RINVOQ® ▼ (upadacitinib)

Healthcare Professional Educational Guide

This document has been reviewed and approved by the Saudi Food and Drug Authority (SFDA).

abbvie

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Information in this guide

This educational guide contains safety information that you need to consider when prescribing upadacitinib to patients, namely:

1. Serious and opportunistic infections including tuberculosis (TB)
   - Testing and screening before prescribing
   - Herpes zoster – varicella zoster viral reactivation
2. Contraception, pregnancy and breast-feeding
3. Major adverse cardiovascular events (MACE)
4. Venous thromboembolic events – deep venous thrombosis (DVT) or pulmonary embolus (PE)
5. Malignancy
6. Gastrointestinal (GI) perforation

In addition, the guide contains information on:

- Indications for use and posology for upadacitinib
- Use in patients aged ≥ 65 years
- Patient Card
- Indications which include doses higher than 15 mg once daily
  - Upadacitinib in atopic dermatitis (AD)
  - Upadacitinib in Inflammatory Bowel Disease (IBD) – ulcerative colitis (UC), Crohn's Disease (CD)

If you prescribe upadacitinib, **please read this guide in full** along with your SPC.

About upadacitinib

Upadacitinib is an oral selective and reversible Janus kinase (JAK) inhibitor. In human cellular assays, upadacitinib preferentially inhibits signaling by JAK1 or JAK1/3 with functional selectivity over cytokine receptors that signal via pairs of JAK2.

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Indications for upadacitinib

Review the indication section of your SPC, remember:

Rheumatoid arthritis

RINVOQ is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs (DMARDs). RINVOQ may be used as monotherapy or in combination with methotrexate.

Psoriatic arthritis

RINVOQ is indicated for the treatment of active psoriatic arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more DMARDs. RINVOQ may be used as monotherapy or in combination with methotrexate.

Axial Spondyloarthritis

• Ankylosing spondylitis

RINVOQ is indicated for the treatment of active ankylosing spondylitis in adult patients who have responded inadequately to conventional therapy.

• Non-radiographic axial spondyloarthritis (nr-axSpA)

RINVOQ is indicated for the treatment of active non-radiographic axial spondyloarthritis in adult patients with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI), who have responded inadequately to nonsteroidal anti-inflammatory drugs (NSAIDs).

Atopic dermatitis

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.

Ulcerative colitis

RINVOQ is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to either conventional therapy or a biologic agent.

Crohn's Disease

RINVOQ is indicated for the treatment of adult patients with moderately to severely active Crohn’s disease who have had an inadequate response, lost response or were intolerant to either conventional therapy or a biologic agent.

Posology

Review the posology section of your SPC on how to use the 15, 30 and 45 mg doses in AD, UC and CD.

- As a reminder, for the AD indication and maintenance dosing in UC and CD, the 15 mg dose is recommended for patients at higher risk of venous thromboembolism (VTE), major adverse cardiovascular events (MACE) and malignancy as described in the Posology and Warning and Precautions section of your SPC.

Use of upadacitinib in patients ≥ 65 years

Given the increased risk of certain clinical outcomes in patients ≥ 65 years of age, as observed with another JAK inhibitor, upadacitinib should only be used if no suitable treatment alternatives are available.

- In patients ≥ 65 years of age, there is an increased risk of adverse reactions with upadacitinib 30 mg once daily.
- Consequently, for indications in which the 30 mg dose may be used for long-term maintenance, the recommended dose for long-term use in patients ≥ 65 years of age is 15 mg.

Patient Card

• Explain the importance of the Patient Card when discussing upadacitinib risks with your patients or patient caregivers.

• It contains information that patients and caregivers need to know before, during, and after treatment with upadacitinib.

- The Patient Card tells patients and caregivers of signs and symptoms they should be aware of when they are using upadacitinib.
- Tell patients and caregivers to read the Patient Card along with the Patient Information Leaflet.
- Tell patients and caregivers that other physicians involved in their care should read the Patient Card.
- Use this HCP guide when discussing the risks of upadacitinib with your patients.

1. Serious and opportunistic infections including TB

• Upadacitinib increases the risk of serious infections, including opportunistic infections and tuberculosis (TB).
- Do not prescribe upadacitinib in patients with active TB or active serious infections, including localised infections.
- There is an increased risk of herpes zoster in patients receiving upadacitinib.
- There is a higher incidence of infections in the elderly and in diabetic populations in general, caution should be used when treating the elderly and patients with diabetes.

Testing and screening before prescribing

- Before and during upadacitinib treatment, check absolute lymphocyte and absolute neutrophil counts (refer to the SPC for guidance on dose initiation and dose interruption based on absolute lymphocyte and absolute neutrophil counts and how frequently to monitor).
- Screen patients to rule out active TB. Do not prescribe upadacitinib to patients with active TB. If latent TB is diagnosed, consider anti-TB therapy before starting upadacitinib. Refer to the SPC for important drug-drug interactions to consider if TB therapy is needed.
- Screen patients for viral hepatitis and monitor for reactivation in accordance with clinical guidelines.
- It is important to tell patients and caregivers to get immediate medical attention if they have signs suggesting infection. This is to ensure rapid evaluation and appropriate treatment.

If a new infection develops

- If a patient develops any new infection during treatment, carry out diagnostic testing appropriate for an immunocompromised patient immediately.
- If the infection is a serious or an opportunistic infection – temporarily stop upadacitinib.
- Use appropriate antimicrobial therapy, and closely monitor the patient.
- If the patient is not responding to antimicrobial therapy – temporarily stop upadacitinib.
- Do not re-start upadacitinib until the infection is controlled.

Vaccines

- Before starting upadacitinib, it is recommended that you bring all patients up to date with all immunisations (including prophylactic zoster vaccinations) – in agreement with current immunisation guidelines.
- Do not use live, attenuated vaccines during, or immediately prior to starting upadacitinib treatment.
- Examples of live, attenuated vaccines include but are not limited to vaccines for measles/mumps/rubella, live attenuated influenza vaccine given as a nasal spray, oral polio vaccine, yellow fever vaccine, Zostavax™ used to prevent herpes zoster, BCG vaccine and varicella vaccine.

2. Contraception, pregnancy, and breast-feeding

Upadacitinib was found to cause birth defects in animals – cardiovascular and bone effects. There are limited data in humans. However, based on animal data, there is a potential risk to a human foetus.

Pregnancy and contraception

- Upadacitinib is contraindicated during pregnancy.
- Female patients who are able to have children should use effective contraception both during treatment, and for 4 weeks after stopping upadacitinib treatment.
- Tell your patient to inform you straight away if they think they could be pregnant, are planning to become pregnant, or if pregnancy is confirmed.
- Do not prescribe upadacitinib for women who are breast-feeding or intend to breast feed. This is because it is not known if upadacitinib passes into human breast milk.

3. Major adverse cardiovascular events (MACE)

Treatment with upadacitinib was associated with dose-dependent increases in lipid parameters, including total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol. Elevations in LDL cholesterol decreased to pre-treatment levels in response to statin therapy, although evidence is limited.

MACE – considerations with upadacitinib use

- Upadacitinib should only be used if no suitable treatment alternatives are available in the following patients who are considered at risk for MACE:
  - ☐ age ≥ 65 years
  - ☐ current smokers or past long-time smokers
  - ☐ history of atherosclerotic cardiovascular disease or other cardiovascular risk factors

- Assess lipid levels 12 weeks after starting upadacitinib. Monitor and manage lipid levels during treatment, according to clinical guidelines for hyperlipidaemia.
- Tell your patients and their caregivers that you will be monitoring their lipid levels.

4. Venous thromboembolic events – DVT or PE

DVT and PE – considerations with upadacitinib use

- In patients with risk factors for MACE or malignancy, upadacitinib should only be used if no suitable treatment alternatives are available.
- In patients with known risk factors for VTE other than MACE or malignancy risk factors, upadacitinib should be used with caution. Risk factors for VTE include:
  - ☐ previous VTE
  - ☐ patients undergoing major surgery
  - ☐ immobilization
  - ☐ use of combined hormonal contraceptives or hormone replacement therapy
  - ☐ inherited coagulation disorder

- Patients should be re-evaluated periodically during upadacitinib treatment to assess for changes in VTE risk.
- Promptly evaluate patients with signs and symptoms of VTE and discontinue upadacitinib in patients with suspected VTE, regardless of dose.

5. Malignancy

Malignancy – considerations with upadacitinib use

- Upadacitinib should only be used if no suitable treatment alternatives are available in the following patients who are considered at risk for malignancy:
  - ☐ age ≥ 65 years
  - ☐ patients who are current smokers or past long-time smokers
  - ☐ other malignancy risk factors (i.e. current malignancy, or history of malignancy prior to initiating therapy

- Periodic skin examination is recommended for patients, particularly those with risk factors for skin cancer.

6. GI perforation

GI perforation- considerations with upadacitinib

- Upadacitinib should be used with caution in patients who may be at risk for gastrointestinal perforation (e.g., patients with diverticular disease, a history of diverticulitis, or who are taking nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or opioids).
- Patients with active Crohn's disease are at increased risk for developing intestinal perforation.
- Patients presenting with new onset abdominal signs and symptoms should be evaluated promptly for early identification of diverticulitis or gastrointestinal perforation.

Upadacitinib in atopic dermatitis (including adolescents)

If considering the 30 mg upadacitinib dose in an adult less than 65 years of age with atopic dermatitis remember:

- There is an increased rate of serious infections and herpes zoster for the 30 mg compared to the 15 mg dose.
- A higher rate of malignancies, was observed with upadacitinib 30 mg compared to 15 mg.
- There is an increase in plasma lipids for the 30 mg compared to the 15 mg dose.
- See SPC for dosing.
- A dose of 15 mg is recommended for patients at higher risk of VTE, MACE and malignancy.
- Use the lowest effective dose to maintain response.

Remember:

- Upadacitinib 30 mg once daily dose is not recommended with strong CYP3A4 inhibitors such as: clarithromycin, itraconazole, ketoconazole, grapefruit products, since upadacitinib is metabolized by CYP3A4. Consider alternatives to strong CYP3A4 inhibitor medicines in the long-term.
- Upadacitinib 30 mg once daily is not recommended for patients with severe renal impairment.

Upadacitinib use in adolescents 12 years and older with atopic dermatitis

- See SPC for the recommended dose in adolescents.
- In considering whether to administer vaccines to adolescents, some vaccines recommended by local guidelines are live, attenuated vaccines (e.g. measles/mumps/rubella, varicella and BCG). These vaccines should not be given during or immediately prior to starting upadacitinib.
- Remind adolescents of the potential pregnancy risks and the appropriate use of effective contraception.
- If your adolescent patient has not experienced menarche, let them or their caregivers know to contact you once they experience menarche while taking upadacitinib.

Upadacitinib in UC or CD

Upadacitinib induction and maintenance dosing should be reviewed in the SPC.

When considering whether to use the 15 or 30 mg dose for maintenance, remember:

- There is an increased rate of serious infections and herpes zoster for the 30 mg compared to the 15 mg dose.
- A higher rate of malignancies, was observed with upadacitinib 30 mg compared to 15 mg.
- See SPC for dosing.
- A dose of 15 mg is recommended for patients at higher risk of VTE, MACE and malignancy.
- For maintenance dosing, use the lowest effective dose to maintain response.

Remember:

- For patients receiving strong inhibitors of CYP3A4 (e.g. clarithromycin, itraconazole, ketoconazole, grapefruit products), upadacitinib 30 mg once daily is the recommended induction dose (for up to 16 weeks) and upadacitinib 15 mg once daily is the recommended maintenance dose. Consider alternatives to strong CYP3A4 inhibitor medicines in the long-term.
- In patients with severe renal impairment: Upadacitinib 30 mg once daily is the recommended induction dose and upadacitinib 15 mg once daily is the recommended. maintenance dose.

Further Information

- As a healthcare professional, it is important that you report any suspected adverse reactions. See SPC for how to report adverse reactions.
- For more details on prescribing upadacitinib, please refer to the SPC.

- Please contact AbbVie medical information at medinfo_saudi@abbvie.com if you have any questions.

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For Extra copies of the Patient Card please contact AbbVie Biopharmaceuticals GmbH 00966 55 828 2010, email: PV.MEA@abbvie.com

To report any side effects for Rinvoq please contact:

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Hotline: 00966 55 828 2010, Email: PV.MEA@abbvie.com

National Pharamacovigilance Center Saudi Food and Drug Authority.
SFDA Unified Call Center: 19999
E-mail: npc.drug@sfda.gov.sa I Website: https://ade.sfda.gov.sa/