RINVOQ® (upadacitinib)

Healthcare Professional Educational Brochure

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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 cardiovascular events - potential risk
4. Venous thromboembolic events - potential risk

In addition, the brochure contains information on:

- Patient Information Card
- Upadacitinib in atopic dermatitis (including adolescents)

If you prescribe upadacitinib, **please read this brochure in full** along with your **Prescribing information (PI).**

About upadacitinib

Upadacitinib is an oral selective and reversible 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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Patient Information Card

Explain the importance of the Patient Information Card (PIC) 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 PIC along with the Patient Information Leaflet.
- The PIC 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 PIC.

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 PI 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 PI 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 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.

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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 PI 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 juice, 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 PI for the recommended dose in adolescents.
- 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.

References:

1. Zegkos T, et al. Ther Adv Musculoskel Dis 2016, Vol. 8(3); 86 –101.
2. Agca R, et al. Ann Rheum Dis 2017, Vol. 76; 17–28.
3. England BR, et al. BMJ 2018, Vol. 361; k1036.
4. Santos Casta~neda et al. Best Practice & Research Clinical Rheumatology 30 (2016); 851-869
5. Zhang AS, J. Association of Atopic Dermatitis With Being Overweight and Obese: A Systematic Review and Metaanalysis. J Am Acad Dermatol. 2015;72(4):606-16e4.
6. Silverberg JI. Atopic disease and cardiovascular risk factors in US children. J Allergy Clin Immunol. 2016;137(3):938-40.e1.
7. Heit JA. Nat Rev Cardiol 2015, Vol. 12; 464– 474.

Further Information

- As a healthcare professional, it is important that you report any suspected adverse reactions. You may report suspected adverse reactions to **AbbVie** via the mailbox *pvisrael@abbvie.com.* In addition, you may report suspected adverse reactions to the **Ministry of Health** via the side effects portal in the link *sideeffects.health.gov.il*.
- For more details on prescribing upadacitinib, please refer to the PI.
- Please contact **AbbVie medical information** at *Abbviemedinfo.com*, if you have any questions or require additional copies of the Patient Information Card.

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.
This HCP Educational Brochure was approved according to the guidelines of the Ministry of Health in **Aug 2021, V.3.0.**

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