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**Certification Statement**

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# RINVOQ® ▼ (upadacitinib) – Healthcare Professional Educational Brochure

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

## Information in this brochure

This educational brochure 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 - potential risk
3. Major adverse cardiovascular events - potential risk
4. Venous thromboembolic events – deep venous thrombosis (DVT) or pulmonary embolus (PE) - potential risk

In addition, the brochure contains information on:

- Patient Alert Card (PAC)
- Upadacitinib in atopic dermatitis (including adolescents)
- Upadacitinib in Inflammatory Bowel Disease (IBD) indications

If you prescribe upadacitinib, **please read this brochure in full** along with your Summary of product characteristics (SPC) approved by SFDA

## 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.

## Patient Alert Card

Explain the importance of the Patient Alert Card (PAC) 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.

- Tell patients and caregivers to read the PAC along with the Patient Information Leaflet.
- The PAC tells patients and caregivers of signs and symptoms they should be aware of when they are using upadacitinib.
- Tell patients and caregivers that other physicians involved in their care should read the PAC.

# 1. Serious and opportunistic infections including TB

Upadacitinib increases the risk of serious infections, including opportunistic infections and tuberculosis (TB) (see also section 'Upadacitinib in atopic dermatitis').

- 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.

## Testing and screening before prescribing

- Before and during upadacitinib treatment, check absolute lymphocyte and absolute neutrophil counts (refer to the Summary of product characteristics (SPC) approved by SFDA 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 Summary of product characteristics (SPC) approved by SFDA 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.
- There is a higher incidence of infections in patients ≥ 65 years of age, caution should be used when treating this population.

## 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)

Management of traditional cardiovascular risk factors (for example hypertension, smoking, diabetes, obesity) should be part of clinical care for patients[1-4]. This is even more important in diseases where cardiovascular risk may be increased or when the prevalence of cardiovascular risk factors may be increased[5,6].

In clinical trials of upadacitinib, there were increases in total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol. Elevations were observed at 2 to 4 weeks of treatment, and remained stable with longer-term treatment. There was no change in the LDL/HDL ratio. The effect of these lipid level elevations on cardiovascular morbidity and mortality has not been determined. Long-term studies are being done to further evaluate this risk (see also section ‘Upadacitinib in atopic dermatitis’).

### Blood lipid levels

It is important to:

- 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.
- Consider all traditional cardiovascular risk factors when managing your patient.

# 4. Venous thromboembolic events – DVT or PE

Events of DVT and PE have been reported in patients receiving JAK inhibitors, including upadacitinib. Use upadacitinib with caution in patients at high risk of DVT or PE. Risk factors that should be considered in determining the patient's risk for DVT or PE include: older age, obesity, a medical history of DVT or PE, whether they are undergoing major surgery, and prolonged immobilisation.[7]

## DVT and PE

- If clinical features of DVT or PE occur, discontinue upadacitinib treatment, promptly evaluate the patient, and give an appropriate treatment.

# Upadacitinib in atopic dermatitis (including adolescents)

## If considering the 30 mg upadacitinib dose in an adult <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.
- There is an increase in plasma lipids for the 30 mg compared to the 15 mg dose. See the Summary of product characteristics (SPC) approved by SFDA for more information on laboratory values observed with the 30 mg and 15 mg doses.
- Eczema herpeticum occurred in both placebo and upadacitinib-treated patients with similar rates in the upadacitinib 15 mg and 30 mg dose groups.

## Remember:

- The 15 mg dose is the recommended dose in patients ≥ 65 years of age.
- Upadacitinib 30 mg once daily dose is not recommended with strong CYP3A4 inhibitors: clarithromycin, itraconazole, ketoconazole, large amounts (>1 litre/day) 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

- 'The recommended dose for adolescents weighing at least 30kg is 15 mg once daily.
- In considering whether to administer vaccines to adolescents, some vaccines recommended by local guidelines are live, attenuated vaccines (ie. 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 IBD

**Upadacitinib induction and maintenance dosing should be reviewed in the Summary of product characteristics (SPC) approved by SFDA**

**Remember:**

- The 15 mg dose is the recommended maintenance dose in patients ≥ 65 years of age.
- For patients receiving strong inhibitors of CYP3A4 (e.g., clarithromycin, itraconazole, ketoconazole, large amounts [>1 litre/day] 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.

## References:


1. Zegkos, T., Kitas, G. and Dimitroulas, T., 2016. Cardiovascular risk in rheumatoid arthritis: assessment, management and next steps. Therapeutic advances in musculoskeletal disease, 8(3), pp.86-101.
2. Agca, R., Heslinga, S.C., Rollefstad, S., Heslinga, M., McInnes, I.B., Peters, M.J.L., Kvien, T.K., Dougados, M., Radner, H., Atzeni, F. and Primdahl, J., 2017. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Annals of the rheumatic diseases, 76(1), pp.17-28.
3. England, B.R., Thiele, G.M., Anderson, D.R. and Mikuls, T.R., 2018. Increased cardiovascular risk in rheumatoid arthritis: mechanisms and implications. Bmj, 361.
4. Castañeda, S., Nurmohamed, M.T. and González-Gay, M.A., 2016. Cardiovascular disease in inflammatory rheumatic diseases. Best Practice & Research Clinical Rheumatology, 30(5), pp.851-869.
5. Zhang, A. and Silverberg, J.I., 2015. Association of atopic dermatitis with being overweight and obese: a systematic review and metaanalysis. Journal of the American Academy of Dermatology, 72(4), pp.606-616.
6. Silverberg, J.I., 2016. Atopic disease and cardiovascular risk factors in US children. The Journal of allergy and clinical immunology, 137(3), p.938.
7. Heit, J.A., 2015. Epidemiology of venous thromboembolism. Nature Reviews Cardiology, 12(8), pp.464-474.


# Further information

- As a healthcare professional, it is important that you report any suspected adverse reactions. See Summary of product characteristics (SPC) approved by SFDA for how to report adverse reactions.
- For more details on prescribing upadacitinib, please refer to the See Summary of product characteristics (SPC) approved by SFDA
- Please contact AbbVie Medical information at medinfo_saudi@abbvie.com

- **Please Contact AbbVie pharmacovigilance at MEAPV@abbvie.com** if you have any questions or require additional copies of the Patient Alert Card.

**www.sfda.gov.sa/npc**

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.

This brochure (Version 4.0) was last updated May 2022

- **For Extra copies please contact AbbVie Biopharmaceuticals GmbH 00966 55 828 2010**

**To report any side effects for Rinvoq please contact AbbVie Biopharmaceuticals GmbH Hot Line: 00966 55 828 2010 - Mailbox: MEAPV@abbvie.com**

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