CASE AUTH/3712/11/22

COMPLAINANT v ABBVIE

Promotion of Rinvoq

CASE SUMMARY

This case concerned allegations about the suitability of imagery used on two Rinvoq (upadacitinib) webpages related to rheumatoid arthritis and psoriatic arthritis.

The Panel ruled a breach of the following clauses of the 2021 Code on the basis that it considered:

- **the use of an image of a young female surfing on the webpage related to psoriatic arthritis might misleadingly imply that patients taking Rinvoq would be able to perform such strenuous exercise which in the Panel's view was unlikely and which was compounded by the claim of 'rapid and sustained joint efficacy' and created a misleading impression in that it did not reflect the typical patient with moderate to severe psoriatic arthritis and could not be substantiated**
- **the image of a woman of childbearing potential on each webpage without including a reference to the fact it was contraindicated in pregnancy or the warning that women of childbearing potential should be advised to use effective contraception during treatment and for 4 weeks following the final dose of Rinvoq was misleading**
- **the use of imagery of a young female, in association with a product with a known risk of foetal harm, without highlighting that there were restrictions on use in this population had the potential to impact patient safety and was such that AbbVie had brought discredit upon, and reduced confidence in, the industry.**

Breach of Clause 2	**Bringing discredit upon, and reducing confidence in, the pharmaceutical industry**
Breach of Clause 5.1	**Failing to maintain high standards**
Breach of Clause 6.1	**Failing to ensure material was sufficiently complete and not misleading**
Breach of Clause 6.2	**Making an unsubstantiated claim**
Breach of Clause 6.3	**Failing to ensure artwork conformed to the letter and spirit of the Code**

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

- **Rinvoq was licensed for rheumatoid arthritis and psoriatic arthritis in adult patients only. Therefore, the Panel did not consider that failure to include the warning, that female paediatric patients taking Rinvoq and/or their**

parents/caregivers should be informed about the need to contact the treating physician once the patient experiences menarche (starting menstruation), on the webpages at issue was, in the particular circumstances of the case, misleading or incapable of substantiation

- **The complainant had not established that an image of a young female sitting on a swing swinging on the rheumatoid arthritis webpage was not representative of a typical patient with moderate to severe rheumatoid arthritis; while some fitness was required to generate the swinging movement, the activity did not appear to require particular stability or strength in the joints.**

No Breach of Clause 6.1	**Requirement that material must be sufficiently complete and not be misleading**
No Breach of Clause 6.2	**Requirement that claims and information must be capable of substantiation**
No Breach of Clause 6.3	**Requirement that all artwork must conform to the letter and spirt of the Code**

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

FULL CASE REPORT

A complainant who described themselves as a health professional and was initially contactable but became non-contactable complained about the promotion of Rinvoq (upadacitinib) by AbbVie Ltd. The material at issue comprised two webpages of the AbbViePro website and links to those pages were provided. Rinvoq was indicated, amongst other things, for the treatment of moderate to severe active rheumatoid arthritis in certain adult patients and the treatment of active psoriatic arthritis in certain adult patients.

COMPLAINT

The complainant noted that Rinvoq was licensed for treatment in moderate to severe rheumatoid arthritis or moderate to severe psoriatic arthritis but was contraindicated in pregnancy and there were extra considerations required during breastfeeding. The complainant alleged that the imagery used of young females on top of the two promotional webpages for this product implied it was suitable for use in all females regardless of pregnancy or breastfeeding status. Women of childbearing potential should be advised to use effective contraception during treatment and for 4 weeks following the final dose of Rinvoq. Female paediatric patients and/or their parents/caregivers should be informed about the need to contact the treating physician once the patient experiences menarche while taking Rinvoq. However, information that Rinvoq was contraindicated in pregnancy, contraception requirements and considerations that needed to be decided during breastfeeding were not provided on the two pages.

The complainant further alleged that the two images chosen were also not reflective of a typical moderate to severe rheumatoid or moderate to severe psoriatic arthritis patient as these patients would not be surfing or performing strenuous activities. Initial impressions would imply the product was suitable for use in all female patients without any considerations when this was not true. This was concerning as Rinvoq is a black triangle drug. The misleading images and omission of pregnancy contraindications, contraception requirements and no information at

breastfeeding considerations alongside images not representative of typical patients were in breach of Clauses 6.1, 6.2, 5.1 and 2.

When writing to AbbVie the Authority asked it to consider the requirements of Clause 6.3 in addition to those cited by the complainant.

RESPONSE

AbbVie stated that it took its responsibility for compliance with all applicable laws and regulations including the ABPI Code of Practice ('Code') very seriously and it continuously endeavoured to maintain these high standards in all its activities.

Suitability of the images used on both pages referred to by the complainant

AbbVie noted that the Code stated that 'care must be taken to ensure artwork does not mislead as to the nature of the medicine'. RINVOQ's licensed indication in rheumatic arthritis and psoriatic arthritis, as stated in the Summary of Product Characteristics (SPC), was:

> *'Treatment of moderate to severe active rheumatoid arthritis (RA) and active psoriatic arthritis (PsA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying antirheumatic drugs (DMARDs). RINVOQ may be used as monotherapy or in combination with methotrexate.'*

Adult age in pharmaceutical and legal terms was defined as aged 18 years and over. There was also no exclusion of female sex in the licensed indications for RINVOQ. The images of females used were clearly those aged 18 or older and they were depicted as neither pregnant nor breastfeeding.

The image on the webpage relating to rheumatoid arthritis (UK-UPAD-220195) showed a female sitting on a swing, an activity AbbVie believed required minimal to no further exertion than an individual would experience in their day to day lives and thus one which could be undertaken by a patient with rheumatoid arthritis. Like most autoimmune diseases, rheumatoid arthritis also primarily affected women, with around two thirds of patients suffering with rheumatoid arthritis being female. Therefore, it would not be unreasonable for the imagery to be reflective of the sex type who were more likely to suffer with rheumatoid arthritis.

The image on the webpage relating to psoriatic arthritis (UK-UPAD-220201) showed a female standing on a surfboard. It was important to note that psoriatic arthritis tended to be diagnosed in younger patients with peak onset between 25-50 years old; compared to those diagnosed with rheumatoid arthritis (peak onset 40-60 years). Patients with PsA were typically of younger age than patients with RA and therefore likely to be more physically active at the time when they were typically diagnosed with the disease. Following diagnosis and while undergoing treatment, patients with PsA were actively encouraged to partake in some level of physical activity, as close as possible to the patient's old normal exercise regimen to support holistic disease management. Also, considering that psoriatic arthritis affected males and females roughly equally, in AbbVie's view there was no reason why this would preclude the use of imagery depicting a female, as females were as likely to be affected by the disease as males.

In the context set out above, AbbVie was of the view that the use of imagery depicting women on both pages was not inappropriate. It was not aware of any provision in the Code or in the

legislation requiring imagery of women to be labelled with pregnancy warnings. AbbVie submitted that it had also included below additional detail as to why it believed that the absence of such warning was highly unlikely to lead a health professional to believe that RINVOQ could be prescribed to pregnant or breastfeeding women with no restrictions or other considerations.

Based on the above, AbbVie believed that the imagery used was consistent with RINVOQ's licensed indications, was not misleading, and therefore not in breach of Clauses 6.1, 6.2 and 6.3. And as such high standards had been maintained (Clause 5.1).

Allegation that information regarding RINVOQ being contra-indicated in pregnancy, and the extra considerations required during breastfeeding were not provided on the two pages in question

AbbVie submitted that it took patient safety extremely seriously and reassured the PMCPA that all the appropriate and relevant information for health professionals to understand the suitability of treatment with RINVOQ for specific categories of patients had been included, details of which were outlined below.

Prescribing Guide for Health professionals

Adjacent to the images at the top of both webpages, was a prescribing guide for health professionals (UK-UPAD-220185), accessed by clicking on the text to open the document, that provided health professionals with all the relevant information for them to understand how to dose RINVOQ, outlining information on dosing, screening, monitoring and safety recommendations.

This document gave specific guidance around contraception, pregnancy and lactation. It stated beneath the heading 'Contraception' that women of childbearing potential should be advised to use effective contraception during treatment and for 4 weeks following the final dose and that if the patient became pregnant while taking RINVOQ they should be informed of the potential risk to the foetus. It further stated beneath the heading 'Pregnancy and lactation' that RINVOQ was contraindicated during pregnancy and should not be used during breastfeeding. AbbVie reproduced the full text.

Prescribing Information for RINVOQ

Also adjacent to the images on both webpages was the prescribing information for RINVOQ (UK-UPAD- 220221). The prescribing information clearly highlighted that RINVOQ was contraindicated in pregnancy:

RINVOQ SPC

AbbVie provided a screenshot which showed that within the prescribing information health professionals were also advised to see the SPC for a full list of special warnings and precautions. A screenshot of Section 4.6 of the SPC was provided showing that it contained further information on contraception, pregnancy and lactation.

Safety Profile Webpage

Further to the above, safety information could clearly be found below both images that the complainant had questioned. The tab entitled "Safety Profile" appeared directly in the line of sight of the images in question, without the need to scroll further down the page. Screenshots were provided.

These Safety Profile tabs accessed from each page contained clear information on how patients should be screened, monitored, information on contraindications, and more specifically information on contraception, pregnancy and lactation as well as direct signposting to the SPC:

Psoriatic Arthritis - Safety Profile webpage details

AbbVie provided a link to the safety profile webpage and screenshots of a list of contraindications and a 'Pregnancy and lactation' section which included the pregnancy contraindication, information regarding the need for women of childbearing age to use effective contraception during treatment and for 4 weeks after the final dose and that RINVOQ should not be used during breastfeeding. The page also referred viewers to the SPC for complete product information.

Rheumatoid Arthritis - Safety Profile webpage details

AbbVie provided a link to the safety profile webpage and screenshots of a list of contraindications and a 'Pregnancy and lactation' section which included the pregnancy contraindication, information regarding the need for women of childbearing age to use effective contraception during treatment and for 4 weeks after the final dose and that RINVOQ should not be used during breastfeeding. The page also referred viewers to the SPC for complete product information.

AbbVie submitted that both webpages were sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine. The Prescribing Guide and the Prescribing Information were prominently signposted at the start of the page, alongside the images in question, providing all the required relevant information around contraception, pregnancy and lactation in a fair and balanced manner so as to not mislead.

Allegation that no information on the promotional pages included advice that 'Female paediatric patients and/or their parents/caregivers should be informed about the need to contact the treating physician once the patient experiences menarche while taking RINVOQ'.

RINVOQ was licensed for rheumatoid arthritis and psoriatic arthritis in adult patients only, whereas there was a licensed indication for atopic dermatitis for patients 12 years and older. Information regarding the use of RINVOQ in paediatric patients under the age of 18 years could be regarded as potentially irrelevant and misleading for the rheumatology indications. As outlined above, for the RA and PsA patient populations the relevant information had been included in the website to ensure that health professionals had the appropriate information at their disposal to make relevant informed treatment decisions. AbbVie believed that the webpage was suitably complete, was fair and balanced in a manner as not to mislead and reflected the relevant patients within the rheumatological indication for RINVOQ.

AbbVie submitted that in addition to the above, it should be noted that Section 4.2 in the SPC stated that treatment with upadacitinib should be initiated and supervised by physicians experienced in the diagnosis and treatment of conditions for which upadacitinib is indicated.

The details relating to RINVOQ on the AbbViePro website were addressed at health professionals that met the level of expertise that would enable them to prescribe RINVOQ in the first place, and it believed this had several important implications:

- There were numerous considerations that a health professional needed to take into account when starting a patient on RINVOQ including for example, blood counts and lab measures, vaccination information, information related to infections, concomitant medical conditions etc. - and this was all described in the Summary of Product Characteristics (SPC), the Prescribing Information and the Prescribing Guide for starting patients on RINVOQ, alongside the points related to pregnancy and lactation;

- On the balance of probabilities, and given the context of the website, experienced health professionals that could prescribe RINVOQ were not likely to interpret the imagery of females as implying that RINVOQ could be taken by pregnant or breastfeeding women. Indeed, the majority of medicines had not been tested in pregnant or breastfeeding females, and it was generally accepted knowledge among health professionals that the majority of medicines were contraindicated or not recommended in pregnancy;

- AbbVie recognised that health professionals were often busy and subject to time pressure. However, it didn't believe it was reasonable to make the assertion that an experienced health professional looking to prescribe an advanced therapy would simply look at the female imagery on the webpages in question and assume therefore that the medication was suitable for pregnant or lactating women. The complainant hadn't provided any evidence that, on the balance of probabilities, this was likely to be the case.

Summary

AbbVie submitted that all relevant information (including that around contraception, pregnancy and lactation) was provided upfront, and at the start of the web page within the Prescribing Guide and Prescribing Information as well as under the safety profile, in a manner to ensure the web pages did not prejudice patient safety.

Care had been taken to ensure that the artwork did not mislead regarding the use of RINVOQ in pregnant or breastfeeding women, did not detract from any warnings or contraindications and did not prejudice patient safety or mislead.

AbbVie took its responsibility for compliance with the ABPI Code very seriously as it continuously endeavoured to maintain high standards in all its activities. It remained available to answer any further questions PMCPA might have, but trusted that its response was sufficient for the Panel to confirm AbbVie was not in breach of any of the Clauses of the Code that AbbVie had been asked to consider.

PANEL RULING

The Panel noted that the complaint related to the suitability of imagery used on two Rinvoq webpages related to rheumatoid arthritis and psoriatic arthritis given that there were additional factors to be considered when the medicine was used in women of childbearing age and further that the imagery was not reflective of a typical moderate to severe rheumatoid arthritis or moderate to severe psoriatic arthritis patient as these patients would not be surfing or performing strenuous activities.

The Panel noted that the two webpages at issue for rheumatoid arthritis and psoriatic arthritis had a similar layout, comprising a banner at the top of the webpage which featured the Rinvoq logo on the left-hand side, and at the top of the banner, three navigation tabs linking to the Rinvoq prescribing guide, the Rinvoq prescribing information and the prescribing information for adalimumab. Beneath the tabs was the Rinvoq indication for moderate to severe rheumatoid arthritis or active psoriatic arthritis, as applicable.

On the webpage relating to rheumatoid arthritis, within the banner and below the indication were three tabs linked to the NICE recommendations for severe rheumatoid arthritis, moderate rheumatic arthritis and the SMC recommendations. An image of a young female swinging on a swing appeared on the right-hand side of the banner.

On the webpage relating to psoriatic arthritis, within the banner and below the indication was the statement that 'NICE recommends Rinvoq as a treatment option for adult patients with active Psoriatic Arthritis after inadequate response to DMARDs, subject to eligibility criteria'. An image of a young female on a surfboard appeared on the right-hand side of the banner.

The product information part of each webpage differed and contained further navigation tabs including product claims. It appeared to the Panel that each could be clicked on to obtain further information on each topic, however, the Panel did not have before it the linked webpages. The Panel noted that the product information section on the rheumatoid arthritis webpage included the following claims for Rinvoq: 'Significantly greater remission vs adalimumab + MTX' and 'Consistent efficacy'.

The product information section on the psoriatic arthritis webpage, included the claims 'rapid and sustained joint efficacy' and 'comprehensive efficacy across key PsA manifestations'.

The Panel noted that pregnancy was listed as a contraindication in Section 4.3 of the Rinvoq SPC and Section 4.6, Fertility, pregnancy and lactation stated, amongst other things that:

- women of childbearing potential should be advised to use effective contraception during treatment and for 4 weeks following the final dose of Rinvoq. Female paediatric patients and/or their parents/caregivers should be informed about the need to contact the treating physician once the patient experiences menarche while taking upadacitinib.
- there are no or limited data on the use of upadacitinib in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). Upadacitinib was teratogenic in rats and rabbits with effects in bones in rat foetuses and in the heart in rabbit foetuses when exposed *in utero*. RINVOQ is contra-indicated during pregnancy. If a patient becomes pregnant while taking upadacitinib the parents should be informed of the potential risk to the foetus, and
- it is unknown whether upadacitinib/metabolites are excreted in human milk. Available pharmacodynamic/toxicological data in animals have shown excretion of upadacitinib

> in milk (see section 5.3). A risk to newborns/infants cannot be excluded. Upadacitinib should not be used during breast-feeding. A decision must be made whether to discontinue breast-feeding or to discontinue upadacitinib therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

The Panel considered that whether a contraindication, special warning or precaution needed to be highlighted within a particular section of promotional material, in addition to its requirement to be included within the prescribing information that was required on all promotional material, depended on a consideration of all of the circumstances including the nature of the contraindication/warning/precaution and the content, layout, audience and intended use of the material.

The Panel noted that the SPC stated that Rinvoq should be initiated and supervised by physicians experienced in the diagnosis and treatment of the licensed indications. The Panel noted, however, that the AbbViePro website appeared to be aimed at all health professionals and that, in addition, Rinvoq was a black triangle product and it was likely that some prescribers might not be wholly familiar with all aspects of the Rinvoq SPC.

The Panel noted that it was well-established that images could constitute a claim and that companies had to carefully consider whether all images used in promotional materials were appropriate and ensure that they were not inconsistent with the summary of product characteristics or likely to create a misleading impression. The Panel noted that the supplementary information to Clause 6.3 stated that care must be taken to ensure that artwork does not mislead as to the nature of the medicine or any claim or comparison and that it does not detract from any warnings or contraindications. Clause 6.1 of the Code required, among other things, that information must not be misleading directly or by implication and must be sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine and Clause 6.2 required that any information be capable of substantiation.

The Panel noted AbbVie's submission that the peak onset of psoriatic arthritis was between 25-50 years old and affected males and females roughly equally whereas the peak onset for those diagnosed with rheumatoid arthritis was 40-60 years with around two thirds of patients suffering with rheumatoid arthritis being female. The Panel was concerned to note, therefore, that a significant proportion of the target population would be women of childbearing age for whom there were a number of important safety matters to be considered before prescribing.

The Panel noted AbbVie's submission that the webpages included links to the Rinvoq prescribing guide that contained all the relevant information and that the prescribing information referred health professionals to the SPC for full information. The Panel noted that there did not appear to be a direct link to the SPC from the webpages at issue. While the Panel noted AbbVie's reference to the availability of qualifying information elsewhere on the website the Panel noted that the supplementary information to Clause 6.1 stated that it should be borne in mind that claims in material which, in the Panel's view, included artwork must be capable of standing alone as regards accuracy etc. In general, claims should not be qualified by the use of footnotes and the like.

The Panel considered the immediate and overall impression of the two product information webpages to a busy health professional and considered that use of an image of a woman of childbearing potential on each webpage without including a reference to the fact it was

contraindicated in pregnancy or the warning that women of childbearing potential should be advised to use effective contraception during treatment and for 4 weeks following the final dose of Rinvoq was misleading. In the Panel's view, the association with use in females of childbearing potential was compounded on the psoriatic arthritis webpage by the further prominent use of the same image as the first screen of a video further down the page. In the Panel's view, the webpages implied that Rinvoq could be used in this patient population with no additional relevant considerations which was not so and detracted from important safety considerations. The inclusion of the information in linked documents was insufficient to negate the misleading impression on the webpages in question which could not be substantiated. The Panel therefore **ruled a breach of Clauses 6.1, 6.2 and 6.3** in relation to each webpage in this regard.

The Panel noted the complainant's comment that female paediatric patients and/or their parents/caregivers should be informed about the need to contact the treating physician once the patient experiences menarche while taking Rinvoq. The Panel noted AbbVie's submission that Rinvoq was licensed for rheumatoid arthritis and psoriatic arthritis in adult patients only, whereas there was a licensed indication for atopic dermatitis for patients 12 years and older. In the Panel's view, information regarding the use of Rinvoq in paediatric patients under the age of 18 years could be regarded as potentially irrelevant and misleading for the rheumatology indications. The Panel noted that the complaint was limited to the product information webpages for Rinvoq in rheumatoid arthritis and psoriatic arthritis only and therefore it did not consider that failure to include the warning that female paediatric patients and/or their parents/caregivers should be informed about the need to contact the treating physician once the patient experiences menarche while taking Rinvoq on these webpages was, in the particular circumstances of this case, misleading or incapable of substantiation and therefore **no breach of Clauses 6.1, 6.2 and 6.3** was ruled in relation to each webpage.

In relation to the complainant's allegation that the images did not reflect typical patients the Panel noted AbbVie's submission that patients with psoriatic arthritis were typically of a younger age than patients with rheumatoid arthritis and therefore likely to be more physically active at the time when they were typically diagnosed with the disease. Following diagnosis and while undergoing treatment, patients with psoriatic arthritis were actively encouraged to partake in some level of physical activity, as close as possible to the patient's old normal exercise regimen to support holistic disease management. The Panel considered that surfing required a degree of physical strength and in particular joint stability. The Panel, however, queried whether surfing was likely to be the normal exercise regimen of the majority of such patients and in particular queried whether a patient with severe psoriatic arthritis would be able to surf in the confident manner depicted. The Panel considered that the use of the image in question of a female surfing might misleadingly imply that patients taking Rinvoq would be able to perform such strenuous exercise which, in the Panel's view, was unlikely. In the Panel's view, this misleading visual impression was compounded by the claim of 'rapid and sustained joint efficacy' which appeared within the visual field of the image in question. Accordingly, the Panel considered that, on the balance of probabilities, the image created a misleading impression in that it did not reflect the typical patient with moderate to severe psoriatic arthritis and that could not be substantiated. The Panel therefore **ruled a breach of Clauses 6.1, 6.2 and 6.3**.

In relation to the image on the rheumatoid arthritis webpage, the Panel noted AbbVie's submission that the image on that webpage showed a female sitting on a swing, an activity AbbVie believed required minimal to no further exertion than an individual would experience in their day to day lives and thus one which could be undertaken by a patient with rheumatoid

arthritis. The Panel noted that the image in question showed that the woman was actively swinging, rather than passively sitting on the swing. Nonetheless, the Panel noted that the woman was in a sitting position. The Panel noted that while some fitness was required to generate the swinging movement the activity did not appear to require particular stability or strength in the joints. On balance, the Panel did not consider that the complainant had established that the use of the image on the rheumatoid arthritis webpage was not representative of a typical patient with moderate to severe rheumatoid arthritis as alleged. The Panel therefore **ruled no breach of Clauses 6.1, 6.2 and 6.3**.

In the Panel's view, it was of the utmost importance that relevant information about safety considerations in particular populations was clearly communicated. The Panel noted that the relevant information was available in the linked prescribing guide, and that the prescribing information advised readers that Rinvoq was contraindicated in pregnancy and to refer to the SPC for full information. However, in the Panel's view, the use of the images of young females in relation to a product with a known risk of foetal harm combined with the failure to include, on the face of the particular webpages, information to alert readers to the need to consider important relevant safety information before prescribing for women of childbearing age amounted to a failure to maintain high standards. The Panel ruled a **breach of Clause 5.1**.

The Panel noted that Clause 2 was a sign of particular censure and was reserved for such use. The supplementary information to Clause 2 included prejudicing patient safety as an example of an activity that was likely to be in breach of this clause. In the Panel's view, the use of imagery of a young female, in association with a product which had the potential to harm a foetus, without highlighting that there were restrictions on use in this population had the potential to impact patient safety and was such that AbbVie had reduced confidence in, and brought discredit upon, the industry. The Panel ruled a **breach of Clause 2**.

Complaint received **22 November 2022**

Case completed **8 August 2023**