Unijak ER

(Upadacitinib)

15mg & 30mg Tablets

یونی جیک اِی آر

(اپاڈاسٹینب)

۱۵ ملی گرام اور ۳۰ ملی گرام

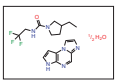
Composition:
UNIJAK 15mg ER Tablet:
Each extended release tablet contains:
Upadacitinib Hemihydrate Eq. to Upadacitinib 15mg

UNIJAK 30mg ER Tablet:
Each extended release tablet contains:
Upadacitinib Hemihydrate Eq. to Upadacitinib 30mg

Product Description
Physical Properties
Chemical Name:
(3S,4R)-3-Ethyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-N-(2,2,2-trifluoroethyl)-1-pyrrolidine-1-carboxamide hemihydrate

Molecular Weight
389.375

Structural Formula



Pharmacodynamics and Pharmacokinetics
Pharmacotherapeutic group: Immunosuppressants, Janus-associated kinase (JAK) inhibitor

Mechanism of action
Upadacitinib is a selective and reversible Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes that transmit cytokine or growth factor signals involved in a broad range of cellular processes including inflammatory responses, hematopoiesis, and immune surveillance. The JAK family of enzymes contains four members, JAK1, JAK2, JAK3 and TYK2 which work in pairs to phosphorylate and activate signal transducers and activators of transcription (STATs). This phosphorylation, in turn, modulates gene expression and cellular function. JAK1 is important in inflammatory cytokine signals while JAK2 is important for red blood cell maturation and JAK3 signals play a role in immune surveillance and lymphocyte function.
In human cellular assays, upadacitinib preferentially inhibits signalling by JAK1 or JAK1/3 with functional selectivity over cytokine receptors that signal via pairs of JAK2. Atopic dermatitis is driven by pro-inflammatory cytokines (including IL-4, IL-13, IL-22, TSLP, IL-31 and IFN-γ) that transduce signals via the JAK1 pathway. Inhibiting JAK1 with upadacitinib reduces the signaling of many mediators which drive the signs and symptoms of atopic dermatitis such as eczematous skin lesions and pruritus. Pro-inflammatory cytokines (primarily IL-6, IL-7, IL-15 and IFNγ) transduce signals via the JAK1 pathway and are involved in the pathology of inflammatory bowel diseases. JAK1 inhibition with upadacitinib modulates the signalling of the JAK-dependent cytokines underlying the inflammatory burden and signs and symptoms of inflammatory bowel diseases.

Pharmacokinetic properties
Absorption
Following oral administration of upadacitinib prolonged-release formulation, upadacitinib is absorbed with a median Tmax of 2 to 4 hours. Coadministration of upadacitinib with a high-fat meal had no clinically relevant effect on upadacitinib exposures (increased AUC by 29% and Cmax by 39% to 60%). In clinical trials, upadacitinib was administered without regard to meals (see section 4.2). In vitro, upadacitinib is a substrate for the efflux transporters P-gp and BCRP.
Distribution
Upadacitinib is 52% bound to plasma proteins. Upadacitinib partitions similarly between plasma and blood cellular components, as indicated by the blood to plasma ratio of 1.0.
Metabolism
Upadacitinib metabolism is mediated by CYP3A4 with a potential minor contribution from CYP2D6. The pharmacologic activity of upadacitinib is attributed to the parent molecule. In a human radiolabeled study, unchanged upadacitinib accounted for 79% of the total radioactivity in plasma while the main metabolite (product of monooxidation followed by glucuronidation) accounted for 13% of the total plasma radioactivity. No active metabolites have been identified for upadacitinib.
Elimination
Following single dose administration of [14C]-upadacitinib immediate-release solution, upadacitinib was eliminated predominantly as the unchanged parent substance in urine (24%) and faeces (38%). Approximately 34% of upadacitinib dose was excreted as metabolites. Upadacitinib mean terminal elimination half-life ranged from 9 to 14 hours.

Recommended Dose
Posology
Rheumatoid Arthritis, Psoriatic Arthritis, and Axial Spondyloarthritis

Recommended Dose: 15 mg once daily.
Discontinuation Consideration: Discontinue if no clinical response after 16 weeks, though partial responders may improve with continued treatment.

- Anaemia.
- Pain in your belly (abdomen).
- Fatigue (feeling unusually tired and weak).
- Headache.
- Hives (urticaria).
- Urinary tract infection.
- Rash.

Uncommon (may affect up to 1 in 100 people)
- Thrush in the mouth (white patches in the mouth)
- Increased levels of triglycerides (a type of fat) in the blood, as shown in tests
- Diverticulitis (painful inflammation of small pockets in the lining of your Intestine)

Overdose and Treatment
Signs and Symptoms
In clinical studies, upadacitinib was administered at doses equivalent to 60 mg once daily, with no new toxicities identified. In case of overdose, patients should be monitored for adverse reactions, and appropriate treatment should be provided if necessary.

Effects on Ability to Drive and Use Machines
Upadacitinib may have a minor influence on the ability to drive and use machines because dizziness and vertigo may occur during its treatment.

Dosage Forms and Packaging Available
Incompatibilities
Not applicable.

Shelf life
2 years

Special precautions for storage
- Store below 30ºC.
- Keep out of reach of children.
- Store away from direct sunlight, heat and moisture.
- To be sold on prescription of a registered medical practitioner only.

Nature and contents of container
Alu-Alu Blister.

Presentation
Unijak ER tablet 15mg is available in blister pack of 10's.
Unijak ER tablet 30mg is available in blister pack of 10's.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات:
- دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر روشنی سے بچا کر خشک جگہ پر رکھیں۔
- صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کریں۔
- بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:
Kaizen Pharmaceuticals (Pvt.) Ltd.
E-127-129, North Western Industrial Zone,
Bin Qasim, Karachi-75020, Pakistan.

Art no: 1003

Atopic Dermatitis

Adults:
15 mg: Recommended for patients at higher risk of venous thromboembolism (VTE), major adverse cardiovascular events (MACE), and malignancy.
30 mg: For patients with high disease burden or inadequate response to 15 mg, and not at higher risk of VTE, MACE, and malignancy.
Age 65 and older: Recommended dose is 15 mg once daily.
Adolescents (12-17 years, weighing at least 30 kg): 15 mg once daily.
Concomitant Topical Therapies: Can be used with or without topical corticosteroids or calcineurin inhibitors for sensitive areas.
Discontinuation Consideration: Discontinue after 12 weeks if no therapeutic benefit.

Ulcerative Colitis
Induction:
Recommended Dose: 45 mg once daily for 8 weeks.
For patients not responding, continue 45 mg for an additional 8 weeks.
Discontinuation: If no therapeutic benefit by week 16, discontinue treatment.
Maintenance:
15 mg: For patients at higher risk of VTE, MACE, and malignancy.
30 mg: For patients with high disease burden or inadequate response to 15 mg.
Age 65 and older: Recommended dose is 15 mg once daily.
Corticosteroid Reduction: May be reduced/discontinued as per standard care in responding patients.

Crohn's Disease
Induction:
Recommended Dose: 45 mg once daily for 12 weeks.
Maintenance:
15 mg: For patients at higher risk of VTE, MACE, and malignancy.
30 mg: For patients with high disease burden or inadequate response to 15 mg.
If no therapeutic benefit by 24 weeks, discontinue treatment.
Age 65 and older: Recommended dose is 15 mg once daily.
Corticosteroid Reduction: May be reduced/discontinued as per standard care in responding patients.

Precautions regarding use and dosage
Atopic Dermatitis: Doses higher than 15 mg once daily are not recommended for patients 65 years and older.
Ulcerative Colitis and Crohn's Disease: For maintenance, doses higher than 15 mg once daily are not recommended for patients 65 years and older. Safety and efficacy have not been established for patients 75 years and older.
Renal Impairment
Mild/Moderate Renal Impairment: No dose adjustment required.
Severe Renal Impairment: Use with caution, as limited data is available. Not recommended for patients with end-stage renal disease due to lack of studies.

Method of administration
Oral

Contraindications
Do not administer to the following patients
Hypersensitivity to the active substance or to any of the excipients listed
Active tuberculosis (TB) or active serious infections
Severe hepatic impairment
Pregnancy

Warnings and Precautions
Upadacitinib should only be used if no suitable treatment alternatives are available in patients:
- 65 years of age and older;
- patients with history of atherosclerotic cardiovascular disease or other cardiovascular risk factors (such as current or past long-time smokers);
- patients with malignancy risk factors (e.g. current malignancy or history of malignancy)

Use in Patients 65 Years of Age and Older
- **Increased Risks:** Higher risk of major adverse cardiovascular events (MACE), malignancies, serious infections, and all-cause mortality. Use only if no suitable alternatives are available.
- **Recommended Dose:** 15 mg once daily for long-term use; higher doses (30 mg) may increase risks.

Immunosuppressive Medicinal Products
- **Avoid Combination:** Do not combine with potent immunosuppressants (e.g., azathioprine, ciclosporin, tacrolimus, biologics, or other JAK inhibitors), as the risk of additive immunosuppression is unknown.

Serious Infections
- Increased Risk: Serious infections like pneumonia, sepsis, and tuberculosis (TB) may occur.
- Screening: Screen for TB before starting therapy.
- Precaution: Discontinue if a serious infection develops. Patients with chronic/recurrent infections or history of TB should be monitored closely.

Viral Reactivation
- Herpes Zoster: Risk of herpes virus reactivation; consider interrupting therapy if herpes zoster occurs.
- Hepatitis Screening: Test for hepatitis before and during therapy. Seek advice from a liver specialist if hepatitis B reactivation occurs.

Vaccination
- **Live Vaccines:** Avoid live vaccines during or just before treatment with upadacitinib. Ensure vaccinations are up to date before starting therapy.

Malignancy
- **Increased Risk:** Possible increased risk of lymphoma, lung cancer, and non-melanoma skin cancer (NMSC), particularly with higher doses (30 mg). Use with caution in patients with cancer risk factors.
- **Skin Exams:** Periodic skin checks are recommended, especially for those with skin cancer risks.
  Haematological Abnormalities
- **Blood Cell Counts:** Low neutrophil, lymphocyte, or hemoglobin levels require discontinuation or interruption of treatment.
  Gastrointestinal Perforations
- **Caution:** Use with caution in patients at risk for gastrointestinal perforations (e.g., with diverticulitis or on NSAIDs). Report any abdominal symptoms immediately.

Major Adverse Cardiovascular Events (MACE)
- **Risk:** Increased rate of MACE observed. Use with caution in elderly patients, smokers, and those with cardiovascular risk factors.
  Lipids
- **Elevated Cholesterol:** Upadacitinib may increase cholesterol levels. Monitor lipid parameters regularly and adjust treatment if needed.

Hepatic Transaminase Elevations
- **Liver Enzyme Monitoring:** Regularly check liver enzymes. If abnormalities occur, suspend therapy until liver injury is excluded.

Venous Thromboembolism (VTE)
- **Increased Risk:** Higher rates of deep vein thrombosis (DVT) and pulmonary embolism (PE) observed. Use with caution in patients with known VTE risk factors.

Hypersensitivity Reactions
- **Severe Reactions:** Discontinue if serious allergic reactions (e.g., anaphylaxis, angioedema) occur.
Hypoglycemia in Diabetic Patients
- **Monitor Blood Sugar:** Hypoglycemia may occur, requiring dose adjustments for diabetes medications.

Interactions with other medicaments
Some medicines may reduce how well Unijak ER Tablet works or may increase the risk of getting side effects such as:
- Medicines to treat fungal infections (such as itraconazole, posaconazole or voriconazole)
- Medicines to treat bacterial infections (such as clarithromycin)
- Medicines to treat Cushing's syndrome (such as ketoconazole)
- Medicines to treat tuberculosis (such as rifampicin)
- Medicines to treat seizures or fits (such as phenytoin)
- Medicines that affect your immune system (such as azathioprine,6-mercaptopurine, ciclosporin and tacrolimus)
- Medicines that may increase your risk of gastrointestinal perforation or diverticulitis such as non-steroidal anti-inflammatory medicines (usually used to treat painful and/or inflammatory conditions of muscle or joints), and/or opioids (used to treat severe pain), and/or corticosteroids (usually used to treat inflammatory conditions).

Pregnancy and lactation
Pregnancy
Do not administer to pregnant women or women who may be pregnant.
Breastfeeding
If you are breast-feeding or are planning to breast-feed, talk to your doctor before taking this medicine. You should not use it while breast-feeding as it is not known if this medicine passes into breast milk.

Undesirable effects
Serious side effects
Talk to your doctor or get medical help straight away if you get any signs of:
- Infection such as shingles or painful skin rash with blisters (herpes zoster) – common (may affect up to 1 in 10 people).
- Infection of the lung (pneumonia), which may cause shortness of breath, fever, and a cough with mucus – common (may affect up to 1 in 10 people).
- Allergic reaction (chest tightness, wheezing, swelling of the lips, tongue or throat, hives) – uncommon (may affect up to 1 in 100 people).

Other side effects
Very Common:
- Throat and nose infections.
- Acne.

Common (may affect up to 1 in 10 people)
- Cough, fever, cold sores (herpes simplex), feeling sick in the stomach (nausea).
- Increase in an enzyme called creatine kinase, shown by blood tests.
- Low white blood cell counts shown in blood tests.
- Increased levels of cholesterol (a type of fat in the blood) as shown in tests.
- Increased levels of liver enzymes, shown by blood tests (sign of liver problems).
- Weight gain.
- Inflammation (swelling) of the hair follicles.
- Flu (influenza).