CASE AUTH/3646/5/22

COMPLAINANT v ROCHE

Concerns about the dosing considerations website for Rozlytrek

CASE SUMMARY

This case was in relation to the dosing webpage of the Rozlytrek (entrectinib) promotional website which missed important information about dose modifications included in the Rozlytrek summary of product characteristics (SPC) that were required to ensure appropriate prescribing and 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 prescribe Rozlytrek in patients with congestive heart failure or QT interval prolongation, elevated ALT and AST, central nervous system adverse reactions, and hyperuricaemia, anaemia or neutropenia which was not so. Noting that Rozlytrek was a black triangle medicinal product subject to additional monitoring, and that important safety information was omitted from the dosing webpage, the Panel considered that Roche had failed to maintain high standards and had brought discredit upon and reduced confidence in the pharmaceutical industry.

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 there were no allegations that the information was not capable of substantiation and the complainant had not established that the webpage gave misleading information regarding fractures or that the information regarding fractures was not substantiated.

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**

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 complainant who described themselves as a health professional complained about the Roche resources website, (www.rocheresources.co.uk) alleging that the dosing considerations website content for Rozlytrek (entrectinib) was misleading and not fair or balanced. There was critical information omitted around dosage reductions/discontinuation during monitoring, which would lead to a patient safety risk as not all information had been provided.

COMPLAINT

The complainant submitted that the webpage, www.rocheresources.co.uk/roche-medicines/oncology/rozyltrek_-entrectinib--/Dosing.html, was dedicated to dosing around Rozlytrek (M-GB-00004833, Date of preparation: November 2021). Towards the bottom of the webpage, there was a suggested monitoring section which noted, heart, liver, CNS (central nervous system), blood and bones. However, the information related to these did not give the relevant and exact information as per the summary of product characteristics (SPC). Table 4 in the SPC, for the product titled 'Recommended Rozlytrek dose modifications for adverse reactions in adult and paediatric patients' was important to consider in this regard. The complainant referred to the table which had specific information around when to stop the product and dosage reductions during monitoring as opposed to just simply monitoring different body systems:

1 Heart – Rozlytrek had to be withheld or resumed at reduced dose in the following cases as per the SPC: 'Symptomatic with middle to moderate activity or exertion, including where intervention is indicated (Grade 2 or 3)' and 'Severe with symptoms at rest, minimal activity, or exertion or where intervention is indicated (Grade 4)'. This information was missing on this promotional page around heart monitoring section. For QTI prolongation, 'QTc [corrected QT interval] 481 to 500 ms', 'Withhold Rozlytrek until recovered to baseline'. For QTc greater than 500 ms, 'Resume at same dose if factors that cause QT prolongation are identified and corrected', 'Resume at reduced dose if other factors that cause QT prolongation are <u>not</u> identified'. This guidance should have been included in the page instead of simply saying 'assess QT interval'.

2 Liver – the SPC stated transaminase elevations where 'ALT [Alanine aminotransaminase] or AST [Aspartate aminotransferase] greater than 3 times ULN [upper limit of normal] with concurrent total bilirubin greater than 2 times ULN (in the absence of cholestasis or haemolysis)' required permanent discontinuation of the product. This crucial information was omitted on the webpage. All the webpage said was monitor liver function tests.

3 CNS – the SPC advice was, 'For prolonged, severe, or intolerable events, discontinue Rozlytrek as clinically appropriate'. This information was not presented on the webpage. The webpage simply stated 'Monitor for signs' under CNS section.

4 Blood – SPC information was at Grade 3 or 4 anaemia or neutropenia 'Withhold Rozlytrek until recovery to less than or equal to Grade 2 or to baseline' and 'Resume at the same dose or reduced dose, as clinically needed'. This was not stated on the webpage. There was also no mention of dosage considerations around anaemia or neutropenia either as dosage reductions were required as per the SPC. This was not made clear in the blood section.

The information in the SPC around Hyperuricaemia (Symptomatic or Grade 4) and needing to withhold the medicine were also not made clear.

To have a monitoring section and not actually list out such specific advice from the SPC around dosage reductions and discontinuation for a black triangle product, demonstrated the lack of understanding by Roche around patient safety. Health professionals had to be able to make informed decisions by being presented all information and the monitoring section of the webpage did not have the exact criteria to align with the SPC.

The complainant alleged breaches of Clauses 6.1 (x5 for each of the monitoring sections), 6.2 (x5 for each of the monitoring sections), 5.1 and 2. One had to question who had approved this content for release considering the danger to patients of such content missing important information.

When writing to Roche, the Authority asked it to consider the requirements of Clauses 6.1, 6.2, 5.1 and 2 of the 2021 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. Roche was therefore disappointed to receive this complaint which it believed had no basis.

For context, Roche submitted that the complaint referred to a page on the Roche resources website, which required the user to confirm that they were a healthcare professional prior to access. 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.

The complaint referred to a Roche Resources webpage which highlighted the dosing requirements for Rozlytrek (entrectinib), an inhibitor of the tropomyosin receptor kinases (TRK1,2,3) a proto-oncogene tyrosine-protein kinase ROS (ROS-1) and anaplastic lymphoma kinase (ALK). Rozlytrek was indicated for treating NTRK [neurotrophic tyrosine receptor kinase] fusion-positive solid tumours and ROS1-positive advanced non-small cell lung cancer.

The Roche Resources webpage referred to by the complainant formed part of a number of pages detailing the different elements of Rozlytrek. All the Roche Resources pages for Rozlytrek contained prominent links, in blue, to Rozlytrek prescribing information – one ‘click’ away. In addition to the blue link, Rozlytrek prescribing information was available from the fixed menu at the top of each webpage, as well as the fixed menu in the grey border at the bottom of each page.

The particular page referred to by the complainant entitled ‘Dosing’ contained information concerning testing requirements and general dosing in the yellow boxes at the top, followed by a summary of dosage modifications under the heading of ‘ROZLYTREK Treatment in Practice – Dose Reductions’. A table in this section provided more details on age and body surface area (BSA) related dosing along with recommended dose reductions. The following text sat above the table: *‘Further information on recommended ROZLYTREK dose modification in response to specific adverse reactions is available in the ROZLYTREK SmPC’*.

Below this, in a section entitled 'Suggested Monitoring', there were five headings: Heart, Liver, CNS, Blood and Bones. Next to each header graphic was a brief sentence to give context about the types of monitoring which might be considered and the rationale. This information was clearly referenced to the Rozlytrek SPC.

The complainant stated, in relation to this specific section, 'the information related to these did not give the relevant and exact information as per the SPC' and went on to reference a table within the SPC which 'had specific information around when to stop the product and dosage reductions during monitoring as opposed to just simply monitoring different body systems'.

Roche's above description and screenshots provided demonstrated that the Roche Resources pages for Rozlytrek directed the reader to refer to further information from the SPC and contained multiple opportunities to access prescribing information. All of which were in place to ensure the promotion of Rozlytrek was done with full consideration for the safety of patients.

Roche also acknowledged and respected the high skill and expertise of the target audience in question and felt the information given was sufficient to enable the health professional to make their own informed decision based on the information provided, including the prescribing information and references to the full SPC. Furthermore, as the reader was required to confirm their healthcare professional status before viewing the page, it was likely that they were already familiar with the management of the indicated conditions. It therefore followed that the reader would already understand the need to consult full prescribing information or an SPC before initiating treatment.

In light of the above, Roche felt that the information provided on the Rozlytrek Roche Resources page was accurate, balanced, fair, objective and unambiguous, reflected the SPC, did not mislead the health professional and enabled them to form their own opinion of the medicine. 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 that it had maintained the high standards expected of the industry and with full consideration for patient safety and therefore denied a breach of Clauses 5.1, 5.2 and 2, fully acknowledging the reservation of the aforementioned Clause for situations of particular censure.

Whilst it was disappointing to receive this complaint, Roche believed that it had demonstrated that the Rozlytrek pages contained content that did not represent any adverse impact to patient safety. Roche maintained that the webpages had been produced in accordance with high standards and expectations of the industry.

PANEL RULING

The Panel noted that the Rozlytrek (entrectinib) dosing webpage at issue on the Roche resources website appeared to sit within the medicines section of the website under Oncology and Rozlytrek (entrectinib); the webpage appeared to comprise of three key sections which sat beneath the brand logo, prescribing information and adverse event reporting links.

The first section titled 'ROZLYTREK Treatment in Practice' featured a box with patient selection criteria for patients with NTRK [neurotrophic tyrosine receptor kinase] gene fusion-positive solid

tumours and ROS1+ NSCLC [non-small cell lung cancer] and another box with Rozlytrek dosage information. The second section titled 'ROZLYTREK Treatment in Practice – Dose Reductions' contained information on adverse events and the table 'Recommended dose reductions for patients receiving ROZLYTREK' which listed the dose reductions for paediatric patients based on BSA [body surface area] and adults. The third section, 'Suggested Monitoring', featured the five headings Heart, Liver, CNS, Blood and Bones with brief sentences adjacent to each heading on monitoring requirements.

The Panel noted the following sections of the Rozlytrek SPC:

> Section 4.2 Posology and method of administration included information on dose modifications and stated 'Management of adverse reactions may require temporary interruption, dose reduction, or discontinuation of treatment with Rozlytrek, in case of specified adverse reactions (see Table 4) or based on the prescriber's assessment of the patient's safety or tolerability'; Table 4 included recommended Rozlytrek dose modifications for adverse reactions.
>
> Section 4.4, Special warnings and precautions for use included a number of warnings and precautions, which covered a number of different clinical issues.
>
> Section 4.8, Undesirable effects included the frequency of adverse reactions occurring in adult and paediatric patients treated with Rozlytrek in clinical trials.

The Panel noted the allegation that the dosing considerations were misleading and not fair or balanced; critical information had allegedly been omitted around dosage reductions/ discontinuation during monitoring, which would lead to a patient safety risk as not all information had been provided.

In this regard, the Panel noted Roche's submission that the webpage directed the reader to refer to further information from the SPC and contained multiple opportunities to access prescribing information, enabling health professionals to make their own informed decision based on the information provided; Roche further submitted that the reader was likely already familiar with the management of the indicated conditions and would already understand the need to consult full prescribing information or an SPC before initiating treatment.

The Panel considered that whether a special warning or precaution needed to be highlighted within a particular section of promotional material depended on all of the circumstances including the nature of the warning/precaution and the content, layout, audience and intended use of the material.

The Panel, noting Rozlytrek was a black triangle medicine subject to additional monitoring, set out its rulings in relation to each body system raised by the complainant.

1 Heart

The Panel noted the following information in the Rozlytrek SPC, under Section 4.2 Posology and method of administration, the section on recommended Rozlytrek dose modifications for adverse reactions in adult and paediatric patients, and Sections 4.4 Special warnings and precautions for use and 4.8 Undesirable effects:

	Section 4.2	Section 4.4	Section 4.8
Congestive heart failure	Symptomatic with middle to moderate activity or exertion, including where intervention is indicated (Grade 2 or 3)' Rozlytrek should be withheld until recovered to less than or equal to Grade 1 and resumed at a reduced dose. For patients with severe congestive heart failure with symptoms at rest, minimal activity, or exertion or where intervention is indicated (Grade 4), Rozlytrek should be withheld until recovered to less than or equal to Grade 1 and resumed at a reduced dose or discontinued as clinically appropriate.	For patients with symptoms or known risk factors of CHF [congestive heart failure], left ventricular ejection fraction (LVEF) should be assessed prior to initiation of Rozlytrek treatment. Patients receiving Rozlytrek should be carefully monitored and those with clinical signs and symptoms of CHF, including shortness of breath or oedema, should be evaluated and treated as clinically appropriate. Based on the severity of CHF, Rozlytrek treatment should be modified.	common (≥1/100 to <1/10)
QT interval prolongation	Patients with QTc 481 to 500 ms Rozlytrek should be withheld until recovered to baseline and treatment resumed at the same dose. In patients with QT interval prolongation with QTc greater than 500 ms Rozlytrek should be withheld until QTc interval recovers to baseline and resumed at the same dose if factors that cause QT prolongation are identified and corrected or resumed at a reduced dose if other factors that cause QT prolongation are not identified.	Use of Rozlytrek should be avoided in patients with a baseline QTc interval longer than 450 ms, in patients with congenital long QTc syndrome, and in patients taking medicinal products that are known to prolong the QTc interval. Rozlytrek should be avoided in patients with electrolyte imbalances or significant cardiac disease, including recent myocardial infarction, congestive heart failure, unstable angina, and bradyarrhythmias. If in the opinion of the treating physician, the potential benefits of Rozlytrek in a patient with any of these conditions outweigh the potential risks, additional monitoring should be performed and a specialist consultation should be	common (≥1/100 to <1/10)

		considered. Assessment of ECG and electrolytes at baseline and after 1 month of treatment with Rozlytrek are recommended. Periodic monitoring of ECGs and electrolytes as clinically indicated throughout Rozlytrek treatment, are also recommended. Based on the severity of QTc prolongation, Rozlytrek treatment should be modified.	

The Panel noted that the heart section under Suggested Monitoring on the Roche Resources webpage at issue stated 'Monitor patients for clinical signs and symptoms of congestive heart failure, including shortness of breath and oedema. For patients with or at risk of QTc-interval [corrected QT interval] prolongation, assess QT interval and electrolytes at baseline and periodically during treatment'.

The Panel noted Roche's submission that the dosing web-page contained the statement 'Further information on recommended ROZLYTREK dose modification in response to specific adverse reactions is available in the ROZLYTREK SmPC' which appeared above the table titled 'Recommended dose reductions for patients receiving ROZLYTREK' and that the web-page contained multiple opportunities to access the prescribing information. The Panel did not have the content of the Rozlytrek prescribing information before it. The Panel noted that the dosing webpage did not contain a link to the SPC for Rozlytrek.

The Panel considered the information in Section 4.2 and 4.4 of the Rozlytrek SPC, which gave specific instructions on when to reduce the dose, avoid, withhold or discontinue treatment with Rozlytrek and when additional monitoring should be performed and a specialist consultation considered. The Panel considered that this was important information that a health professional would expect to have been made aware of on a webpage dedicated to dosing. The Panel noted that this important information was not within the body of the webpage, nor was there a signpost on the webpage to indicate that there was additional important information in the SPC regarding evaluation in patients who experience congestive heart failure or when additional monitoring should be performed, and no link to the SPC was provided.

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

In the Panel's view, the statement 'Further information on recommended ROZLYTREK dose modification in response to specific adverse reactions is available in the ROZLYTREK SmPC' was insufficient to negate the misleading impression given that the webpage contained all the important information in relation dosage and monitoring.

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 that health professionals needed to prescribe Rozlytrek in patients with congestive heart failure or QT interval prolongation which was not so. The Panel thus 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 the information was not capable of substantiation; it was not for the Panel to infer detailed reasons to support the allegation on behalf of the complainant. The Panel therefore ruled **no breach of Clause 6.2.**

2 Liver

The Panel summarised the following information in the Rozlytrek SPC under Section 4.2 Posology and method of administration, and Section 4.8 Undesirable effects of the Rozlytrek SPC:

	Section 4.2		**Section 4.8**
Transaminase elevations	Grade 3	• Withhold Rozlytrek until recovery to less than or equal to Grade 1 or to baseline • Resume at same dose if resolution occurs within 4 weeks • Permanently discontinue if adverse reaction does not resolve within 4 weeks • Resume at a reduced dose for recurrent Grade 3 events that resolve within 4 weeks	Hepatobiliary disorders, increased AST and ALT very common (≥1/10)
	Grade 4	• Withhold Rozlytrek until recovery to less than or equal to Grade 1 or to baseline • Resume at reduced dose if resolution occurs within 4 weeks • Permanently discontinue if adverse reaction does not resolve within 4 weeks • Permanently discontinue for recurrent Grade 4 events	
	ALT or AST greater than 3 times ULN [upper limit of normal] with concurrent total bilirubin greater than 2 times ULN (in the absence	• Permanently discontinue Rozlytrek	

	of cholestasis or haemolysis)		

The Panel noted that the Suggested Monitoring section on the dosing webpage stated 'Monitor liver function tests, including ALT [alanine aminotransaminase] and AST [aspartate aminotransferase], every 2 weeks during the first month of treatment, then monthly thereafter, and as clinically indicated'.

The Panel considered the information in Section 4.2 of the Rozlytrek SPC, which gave specific instructions on when to reduce the dose, withhold or discontinue treatment with Rozlytrek. The Panel considered that this was important information that a health professional would expect to have been made aware of on a webpage dedicated to dosing. The Panel noted that elevated AST and ALT levels were very common adverse reactions for Rozlytrek and that the important information regarding dose modifications due to these adverse reactions was not within the body of the webpage, nor was there a signpost on the webpage to indicate that there was additional important information in the SPC, and no link to the SPC was provided. In the Panel's view, the statement 'Further information on recommended ROZLYTREK dose modification in response to specific adverse reactions is available in the ROZLYTREK SmPC' was insufficient to negate the misleading impression given that the webpage contained all the important information in relation dosage and monitoring.

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 that health professionals needed to prescribe Rozlytrek in patients with elevated ALT and AST which was not so. The Panel thus ruled a **breach of Clause 6.1**.

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

3 CNS

The Panel summarised the following information in the Rozlytrek SPC, under Section 4.2 Posology and method of administration and Sections 4.4 Special warnings and precautions for use and 4.8 Undesirable effects:

	Section 4.2	**Section 4.4**	**Section 4.8**
Cognitive Disorders	In patients with intolerable, but moderate changes interfering with activities of daily living (Intolerable Grade 2) and severe changes limiting activities of daily living (Grade 3), Rozlytrek should be withheld until recovery to less than or equal to Grade 1 or to baseline. For intolerable Grade 2 disorders Rozlytrek should be resumed at the same or reduced dose as clinically needed and for intolerable	Cognitive disorders, including confusion, mental status changes, memory impairment, and hallucinations, were reported in clinical trials with Rozlytrek. Patients should be monitored for signs of cognitive changes. Based on the severity of cognitive disorders, Rozlytrek treatment should be modified as described in Table 4 in section 4.2.	Nervous system disorders - very common (≥1/10) and common (≥1/100 to <1/10)

	Grade 3 disorders Rozlytrek should be resumed at a reduced dose. In patients with urgent intervention indicated for an event (Grade 4) such as prolonged, severe or intolerable events, Rozlytrek should be discontinued as clinically appropriate.	Patients should be counselled on the potential for cognitive changes with Rozlytrek treatment. Patients should be instructed not to drive or use machines until symptoms resolve if they experience cognitive disorders.	

The Panel noted that the Suggested Monitoring section on the dosing webpage stated 'Monitor for signs of CNS [central nervous system] adverse reactions, including cognitive impairment, mood disorders, dizziness and sleep disturbances'.

The Panel considered the information in Section 4.2 and 4.4 of the Rozlytrek SPC, which gave specific instructions on when to reduce the dose, withhold or discontinue treatment with Rozlytrek and that patients should be counselled on potential cognitive changes and instructed not to drive or use machines until cognitive symptoms resolve. The Panel considered that this was important information that a health professional would expect to have been made aware of on a webpage dedicated to dosing. The Panel noted that cognitive disorders were very common adverse reactions for Rozlytrek and that the important information regarding dose modifications and counselling patients due to these adverse reactions was not within the body of the webpage, nor was there a signpost on the webpage to indicate that there was additional important information in the SPC, and no link to the SPC was provided. In the Panel's view, the statement 'Further information on recommended ROZLYTREK dose modification in response to specific adverse reactions is available in the ROZLYTREK SmPC' was insufficient to negate the misleading impression given that the webpage contained all the important information in relation dosage and monitoring.

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 that health professionals needed to prescribe Rozlytrek in patients with central nervous system adverse reactions which was not so. The Panel thus ruled a **breach of Clause 6.1**.

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

4 Blood

The Panel noted the following information in the Rozlytrek SPC, under Section 4.2 Posology and method of administration and Sections 4.4 Special warnings and precautions for use and 4.8 Undesirable effects:

	Section 4.2	**Section 4.4**	**Section 4.8**
Hyperuricaemia	In patients with symptomatic or Grade 4 hyperuricemia, urate-lowering medication should	Hyperuricemia has been observed in patients treated with entrectinib. Serum uric acid levels	Common (≥1/100 to <1/10).

	be initiated, Rozlytrek should be withheld until improvement of signs or symptoms and resumed at the same or a reduced dose	should be assessed prior to initiating Rozlytrek and periodically during treatment. Patients should be monitored for signs and symptoms of hyperuricemia. Treatment with urate-lowering medicinal products should be initiated as clinically indicated and Rozlytrek withheld for signs and symptoms of hyperuricemia. Rozlytrek dose should be modified based on severity as described in Table 4 in section 4.2.	
Anaemia or neutropenia	In patients with anaemia or neutropenia at Grade 3 or 4 Rozlytrek should be withheld until recovery to less than or equal to Grade 2 or to baseline and resumed at the same or reduced dose, as clinically needed.		Very common adverse events (≥1/10).

The Panel noted that the Suggested Monitoring section on the dosing webpage stated 'Assess serum urate prior to initiating ROZLYTREK and periodically during treatment. Monitor patients for signs and symptoms of hyperuricaemia'.

The Panel considered the information in Section 4.2 and 4.4 of the Rozlytrek SPC, which gave specific instructions on when to reduce the dose or withhold treatment with Rozlytrek in patients with hyperuricaemia and that treatment with urate-lowering medicinal products should be initiated as clinically indicated and Rozlytrek withheld for signs and symptoms of hyperuricemia. The Panel further noted that information regarding dose modifications due to anaemia or neutropenia was not stated on the webpage.

The Panel considered that this was important information that a health professional would expect to have been made aware of on a webpage dedicated to dosing. The Panel noted that hyperuricemia was a common adverse event for Rozlytrek and that the important information regarding dose modifications and initiating treatment with urate-lowering medicinal products due to such adverse reactions was not within the body of the webpage, nor was there a signpost on the webpage to indicate that there was additional important information in the SPC, and no link to the SPC was provided. In the Panel's view, the statement 'Further information on recommended ROZLYTREK dose modification in response to specific adverse reactions is available in the ROZLYTREK SmPC' was insufficient to negate the misleading impression given that the webpage contained all the important information in relation dosage and monitoring.

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 that health professionals needed to prescribe Rozlytrek in patients with hyperuricaemia, anaemia or neutropenia which was not so. The Panel thus ruled **a breach of Clause 6.1**.

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

5 Bones

The Panel noted the following information in Sections 4.4 Special warnings and precautions for use and 4.8 Undesirable effects of the Rozlytrek SPC:

	Section 4.4	**Section 4.8**
Fractures	Patients with signs or symptoms of fractures (e.g., pain, abnormal gait, changes in mobility, deformity) should be evaluated promptly	Common (≥1/100 to <1/10).

The Panel noted that the Suggested Monitoring section on the dosing web page stated 'As ROZLYTREK increases the risk of fractures, promptly evaluate with signs or symptoms of a fracture, including pain, changes in mobility and deformity'.

The Panel did not consider that the complainant had established that the webpage gave misleading information regarding fractures or that information was not substantiated. The Panel thus ruled **no breach of Clause 6.1** and **Clause 6.2** in this regard.

The Panel noted Roche's submission that it acknowledged and respected the high skill and expertise of the target audience in question and felt the information given was sufficient to enable the health professional to make their own informed decision based on the information provided. The Panel noted that treatment with Rozlytrek should be initiated by a physician experienced in the use of anticancer medicinal products and considered that such health professionals would take particular care when prescribing Rozlytrek. Nonetheless, the Panel considered that material must not be misleading and must be sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine. The Panel, noting it's ruling of breaches of the Code above, and noting that Rozlytrek was a black triangle medicinal product, considered that high standards had not been maintained, and ruled **a breach of Clause 5.1** in this regard.

The Panel considered that patient safety was of the utmost importance. Examples of activities likely to lead to a breach of Clause 2 included prejudicing patient safety. The Panel, noting that Rozlytrek was a black triangle medicinal product subject to additional monitoring, and that important safety information was omitted from the dosing webpage, considered that Roche had brought discredit upon and reduced confidence in the pharmaceutical industry, and **a breach of Clause 2** was ruled.

Complaint received	**12 May 2022**
Case completed	**23 May 2023**