Reucent™ XR

Upadacitinib Tablet

Presentation
Reucent™ XR 15 Tablet: Each extended release tablet contains Upadacitinib Hemihydrate INN equivalent to Upadacitinib 15 mg.

Description
Upadacitinib is a Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Within the signaling pathway, JAKs phosphorylate and activate signal transducers and activators of transcription (STATs) which modulate intracellular activity including gene expression. Upadacitinib modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs.

Upadacitinib had greater inhibitory potency at JAK1 and JAK2 relative to JAK3 and TYK2. In human leukocyte cellular assays, Upadacitinib inhibited cytokine-induced STAT phosphorylation mediated by JAK1 and JAK1/JAK3 more potently than JAK2/JAK2 mediated STAT phosphorylation.

Indications and Uses
Limitations of Use: Upadacitinib is not recommended for use in combination with other JAK inhibitors, biologic DMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine.

Upadacitinib is a Janus kinase (JAK) inhibitor indicated for the treatment of:

• Adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more TNF blockers.
• Adults with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers.
• Adults and pediatric patients 12 years of age and older with refractory, moderate to severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies are inadvisable.
• Adults with moderately to severely active ulcerative colitis who have had an inadequate response or intolerance to one or more TNF blockers.
• Adults with active ankylosing spondylitis who have had an inadequate response or intolerance to one or more TNF blockers.
• Adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation who have had an inadequate response or intolerance to TNF blocker therapy.

Dosage and Administrations
Prior to treatment update immunizations and consider evaluating for active and latent tuberculosis, viral hepatitis, hepatic function, and pregnancy status. Avoid initiation or interrupt UPADACITINIB if absolute lymphocyte count is less than 500 cells/mm^3, absolute neutrophil count is less than 1000 cells/mm^3, or hemoglobin level is less than 8 g/dL.

Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis:
The recommended dosage is 15 mg once daily.

Atopic Dermatitis:
• Pediatric Patients 12 Years of Age and Older Weighing at Least 40 kg and Adults Less Than 65 Years of Age: Initiate treatment with 15 mg orally once daily. If an adequate response is not achieved, consider increasing the dosage to 30 mg orally once daily.
• Adults 65 Years of Age and Older & Severe Renal Impairment: Recommended dosage is 15 mg once daily.

Ulcerative Colitis:
Adults: The recommended induction dosage is 45 mg once daily for 8 weeks. The recommended maintenance dosage is 15 mg once daily. A maintenance dosage of 30 mg once daily may be considered for patients with refractory, severe, or extensive disease. Discontinue UPADACITINIB if adequate therapeutic response is not achieved with the 30 mg dosage. Use the lowest effective dosage needed to maintain response.

Side Effects
Rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, and nonradiographic axial spondyloarthritis: Adverse reactions (≥ 1%) were- upper respiratory tract infections, herpes zoster, herpes simplex, bronchitis, nausea, cough, pyrexia, acne, and headache.

Atopic Dermatitis: Adverse reactions (≥ 1%) are- upper respiratory tract infections, acne, herpes simplex, headache, blood creatine phosphokinase increased, cough, hypersensitivity, folliculitis, nausea, abdominal pain, pyrexia, increased weight, herpes zoster, influenza, fatigue, neutropenia, myalgia and influenza like illness.

Ulcerative colitis: Adverse reactions (≥ 5%) reported during induction or maintenance are- upper respiratory tract infections, increased blood creatine phosphokinase, acne, neutropenia, elevated liver enzymes, and rash.

Precautions
• Serious Infections: Avoid use in patients with active, serious infection, including localized infections.
• Hypersensitivity: Serious hypersensitivity reactions (e.g., anaphylaxis) have been reported. Discontinue if a serious hypersensitivity reaction occurs.
• Gastrointestinal (GI) Perforations: Monitor patients at risk for GI perforations and promptly evaluate patients with symptoms.
• Laboratory Abnormalities: Monitoring recommended due to potential changes in lymphocytes, neutrophils, hemoglobin, liver enzymes and lipids.
• Embryo-Fetal Toxicity: May cause fetal harm based on animal studies. Advise female patients of reproductive potential of the potential risk to a fetus and to use effective contraception.
• Vaccinations: Avoid use with live vaccines.

Contraindications
Known hypersensitivity to Upadacitinib or any of the excipients in UPADACITINIB.

Use in specific population
Pregnancy: UPADACITINIB has the potential to adversely affect a developing fetus. Advise patients of reproductive potential and pregnant patients of the potential risk to the fetus
Lactation: Advise not to breastfeed.

Pediatric Use:
• Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, and Non-radiographic Axial Spondyloarthritis- The safety and effectiveness of UPADACITINIB in pediatric patients with juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, and non-radiographic axial spondyloarthritis have not been established.
• Atopic Dermatitis- The safety and effectiveness of UPADACITINIB in pediatric patients 12 years of age and older weighing at least 40 kg with atopic dermatitis have been established

Geriatric Use
• Rheumatoid Arthritis and Psoriatic Arthritis- No differences in effectiveness were observed between these patients and younger patients; however, there was a higher rate of overall adverse events, including serious infections, in patients 65 years of age and older
• Atopic Dermatitis- No differences ineffectiveness were observed between these patients and younger patients; however, there was a higher rate of serious infections and malignancies in those patients 65 years of age or older in the 30 mg dosing group in the long-term trials.
• Ulcerative Colitis- Clinical studies of UPADACITINIB did not include sufficient numbers of patients 65 years of age and older with ulcerative colitis to determine whether they respond differently from younger adult patients.
• Ankylosing Spondylitis- Clinical studies of UPADACITINIB did not include sufficient numbers of patients 65 years of age and older with ankylosing spondylitis to determine whether they respond differently from younger adult patients.
• Non-radiographic Axial Spondyloarthritis- Clinical studies of UPADACITINIB did not include sufficient numbers of patients 65 years of age and older with non-radiographic axial spondyloarthritis to determine whether they respond differently from younger adult patients.

Renal Impairment
• For patients with rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, and nonradiographic axial spondyloarthritis, no dosage adjustment is needed in patients with mild (eGFR 60 to < 90 mL/min/1.73 m2), moderate (eGFR 30 to < 60 mL/min/1.73 m2), or severe renal impairment (eGFR 15 to < 30 mL/min/1.73 m2)
• For patients with atopic dermatitis, the maximum recommended dosage is 15 mg once daily for patients with severe renal impairment. No dosage adjustment is needed in patients with mild or moderate renal impairment.
• For patients with ulcerative colitis, the recommended dosage for severe renal impairment is 30 mg once daily for induction and 15 mg once daily for maintenance. No dosage adjustment is needed in patients with mild or moderate renal impairment.
• UPADACITINIB has not been studied in patients with end stage renal disease (eGFR <15 mL/min/1.73m2). Use in patients with atopic dermatitis or ulcerative colitis with end stage renal disease is not recommended

Hepatic Impairment
• The use of UPADACITINIB has not been studied in patients with severe hepatic impairment (Child Pugh C), and therefore not recommended for use in patients with rheumatoid arthritis, psoriatic arthritis, atopic dermatitis, ulcerative colitis, ankylosing spondylitis, and non-radiographic axial spondyloarthritis
• For patients with rheumatoid arthritis, psoriatic arthritis, atopic dermatitis, ankylosing spondylitis, and non-radiographic axial spondyloarthritis no dosage adjustment is needed in patients with mild (Child Pugh A) or moderate (Child Pugh B) hepatic impairment impairment is 30 mg once daily for induction and 15 mg once daily for maintenance.

Drug Interaction
Strong CYP3A4 Inhibitors: Upadacitinib exposure is increased when UPADACITINIB is co-administered with a strong CYP3A4 inhibitor (such as ketoconazole and clarithromycin), which may increase the risk of UPADACITINIB adverse reactions.
Strong CYP3A4 Inducers: Coadministration of UPADACITINIB with strong CYP3A4 inducers is not recommended.

Storage
Do not store above 30°C. Keep away from light and out of the reach of children.

Commercial Packaging
Reucent™ XR 15 Tablet: Each box contains 1 blister strip of 10 tablets.

Manufactured by
Incepta Pharmaceuticals Ltd
Savar, Dhaka, Bangladesh