted this was further evidenced by the complainant's ability to find the relevant information on the product in the SPC. Roche therefore denied a breach of Clauses 6.1 and 6.2.

Roche believed it had maintained the high standards expected of the industry and with full consideration for patient safety, therefore it denied a breach of Clauses 5.1 and 2, and fully acknowledged the reservation of the aforementioned clause for situations of particular censure.

Whilst it was disappointed to receive this complaint, in light of the above response, Roche submitted it had maintained the high standards expected of the industry, and with no direct impact to patient safety in these matters, Roche believed the high standards expected, and confidence in the industry, had been upheld.

PANEL RULING

The Panel noted that the complainant had provided a link to the dosing webpage for Polivy that appeared to form part of the Polivy promotional website.

The Panel noted Roche's submission that each product page on its resources website contained a menu with links to separate pages of detailed information on efficacy, safety and dosing in addition to other product dependent pages; the Polivy dosing webpage in question included, amongst other things, a link to the prescribing information, a link to the Polivy safety profile and referred readers to the SPC and hospital guidelines for further information and monitoring recommendations.

The Panel reviewed the layout of the dosing webpage and noted the image with four blue boxes which summarised the dosing schedule for the Polivy + R-Benda treatment regimen. The first box included a statement that the Day 1 dose of Polivy was 1.8mg/kg IV* and the doses of the other medicines administered on Day 1 of the treatment regimen. The second box referred to the administration of Bendamustine 90mg/m^2 IV on Day 2 while the third and fourth boxes referred respectively to the 21 day wait period between Polivy infusions and the total number of cycles. The Panel noted the Day 1 and Day 2 blue boxes also contained a picture of an infusion bag and that below the blue boxes were two red/pink boxes titled 90-Minute initial IV infusion and 30-Minute subsequent infusions. These boxes also contained instructions to monitor

patients during infusions and for a period of time afterwards. This was followed by an image of a downloadable dosing and administration postcard, beneath which was a statement associated with the asterisk in the Day 1 blue box, which stated that it was recommended not to exceed 240mg Polivy/cycle, and guidance to health professionals to refer to the SPC and hospital guidelines for further information and monitoring recommendations and to Section 4.4 of the SPC for special warnings and precautions. Links to the prescribing information and the Polivy safety profile were included near the top of the webpage and to the right of the dosing and administration information, respectively.

1. Polivy 1.8mg/kg IV* dosing statement

The Panel noted the complainant's allegation that stating the Day 1 dose of Polivy as 1.8mg/kg IV* was misleading as it could be misinterpreted as an IV bolus or IV push and as such represented a material risk to patients.

Clause 6.1 stated, amongst other things, that information must be accurate, not mislead and be sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine; Clause 6.2 required information to be capable of substantiation.

Having carefully considered the overall and immediate impression of the webpage to a busy health professional, and the content and layout of the section titled Polivy + R-Benda dosing and administration, and noting that there were several references to Polivy being administered via IV infusion within the same field of vision as the statement in question, the Panel considered, on the balance of probabilities, and in the context of the particular webpage at issue, it was unlikely that health professionals would be misled regarding the route of administration. Accordingly, the Panel ruled **no breach of Clauses 6.1** and **6.2.**

2. Requirement to administer Polivy through a particular infusion line

The Panel noted the complainant's allegation that important instructions about administering Polivy through a dedicated infusion line equipped with a sterile, non-pyrogenic, low-protein binding in-line or add-on filter (0.2 or 0.22 micrometer pore size) and catheter, included in the SPC and required to ensure patient safety, were missing from the webpage.

The Panel noted Section 4.2 (Posology and method of administration) of the SPC set out detailed information for the reconstitution, dilution and administration for Polivy including:

> 'Polivy must be reconstituted and diluted using aseptic technique under the supervision of a healthcare professional. It should be administered as an intravenous infusion through a dedicated infusion line equipped with a sterile, non-pyrogenic, low-protein binding in-line or add-on filter (0.2 or 0.22 micrometer pore size) and catheter. Polivy must not be administered as intravenous push or bolus.'

Additionally, Section 6.6 (Special precautions for disposal and other handling) of the SPC provided instructions for the reconstitution and dilution of Polivy and included that Polivy must be administered using a dedicated infusion line equipped with sterile, non-pyrogenic, low-protein binding in-line or add-on filter (0.2 or 0.22 micrometer pore size) and catheter.

The Panel noted Roche's submission that the webpage in question provided a top-line overview of the dosing and administration of the licensed regimen for Polivy and included a number of

recommendations to refer to the SPC and hospital guidelines for further information as well as opportunities for health professionals to access further information including the prescribing information.

However, the Panel noted that the prescribing information, accessible from the webpage in question, made no reference to the SPC requirement that Polivy must be administered using a dedicated infusion line equipped with a sterile, non-pyrogenic, low-protein binding in-line or add-on filter (0.2 or 0.22 micrometer pore size) and catheter, and that it must not be administered as intravenous push or bolus.

Furthermore, this information was also not included in the 'handy dosing and administration postcard' which readers were encouraged to download from the webpage. There was also no link to the Polivy SPC on the webpage.

The Panel considered the overall structure of the Polivy promotional website, noting it had specific sections dedicated to efficacy, safety, dosing, patient flow, mechanism of action (MOA) and expert discussions. The Panel considered that within this structure readers would expect to find all the important dosing and administration information they needed from the dosing webpage which was headed 'Polivy + R-Benda dosing and administration'.

The Panel considered that the information in Section 4.2 of the SPC, which gave specific instructions about a particular infusion line, was important information that a health professional would expect to have been made aware of on a webpage dedicated to dosing and administration.

The Panel noted, however, that this important information was neither within the body of the webpage, nor within the downloadable dosing and administration postcard, nor in the prescribing information. Furthermore, there was no signpost on the webpage to indicate that there was additional important administration information within the SPC and no link to the SPC was provided. The statement 'Please refer to the SmPC and your hospital guidelines for further information and monitoring recommendations. Please refer to section 4.4 of the SmPC for special warnings and precautions for use', towards the bottom of the webpage, was insufficient to negate the misleading impression given that the webpage contained all the important information in relation to the administration of Polivy. Furthermore, the information about the particular infusion line required was within Sections 4.2 and 6.6 of the SPC which had not been referred to on the webpage.

It was a well-established principle that material had to be capable of standing alone with regard to the requirements of the Code. The Panel considered the immediate and overall impression of the webpage to a busy health professional and, in its view, the webpage gave the misleading impression that it contained all the important information health professionals needed to administer Polivy. The Panel ruled **a breach of Clause 6.1**.

Noting that the matter related to incomplete information in relation to IV administration of an antineoplastic agent, the Panel considered that Roche had failed to maintain high standards and **a breach of Clause 5.1** was ruled.

The Panel noted the complainant had raised Clause 6.2 which stated, amongst other things, that any information, claim or comparison must be capable of substantiation. However, in the

Panel's view, there was no allegation that information was not capable of substantiation. The Panel therefore ruled **no breach of Clause 6.2**.

The Panel considered that patient safety was of the utmost importance and health professionals should be able to rely on company produced materials to be complete and unambiguous in this regard. Examples of activities likely to lead to a breach of Clause 2 included prejudicing patient safety. The Panel considered that by providing some, but not all, of the important information in relation to the administration of Polivy, within a section of the website that was intended to advise health professionals on the appropriate administration of the medicine, was such that Roche had reduced confidence in and brought discredit upon the pharmaceutical industry, and a **breach of Clause 2** was ruled.

3. Slowing the infusion rate or interrupting it if a patient develops an infusion-related reaction.

The Panel noted the complainant's allegation that the absence of information about slowing down the infusion rate or interrupting it if a patient developed an infusion-related reaction, on the dosing webpage in question, meant that the webpage was not balanced or accurate around administration instructions.

The Panel acknowledged Roche's submission that to the right of the dosing information was a link titled 'Find out about the Polivy safety profile' which took readers to the Polivy safety webpage; this included a section titled 'Dose modifications' and the statement, *'The infusion rate of POLIVY should be slowed or interrupted if a patient develops an infusion-related reaction'* as well as detailing dose modifications required in specified settings.

Nonetheless the Panel was mindful that the complainant's allegation related specifically to the absence of the information on the Polivy dosing webpage itself.

Noting that the dose modifications information following an infusion-related reaction was set out in Section 4.2 (Posology and method of administration) of the SPC, the Panel considered that health professionals might expect to have seen the information on the dosing webpage, or a clear and prominent signpost to the reader that additional important information relevant to dosing and administration was available on the safety webpage.

The Panel noted the dosing and administration webpage in question contained the statement 'Find out about the Polivy safety profile' and was linked to the safety webpage, however, the reader was not made aware that this safety page contained additional important information in relation to dosing.

The Panel considered that not highlighting to the reader, on the dosing webpage, that additional important information in relation to dose modifications was within the safety webpage of the website was misleading and therefore the Panel ruled **a breach of Clause 6.1**.

The Panel noted the complainant had raised Clause 6.2 which stated, amongst other things, that any information, claim or comparison must be capable of substantiation. However, in the Panel's view there was no allegation that information was not capable of substantiation. The Panel therefore ruled **no breach of Clause 6.2**.

The Panel noted that the dose modifications information in relation to an infusion-related reaction was provided in detail on the safety webpage. In the particular circumstances of this case, the Panel considered that the complainant had not established that the inclusion of the information on dose modifications following an infusion-related reaction on the safety webpage, as opposed to the dosing webpage of the website, meant that Roche had failed to maintain high standards or reduced confidence in, or brought discredit upon, the industry and therefore the Panel ruled **no breach of Clauses 5.1 and 2**.

Complaint received **25 April 2022**

Case completed **24 April 2023**