CASE AUTH/3834/10/2023 ***NO BREACH OF THE CODE***

COMPLAINANT v ABBVIE

Allegations about a Rinvoq (Upadacitinib) webpage

CASE SUMMARY

This case was in relation to a webinar registration webpage for health professionals. The complainant's allegations related to the absence of important information relating to the consumption of food or drink containing grapefruit when taking Rinvoq not being included on the webpage.

The outcome under the 2021 Code was:

No Breach of Clause 2	**Requirement that activities or materials must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**
No Breach of Clause 5.1	**Requirement to maintain high standards at all times**
No Breach of Clause 6.1	**Requirement that claims/information/comparisons 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 AbbVie was received from a complainant who described themselves as a health professional.

COMPLAINT

The complaint wording is reproduced below:

> "Information was provided on dosing of Rinvoq but important information about avoiding grapefruit juice were omitted. A webinar event page with information about Rinvoq was advertised on the following link: [weblink address provided]. The following information was provided on this standalone promotional webpage: The recommended dose of upadacitinib is a 15 mg or 30 mg once daily based on individual patient presentation. The recommended dose of upadacitinib is 15 mg once daily for adolescents weighing at least 30 kg. For patients ≥65 years of age, the recommended dose is 15 mg once daily. However, the SPC (section 4.2) clearly mentioned the following within the method of administration section where dosing info was given: Food or drink containing grapefruit should be avoided during treatment with upadacitinib (see section 4.5). This information around avoidance of grapefruit during treatment was criticial [sic] in ensuring patient safety. If an individual took grapefruit

alongside Rinvoq, this could risk patient safety. As Rinvoq is a black triangle product, it is even more important to provide all information to HCPs around avoidance of grapefruit. As the webpage in question was providing dosing information (take once daily), all information (avoiding grapefruit) around dosing should have been provided fo [sic] prescribers to ensure patient safety as stipulated in the SPC. Breaches of clauses 6.1, 5.1 and 2 had occurred [*sic*]."

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

ABBVIE'S RESPONSE

The response from AbbVie is reproduced below:

"**Complaint:**

The complainant alleges that 'Information was provided on dosing of Rinvoq but important information about avoiding grapefruit juice were (sic) omitted' from an AbbVie promotional registration webpage'.

Specifically, the complainant alleges that 'As Rinvoq is a black triangle product, it is even more important to provide all information to HCPs around avoidance of grapefruit.'

The complainant alleges breaches of clauses: 2, 5.1, 6.1 of the 2021 ABPI Code.

Background:

The complainant has referred to an AbbVie registration webpage. AbbVie hosted this registration webpage for UK healthcare professionals (HCPs) with the primary purpose of allowing HCPs to register their contact details in order to access on-demand content included in the AbbVie promotional medical educational series 'Clear Horizons'.

'Clear Horizons' is a series that aims to provide educational product related, and therefore promotional information relating to AbbVie medicines within the dermatology therapy area. This registration webpage was accessible via a direct link on the AbbVie promotional website addressed to UK HCPs, specifically via the 'Expert Perspectives' page on [website address provided].

Considerations:

AbbVie ensures all its promotional webhosted content has prescribing information included in the digital material itself or by way of a single click link as per clause 12.5 of the Code. AbbVie also considers that whether an interaction, special warning or precaution should be highlighted in addition to the prescribing information within a particular section of a promotional material, is dependent on the intended use, audience, content and layout of the material.

Intended use of the material:

The intent and focus of this registration webpage was solely to act as a platform for UK HCPs to register their contact details in order to then access HCP directed, on demand promotional content. The intent of the registration webpage was not to act as a complete data source regarding Rinvoq, and therefore contained minimal product information. The prescribing information was available to HCPs accessing the registration webpage as a single click link. Within the prescribing information, information relating to interactions could be found with specific reference to food/drink containing grapefruit. In addition, the registration webpage in question included a reference to the Rinvoq summary of product characteristics and where it could be found, all with a view to ensure UK HCPs had all the relevant documents signposted.

Audience:

The registration webpage was intended for access by UK HCPs only, who could reach this registration webpage through a link hosted on the 'Expert Perspectives' page within the AbbVie promotional website [address provided]. This promotional website contained the necessary and obligatory attestation ramp to ensure only UK HCPs would access the promotional content.

Content and layout of the material:

As noted above, the page in question was a registration page for on demand content and contained information on registration details, summary of the on-demand content, speakers' details, and the following statements:

- *'for UK healthcare professional only',*
- *'Some patients may not be suitable for RINVOQ. You are strongly advised to read the RINVOQ (upadacitanib) prescribing and adverse event reporting information, which can be found below'*
- *and in bold, '**Click here for RINVOQ (upadacitinib) prescribing information**' - a direct single click to the full prescribing information.*

Rinvoq has multiple licensed indications with 3 different doses (15mg, 30mg, and 45mg) and with posology that is indication specific. The registration webpage was a pre-requisite for HCPs accessing content specifically related to Atopic Dermatitis, which is one of Rinvoq's licensed indications. Therefore, AbbVie considered it would be appropriate to give HCPs clarity and context with respect to the content they were registering for by including upfront an explicit reference to the relevant licensed indication:

> *'RINVOQ is indicated for the treatment of moderate to severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy'.*

As the indication statement includes reference to both adolescent and adult populations and only two of the three Rinvoq presentations are licensed for use in Atopic Dermatitis, the corresponding dosing information was included to provide context of the differing dosage. Specifically, 15mg is recommended for adolescent patients and adults >65 years old, and 15mg or 30mg is recommended for adults

based on individual presentation. This information was provided on the registration page in the following statement:

> *'The recommended dose of upadacitinib is a 15mg or 30mg once daily based on individual patient presentation. The recommended dose of upadacitinib is 15 mg once daily for adolescents weighing at least 30 kg. For patients > 65 years of ages, the recommended dose is 15 mg once daily'*

Alleged omissions of information regarding avoidance of grapefruit on the registration page:

As outlined, the purpose of the registration webpage was to enable HCPs to provide their contact details in order to access on-demand content. The registration webpage was designed to provide the necessary information about the subject matter of the on-demand content: Atopic Dermatitis in adolescents and adults. The registration webpage was not intended to be a complete overview of all the information relevant to the prescription of Rinvoq and a link to the prescribing information was provided and highlighted on the page.

The registration webpage clearly stated that some patients may not be suitable for Rinvoq and HCPs are strongly advised to read the Rinvoq prescribing information available as a single click directly on the page, which contained the information regarding avoidance of grapefruit among other considerations.

As part of this case, the complainant stated:

> *'This information around avoidance of grapefruit during treatment was criticial (sic) in ensuring patient safety. If an individual took grapefruit alongside Rinvoq, this could risk patient safety.'*

With relation to the complainant stating that this information is 'critical' for patient safety, AbbVie would like to provide some further context. The recommendation to avoid food/drink containing grapefruit during treatment with upadacitinib is based on data demonstrating upadacitinib exposure is increased when co-administered with strong CYP3A4 inhibitors (such as ketoconazole, itraconazole, posaconazole, voriconazole, clarithromycin, and grapefruit juice). There is no specific data to show that there is an increase in Rinvoq side effects with consumption of grapefruit-containing products. The SmPC states: '*Coadministration of upadacitinib with grapefruit may increase exposure to upadacitinib. Food or drink containing grapefruit should be avoided during treatment with upadacitinib.*' Co-ingestion of Rinvoq and grapefruit is not listed as a contraindication within 4.3 of the Rinvoq SmPC and is not considered a critical patient safety event.

In addition, AbbVie would emphasise that the information regarding grapefruit was readily available to the HCPs within the prescribing information.

AbbVie believe that in respect to the allegation of Code breaches, the registration webpage in question was appropriate in the intended use, audience, content and layout of the material with the relevant information correctly presented in context and complete for the intended purpose, with information accurate, balanced, fair, objective and unambiguous and so there is no breach of clause 6.1. As such, AbbVie believes

high standards have been maintained and there is no breach of clause 5.1. AbbVie does not consider the registration webpage in question jeopardised patient safety or was such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry and so there is no breach of clause 2.

Voluntary Admission

Whilst responding to this case, AbbVie noted that the material in question had not been correctly certified. AbbVie engaged a third-party agency to develop the registration webpage for HCPs. The agency uploaded the registration webpage UK-RISN-210528 to the internal approval platform, and this material was certified by AbbVie. The third-party agency directly accessed this internal approval platform to obtain the certified copy which should have been used for the hosted registration webpage.

The third-party agency then inadvertently uploaded an incorrect version of the registration webpage with the same job code as the final certified material. The difference between the 2 pages was that the certified version had a checkbox list of 3 of the episodes of 'Clear Horizons' that HCPs could register for and the unapproved version had only the episode 3 listed. Therefore, the registration webpage flagged by the complainant, was not the correctly certified version and a certificate is unavailable.

AbbVie has reviewed the certification process related to this page and has identified this to be an isolated incident. To prevent any further incidents, AbbVie has conducted further training with the relevant teams including our partner agencies to mitigate any future issues. AbbVie would therefore like to make a voluntary admission of breach of clause 8.1: Failure to certify material in its final form.

Summary

In summary as outlined above, AbbVie does not believe that the registration page in question has breached clauses 2, 5.1, 6.1 of the 2021 ABPI Code. In addition, AbbVie are making a voluntary admission of a breach of clause 8.1.

AbbVie takes its responsibility for compliance with the ABPI Code very seriously as we continuously endeavour to maintain high standards in all our activities."

PANEL RULING

The Panel noted this complaint concerned a webpage where UK health professionals could register for access to an on-demand promotional webinar for Rinvoq (upadacitinib). The complainant alleged that information about avoiding consumption of food or drink containing grapefruit should have been provided on the webpage because the webpage provided dosing information and, particularly, because Rinvoq was a black triangle product.

From the screenshot provided by AbbVie, the Panel noted the webpage was split into two columns. The left-hand side had an 'Overview' of the webinar and registration fields for health professionals to complete and submit. The right-hand side of the page presented a summary which included the licensed indication for Rinvoq®, the areas the webinar would focus on and the names of the speakers for the webinar. Beneath this, in smaller text, was the licensed indication for Rinvoq, information on recommended dosages, a reference to the summary of

product characteristics (SPC) (available via the emc website) and a sentence reading: “Some patients may not be suitable for Rinvoq®. You are strongly advised to read the Rinvoq® (upadacitinib) prescribing and adverse event reporting information, which can be found below.” At the bottom of the right-hand column, there was a prominent single click link to the prescribing information for Rinvoq, the adverse events reporting statement, a statement that AbbVie had organised and funded the website and the job code and date of preparation.

The Panel noted that the statement about recommended dosages read: “The recommended dose of upadacitinib is a 15 mg or 30 mg once daily based on individual patient presentation. The recommended dose of Upadacitinib is 15 mg once daily for adolescents weighing at least 30 kg. For patients >65 years of age, the recommended dose is 15 mg once daily.”

The Panel noted AbbVie’s submission that the prescribing information was provided on the registration webpage as a single click link and within that, information relating to interactions, particularly with reference to avoiding food and drink containing grapefruit was included. Furthermore, the registration webpage included a reference to the Rinvoq SPC which also contained the statement about grapefruit.

The Panel considered the content, layout and impression created by the webpage as a whole; it determined that its purpose was to enable health professionals to register for access to a webinar which would focus on the burden of disease in atopic dermatitis and the latest Rinvoq data. In the Panel’s view it was clear that the webpage was not intended to be a source of safety information for Rinvoq, The Panel considered it was highly unlikely that health professionals would rely solely on the information contained in a registration webpage to inform prescribing decisions.

Furthermore, the Panel considered the inclusion of the statement that Rinvoq was not suitable for all patients and strongly advising health professionals to refer to the prescribing information was sufficient to alert prescribers that consideration had to be given to specific safety issues in determining the suitability of the product for an individual patient.

Accordingly, the Panel did not consider the complainant had established that the absence of information regarding avoidance of food or drink containing grapefruit on the registration webpage constituted a risk to patient safety, or that the webpage as a whole was misleading. The Panel therefore ruled **no breach of Clause 6.1**.

Based on its ruling of no breach of the Code above, the Panel did not consider that it had been established that AbbVie had failed to maintain high standards, nor that it had brought discredit upon, or reduced confidence in, the pharmaceutical industry. The Panel ruled **no breaches of Clauses 5.1 and 2,** accordingly.

The Panel noted that the voluntary admission was considered within Case AUTH 3852/11/23 and therefore made no ruling on this matter.

Complaint received **9 October 2023**

Case completed **6 September 2024**