Contributor Disclosures

For additional information see "Upadacitinib: Patient drug information" and "Upadacitinib: Pediatric drug information"

For abbreviations, symbols, and age group definitions show table

ALERT: US Boxed Warning

Serious infections:

Patients treated with upadacitinib are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. If a serious infection develops, interrupt upadacitinib until the infection is controlled. Reported infections include:

Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before upadacitinib use and during therapy. Treatment for latent infection should be considered prior to upadacitinib use.

Invasive fungal infections, including cryptococcosis and pneumocystosis.

Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.

The risks and benefits of treatment with upadacitinib should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with upadacitinib, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy

Mortality:

In a large, randomized, postmarketing safety study in rheumatoid arthritis (RA) patients ≥50 years of age with ≥1 cardiovascular risk factor comparing another Janus kinase (JAK) inhibitor to tumor necrosis factor (TNF) blockers, a higher rate of all-cause mortality, including sudden cardiovascular death, was observed with the JAK inhibitor.

Malignancies:

Lymphoma and other malignancies have been observed in patients treated with upadacitinib. In RA patients treated with another JAK inhibitor, a higher rate of malignancies (excluding nonmelanoma skin cancer) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk.

Major adverse cardiovascular events:

In RA patients ≥50 years of age with ≥1 cardiovascular risk factor treated with another JAK inhibitor, a higher rate of major adverse cardiovascular events (defined as cardiovascular death, myocardial infarction [MI], and stroke) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. Discontinue upadacitinib in patients that have experienced an MI or stroke.

Thrombosis:

Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis have occurred in patients treated with JAK inhibitors used to treat inflammatory conditions. Many of these adverse events were serious and some resulted in death. In RA patients ≥50 years of age with ≥1 cardiovascular risk factor treated with another JAK inhibitor, a higher rate of thrombosis was observed when compared with TNF blockers. Avoid upadacitinib in patients at risk. Patients with symptoms of thrombosis should discontinue upadacitinib and be promptly evaluated.

Brand Names: US

Rinvoq; Rinvoq LQ

Brand Names: Canada

Rinvoq

Pharmacologic Category

Antirheumatic, Disease Modifying; Antirheumatic, Miscellaneous; Janus Kinase Inhibitor

Dosing: Adult

Note: Do **not** use in combination with biologic disease-modifying antirheumatic drugs (DMARDs) or potent immunosuppressants (eg, azathioprine, cyclosporine); do **not** initiate in patients with an absolute lymphocyte count <500/mm^3, ANC <1,000/mm^3, or Hb <8 g/dL.

Ankylosing spondylitis

Ankylosing spondylitis: Oral: 15 mg once daily.

Atopic dermatitis, refractory, moderate to severe

Atopic dermatitis, refractory, moderate to severe: Note: Reserve for patients who had an inadequate response or intolerance to other systemic drug products, including biologics, or when use of those therapies is inadvisable.

Oral: 15 mg once daily; may increase to 30 mg once daily if inadequate response. Discontinue if an adequate response is not achieved with the 30 mg dose; use the lowest effective dose needed to maintain response.

Crohn disease

Crohn disease: Oral: Induction: 45 mg once daily for 12 weeks; maintenance: 15 mg once daily; may increase to 30 mg once daily in patients with refractory, severe, or extensive disease. Discontinue if an adequate response is not achieved with the 30 mg dose; use the lowest effective dose needed to maintain response.

Nonradiographic axial spondyloarthritis

Nonradiographic axial spondyloarthritis: Oral: 15 mg once daily.

Psoriatic arthritis

Psoriatic arthritis: Oral: 15 mg once daily.

Rheumatoid arthritis

Rheumatoid arthritis:

Note: For use as adjunctive therapy in patients who have not met treatment goals despite maximally tolerated methotrexate therapy; may also be used off-label as an alternative to methotrexate in DMARD–naive patients with moderate to high disease activity (Ref).

Oral: 15 mg once daily.

Ulcerative colitis

Ulcerative colitis: Oral: Induction: 45 mg once daily for 8 weeks; maintenance: 15 mg once daily; may increase to 30 mg once daily in patients with refractory, severe, or extensive disease. Discontinue if an adequate response is not achieved with the 30 mg dose; use the lowest effective dose needed to maintain response.

Dosage adjustment for concomitant therapy: Significant drug interactions exist, requiring dose/frequency adjustment or avoidance. Consult drug interactions database for more information.

Dosing: Kidney Impairment: Adult

Ankylosing spondylitis, nonradiographic axial spondyloarthritis, psoriatic arthritis, rheumatoid arthritis:

Altered kidney function:

eGFR ≥15 mL/minute/1.73 m^2: No dosage adjustment necessary.

eGFR <15 mL/minute/1.73 m^2: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Atopic dermatitis:

Altered kidney function:

eGFR ≥30 mL/minute/1.73 m^2: No dosage adjustment necessary.

eGFR 15 to <30 mL/minute/1.73 m^2: 15 mg once daily.

eGFR <15 mL/minute/1.73 m^2: Use is not recommended.

Crohn disease:

Altered kidney function:

eGFR ≥30 mL/minute/1.73 m^2: No dosage adjustment necessary.

eGFR 15 to <30 mL/minute/1.73 m^2: Induction: 30 mg once daily for 12 weeks; maintenance: 15 mg once daily.

eGFR <15 mL/minute/1.73 m^2: Use is not recommended.

Ulcerative colitis:

Altered kidney function:

eGFR ≥30 mL/minute/1.73 m^2: No dosage adjustment necessary.

eGFR 15 to <30 mL/minute/1.73 m^2: Induction: 30 mg once daily for 8 weeks; maintenance: 15 mg once daily.

eGFR <15 mL/minute/1.73 m^2: Use is not recommended.

Dosing: Liver Impairment: Adult

Hepatic impairment **prior** to treatment initiation:

Ankylosing spondylitis, atopic dermatitis, nonradiographic axial spondyloarthritis, psoriatic arthritis, rheumatoid arthritis :

Mild to moderate impairment (Child-Pugh class A or B): No dosage adjustment is necessary.

Severe impairment (Child-Pugh class C): Use is not recommended.

Crohn disease:

Mild to moderate impairment (Child-Pugh class A or B): Induction: 30 mg once daily for 12 weeks; maintenance: 15 mg once daily.

Severe impairment (Child-Pugh class C): Use is not recommended.

Ulcerative colitis :

Mild to moderate impairment (Child-Pugh class A or B): Induction: 30 mg once daily for 8 weeks; maintenance: 15 mg once daily.

Severe impairment (Child-Pugh class C): Use is not recommended.

Hepatotoxicity **during** treatment: Treatment should be interrupted if drug-induced liver injury is suspected.

Dosing: Adjustment for Toxicity: Adult

Hematologic:

Absolute lymphocyte count (ALC) <500/mm^3: Interrupt therapy until ALC ≥500/mm^3.

ANC <1,000/mm^3: Interrupt therapy until ANC ≥1,000/mm^3.

Hemoglobin <8 g/dL: Interrupt therapy until hemoglobin ≥8 g/dL.

Hypersensitivity reaction (severe): Discontinue therapy.

Infection (serious), including herpes zoster: Interrupt treatment until the infection is controlled.

Dosing: Older Adult

Ankylosing spondylitis, Crohn disease, nonradiographic axial spondyloarthritis, psoriatic arthritis, rheumatoid arthritis, ulcerative colitis : Refer to adult dosing.

Atopic dermatitis: ≥65 years of age: **Oral:** 15 mg once daily.

Dosing: Pediatric

(For additional information see "Upadacitinib: Pediatric drug information")

Dosage guidance:

Safety: Do not initiate therapy in patients with an absolute lymphocyte count (ALC) <500/mm^3, ANC <1,000/mm^3, or hemoglobin <8 g/dL.

Dosage form information: Upadacitinib extended-release tablets (Rinvoq) and oral solution (Rinvoq LQ) are NOT substitutable on a mg:mg basis.

Atopic dermatitis, refractory, moderate to severe

Atopic dermatitis, refractory, moderate to severe:

Children ≥12 years and Adolescents, weighing ≥40 kg: Extended-release tablet: Oral: 15 mg **once** daily; may increase to 30 mg once daily if inadequate response; in clinical trials, used as either monotherapy or in combination with topical corticosteroids (Ref).

Juvenile idiopathic arthritis, polyarticular

Juvenile idiopathic arthritis, polyarticular:

Children ≥2 years and Adolescents:

10 to <20 kg: Oral solution: Oral: 3 mg twice daily.

20 to <30 kg: Oral solution: Oral: 4 mg twice daily.

≥30 kg:

Oral solution: Oral: 6 mg twice daily.

Extended-release tablet: Oral: 15 mg **once** daily.

Psoriatic arthritis, active

Psoriatic arthritis, active:

Children ≥2 years and Adolescents <18 years:

10 to <20 kg: Oral solution: Oral: 3 mg twice daily.

20 to <30 kg: Oral solution: Oral: 4 mg twice daily.

≥30 kg:

Oral solution: Oral: 6 mg twice daily.

Extended-release tablet: Oral: 15 mg **once** daily.

Adolescents ≥18 years: Extended-release tablet: Oral: 15 mg **once** daily.

Dosage adjustment for concomitant therapy: Significant drug interactions exist, requiring dose/frequency adjustment or avoidance. Consult drug interactions database for more information.

Dosing adjustment for toxicity: Children ≥2 years and Adolescents: Extended-release tablets, oral solution:

Hematologic:

ALC <500/mm^3: Interrupt therapy until ALC ≥500/mm^3.

ANC <1,000/mm^3: Interrupt therapy until ANC ≥1,000/mm^3.

Hemoglobin <8 g/dL: Interrupt therapy until hemoglobin ≥8 g/dL.

Hypersensitivity reaction (severe): Discontinue therapy.

Infection (serious), including herpes zoster: Interrupt treatment until the infection is controlled.

Dosing: Kidney Impairment: Pediatric

Atopic dermatitis:

Altered kidney function:

Children ≥12 years and Adolescents, weighing ≥40 kg: Extended-release tablets: Oral:

eGFR ≥30 mL/minute/1.73 m^2: No dosage adjustment necessary.

eGFR 15 to <30 mL/minute/1.73 m^2: 15 mg once daily.

eGFR <15 mL/minute/1.73 m^2: Use not recommended.

Juvenile idiopathic or psoriatic arthritis:

Altered kidney function:

Children ≥2 years and Adolescents: Extended-release tablets, oral solution: Oral:

eGFR ≥15 mL/minute/1.73 m^2: No dosage adjustment is necessary.

eGFR <15 mL/minute/1.73 m^2: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Liver Impairment: Pediatric

Atopic dermatitis, juvenile idiopathic arthritis, or psoriatic arthritis:

Children ≥2 years and Adolescents: Extended-release tablets, oral solution: Oral:

Baseline hepatic impairment:

Mild to moderate impairment: No dosage adjustment is necessary.

Severe impairment: Use is not recommended.

*Hepatotoxicity **during** treatment:* Treatment should be interrupted if drug-induced liver injury is suspected.

Adverse Reactions (Significant): Considerations

GI perforation

Gastrointestinal (GI) **perforation** is a rare but serious adverse event that may occur with upadacitinib and other Janus kinase (JAK) inhibitors (Ref). A meta-analysis of multiple clinical trials found no significant difference in the risk of GI perforation with upadacitinib compared to conventional synthetic disease-modifying antirheumatic drugs (Ref). A cohort study found no significant difference between groups in the rate of GI perforation between JAK inhibitors as a class and adalimumab, a tumor necrosis factor blocker (Ref).

Mechanism: Inhibits JAK signal transducers and activators of transcription pathway involved in IL-6 signaling and may be associated with decreased intestinal repair and increased risk of GI perforation (Ref).

Onset: Delayed; median ~8 months (IQR ~4 to 21 months) (Ref).

Risk factors:

- Age ≥65 years (Ref)
- Concurrent systemic glucocorticoids (>7.5 mg/day) (Ref)
- History of GI perforation (Ref)
- History of GI disease (eg, diverticulitis, peptic ulcer disease) (Ref)
- History of hypertension (Ref)

Hematologic toxicity

Hematologic toxicity, including **anemia**, **lymphocytopenia**, and **neutropenia**, may occur. Most abnormalities reported were mild and transient and resolved upon therapy discontinuation (Ref).

Onset: Varied; may occur at any time but usually transient (Ref).

Risk factors:

- Higher dose (Ref)

Hepatic effects

Studies pooling data from clinical trials have shown **increased liver enzymes** and hepatic events with upadacitinib compared to placebo or active comparators (Ref). However, a meta-analysis of multiple clinical trials found no significant difference in the risk of serious hepatic events with upadacitinib compared to conventional synthetic disease-modifying antirheumatic drugs (Ref). Most **increased serum alanine aminotransferase**, **increased serum aspartate aminotransferase**, or **increased creatinine phosphokinase in blood specimen** were modest, asymptomatic, and transient (Ref).

Mechanism: Dose-related; not clearly established. In vitro data suggest Janus kinase inhibitor-associated increases in creatinine phosphokinase may represent restoration of myoblast differentiation (Ref).

Onset: Varied; may occur at any time but usually transient (Ref).

Risk factors:

• Higher dose (Ref)

Infection

Patients treated with upadacitinib are at increased risk for developing **serious infections** that may lead to hospitalization or death, including **bacterial infection**, **viral infection** (including **reactivation of HBV** and **herpes zoster infection**), **fungal infection** (including **cryptococcosis** and **infection due to an organism in genus *Pneumocystis***), and other **opportunistic infections**. The most common serious infections reported included **pneumonia** and cellulitis. Other infections reported include **urinary tract infections** and **nasopharyngitis** (Ref).

Mechanism: Dose-related; related to pharmacologic action; immunosuppressive effects predispose to infection; Janus kinase signal transducers and activators of transcription pathway have several key functions in inflammatory cytokines and immune response (Ref).

Onset: Varied (Ref).

Risk factors:

• Higher dose (Ref)

• Concurrent non-methotrexate conventional synthetic disease-modifying antirheumatic drugs (Ref)

• Smoking (Ref)

• Age ≥65 years (Ref)

• Asian patients (herpes zoster) (Ref)

Major cardiovascular events

Studies pooling data from clinical trials have shown no major increase in cardiovascular events with upadacitinib compared to placebo or active comparators (Ref). More data are needed to determine if Janus kinase (JAK) inhibitors or the proatherogenic nature of inflammatory diseases increase the risk of major adverse cardiovascular events (Ref).

Mechanism: Unknown; although, JAK inhibitors increase lipid levels by reducing cholesterol ester metabolism (Ref).

Onset: Varied; no clear time-to-event pattern. In rheumatoid arthritis patients, more events occurred in the first 12 months vs >12 months (Ref).

Risk factors:

- Age ≥65 years (Ref)
- Males (Ref)
- Previous cardiovascular event (Ref)
- History of hypertension (Ref)
- History of diabetes mellitus (Ref)
- History of tobacco/nicotine use (Ref)
- Concurrent glucocorticoid, antithrombotic, statin, and aspirin use (Ref)

Malignancies

Malignant lymphoma and other **malignant neoplasms** have been observed in patients treated with upadacitinib, including **skin carcinoma** and **lung carcinoma** (Ref).

Mechanism: Dose-related; related to pharmacologic action; immunosuppressive effects predispose to malignancies; Janus kinase signal transducers and activators of transcription pathway have several key functions in inflammatory cytokines and immune response (Ref).

Onset: Varied; most malignancies were diagnosed within 3 months after the first dose (Ref).

Risk factors:

- Higher dose (Ref)
- Age ≥65 years (Ref)

Thrombosis

Thrombosis, including **deep vein thrombosis**, **pulmonary embolism**, and **arterial thrombosis**, has occurred in patients treated with Janus kinase (JAK) inhibitors in general when used to treat inflammatory conditions. Studies pooling data from clinical trials have shown no major increase in thrombotic events with upadacitinib compared to placebo or active comparators (Ref).

Mechanism: Unknown; may be related to JAK inhibition specificity, resulting in an imbalance between pro- and anti-thrombotic pathway activity (Ref).

Onset: Varied; no clear time-to-event pattern. Event rates in the first 12 months were similar to rates >12 months (Ref).

Risk factors:

- Age ≥65 years (Ref)
- Males (Ref)
- Obesity (Ref)
- History of hypertension or cardiovascular disease (Ref)
- History of venous thromboembolism (Ref)
- History of tobacco/nicotine use (Ref)
- Concurrent antithrombotic, statin, and aspirin use (Ref)

Tuberculosis

Tuberculosis (TB), pulmonary or extrapulmonary, has been reported (Ref). In a meta-analysis of multiple trials with various Janus kinase (JAK) inhibitors and tumor necrosis factor blockers, no sign of increased risk for TB vs placebo was found, but power was limited (Ref).

Mechanism: Dose-related; related to pharmacologic action; immunosuppressive effects predispose to infection; JAK signal transducers and activators of transcription pathway have several key functions in inflammatory cytokines and immune response (Ref).

Risk factors:

• Residence in an area with high TB prevalence

• Known TB exposure or ongoing risk factors for TB exposure (eg, travel to areas with high TB prevalence)

Adverse Reactions

The following adverse drug reactions and incidences are derived from product labeling unless otherwise specified. Adverse reactions reported in adults and adolescents.

>10%:

Dermatologic: Acne vulgaris (1% to 16%)

Respiratory: Upper respiratory tract infection (9% to 25%)

1% to 10%:

Dermatologic: Folliculitis (2% to 4%), skin carcinoma (0% to 1%; including non-melanoma) (table 1), skin rash (4% to 5%)

Endocrine & metabolic: Hypercholesterolemia (2% to 4%), hyperlipidemia (2%), weight gain (2%)

Gastrointestinal: Abdominal pain (2% to 3%), gastroenteritis (3%), nausea (3% to 4%), oral candidiasis (<2%)

Hematologic & oncologic: Anemia (<1% to 7%) (table 2), leukopenia (1% to 2%), lymphocytopenia (2% to 3%) (table 3), neutropenia (1% to 6%) (table 4)

Hepatic: Increased liver enzymes (2% to 6%; including cholestasis, drug-induced liver injury, increased gamma-glutamyl transferase, increased serum alanine aminotransferase, increased serum alkaline phosphatase, increased serum aspartate aminotransferase, increased serum bilirubin) (table 5)

Hypersensitivity: Hypersensitivity reaction (3%)

Infection: Herpes simplex infection (≤8%), herpes zoster infection (<1% to 5%) (table 6), influenza (2% to 3%)

Nervous system: Fatigue (2% to 3%), headache (3% to 6%)

Neuromuscular & skeletal: Increased creatine phosphokinase in blood specimen (1% to 8%) (table 7), myalgia (2%)

Respiratory: Bronchitis (1% to 4%), cough (2% to 3%), flu-like symptoms (2%), pneumonia (<1% to 4%) (table 8)

Miscellaneous: Fever (1% to 7%)

<1%:

Gastrointestinal: Gastrointestinal perforation (table 9), oral herpes simplex infection

Ophthalmic: Retinal detachment

Frequency not defined:

Cardiovascular: Arterial thrombosis, thrombosis

Dermatologic: Cellulitis

Hypersensitivity: Anaphylaxis, angioedema

Infection: Reactivation of HBV

Postmarketing:

Cardiovascular: Acute myocardial infarction (Ref), deep vein thrombosis (Ref), pulmonary embolism (Ref), venous thrombosis (Ref)

Dermatologic: Eczema (herpeticum) (Ref), varicella-like rash (Kaposi varicelliform eruption) (Ref)

Gastrointestinal: Appendicitis (Ref), esophageal candidiasis (Ref)

Genitourinary: Urinary tract infection (Ref)

Hematologic & oncologic: Malignant lymphoma (Ref), malignant neoplasm (Ref)

Infection: Infection (including bacterial infection, cryptococcosis, fungal infection, opportunistic infection, serious infection, viral infection) (Ref)

Nervous system: Cerebrovascular accident (Ref)

Respiratory: Infection due to an organism in genus *Pneumocystis* (Ref), lung carcinoma (Ref), nasopharyngitis (Ref), tuberculosis (Ref)

Contraindications

Hypersensitivity to upadacitinib or any component of the formulation.

Warnings/Precautions

Concerns related to adverse effects:

• GI perforation: Use with caution in patients at increased risk for GI perforation (eg, history of diverticulitis, concomitant nonsteroidal anti-inflammatory drugs, corticosteroids); perforations have been reported in clinical trials. Promptly evaluate new-onset abdominal symptoms in patients taking upadacitinib.

• Hematologic toxicity: Hematologic toxicity, including lymphopenia, anemia, and neutropenia, may occur and is generally reversible and managed by treatment interruption. Do not initiate therapy in patients with an absolute lymphocyte count <500/mm^3, ANC <1,000/mm^3, or hemoglobin <8 g/dL. Monitor CBC at baseline and periodically thereafter.

• Hepatic effects: Liver enzyme elevation has been observed. Monitor LFTs at baseline and periodically thereafter; interrupt therapy if LFTs increased and drug-induced liver injury is suspected.

• Hypersensitivity reactions: Severe hypersensitivity, including anaphylaxis and angioedema, has been reported.

• Infections: Patients receiving upadacitinib are at increased risk for serious infections, which may result in hospitalization and/or fatality; rate of serious infections was increased in patients on higher doses. The most common serious infections reported included pneumonia and cellulitis. Reactivation of viral infections (eg, herpes zoster, hepatitis B) have been observed; the incidence of chronic viral hepatitis reactivation is unknown. If herpes zoster is reported, consider interrupting therapy until herpes zoster has resolved. Consultation with a hepatologist may be necessary if hepatitis B virus DNA is detected.

• Lipid abnormalities: Increased lipid parameters (eg, total, low-density lipoprotein [LDL], and high-density lipoprotein [HDL] cholesterol) have been observed. Mean LDL and HDL increased by ~15 mg/dL and ~8 mg/dL, respectively, 2 months after starting upadacitinib. Assess lipids 12 weeks after upadacitinib initiation and manage lipid abnormalities according to current clinical guidelines.

• Malignancy: Lymphoma and other malignancies have been reported in patients receiving upadacitinib. Consider risks versus benefits prior to use in patients with a known malignancy (other than successfully treated nonmelanoma skin cancers [NMSCs]) or when continuing upadacitinib in patients who develop a new malignancy. NMSCs have been reported.

• Medication residue in stool: Medication residue in stool or ostomy output has been reported in patients with anatomical conditions (eg, ileostomy, colostomy, intestinal resection) or functional conditions that slow GI transit times. Instruct patients to report medication residue in stool to a health care provider. Monitor patients for clinical response and consider alternative therapy if there is a lack of therapeutic response.

• Tuberculosis: Tuberculosis (TB) (pulmonary or extrapulmonary) has been reported in patients receiving upadacitinib. Use with caution in patients who have resided or traveled in regions where TB is endemic. Consider anti-TB therapy if an adequate course of treatment cannot be confirmed in patients with a history of TB infection or disease (latent or active TB) or for patients with risk factors despite negative skin test.

Special populations:

• Patients with rheumatic musculoskeletal disease undergoing hip or knee replacement surgery: Hold upadacitinib for at least 3 days prior to surgery to reduce infection risk; therapy can be restarted once surgical wound shows evidence of healing (eg, no swelling, erythema, or drainage), sutures/staples are removed, and no ongoing nonsurgical site infections (typically ~14 days to reduce infection risk) (ACR/AAHKS [Goodman 2022]).

Dosage form specific issues:

• Benzyl alcohol and derivatives: Some dosage forms may contain benzyl alcohol and/or sodium benzoate/benzoic acid; benzoic acid (benzoate) is a metabolite of benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates; the "gasping syndrome" consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage), hypotension, and cardiovascular collapse (AAP ["Inactive" 1997]; CDC 1982); some data suggest that benzoate displaces bilirubin from protein binding sites (Ahlfors 2001); avoid or use dosage forms containing benzyl alcohol and/or benzyl alcohol derivatives with caution in neonates. See manufacturer's labeling.

• Product interchangeability: Oral solution should not be substituted for the ER tablets; products are not bioequivalent and not interchangeable on a milligram-per-milligram basis.

Oral solution is intended for pediatric use only.

Other warnings/precautions:

• Immunizations: Immunization status should be current before initiating therapy. Live vaccines should not be given concomitantly, or immediately prior to, upadacitinib; recommended interval between receipt of live vaccines and initiation of immunosuppressive agents such as upadacitinib should follow current vaccination clinical guidelines.

Dosage Forms: US

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Oral:

Rinvoq LQ: 1 mg/mL (180 mL) [contains sodium benzoate]

Tablet Extended Release 24 Hour, Oral:

Rinvoq: 15 mg, 30 mg, 45 mg

Generic Equivalent Available: US

No

Pricing: US

Solution (Rinvoq LQ Oral)

1 mg/mL (per mL): $21.61

Tablet, 24-hour (Rinvoq Oral)

15 mg (per each): $270.11

30 mg (per each): $270.11

45 mg (per each): $540.22

Disclaimer: A representative AWP (Average Wholesale Price) price or price range is provided as reference price only. A range is provided when more than one manufacturer's AWP price is available and uses the low and high price reported by the manufacturers to determine the range. The pricing data should be used for benchmarking purposes only, and as such should not be used alone to set or adjudicate any prices for reimbursement or purchasing functions or considered to be an exact price for a single product and/or manufacturer. Medi-Span expressly disclaims all warranties of any kind or nature, whether express or implied, and assumes no liability with respect to accuracy of price or price range data published in its solutions. In no event shall Medi-Span be liable for special, indirect, incidental, or consequential damages arising from use of price or price range data. Pricing data is updated monthly.

Dosage Forms: Canada

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Tablet Extended Release 24 Hour, Oral:

Rinvoq: 15 mg, 30 mg, 45 mg

Administration: Adult

Oral: Administer with or without food. Swallow tablet whole; do not crush, split, or chew.

Administration: Pediatric

Oral: Administer with or without food.

Oral solution: Administer using provided press-in bottle adaptor and oral dosing syringe; must be administered within 1 hour after drawing up solution in syringe.

Extended-release tablet: Swallow tablet whole; do not crush, split, or chew.

Hazardous Drugs Handling Considerations

This medication is not on the NIOSH (2024) list; however, it may meet the criteria for a hazardous drug. Upadacitinib may cause carcinogenicity and teratogenicity.

Use appropriate precautions for receiving, handling, storage, preparation, dispensing, transporting, administration, and disposal. Follow NIOSH and USP 800 recommendations **and** institution-specific policies/procedures for appropriate containment strategy (NIOSH 2023; NIOSH 2024; USP-NF 2020).

Note: Facilities may perform risk assessment of some hazardous drugs to determine if appropriate for alternative handling and containment strategies (USP-NF 2020). Refer to institution-specific handling policies/procedures.

Medication Guide and/or Vaccine Information Statement (VIS)

An FDA-approved patient medication guide, which is available with the product information and as follows, must be dispensed with this medication:

Rinvoq: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/211675s019lbl.pdf

Use: Labeled Indications

Ankylosing spondylitis: Treatment of active ankylosing spondylitis in adults who have had an inadequate response or intolerance to one or more tumor necrosis factor (TNF) blockers.

Limitation of use: Use of upadacitinib in combination with other Janus-associated kinase inhibitors, biologic disease-modifying antirheumatic drugs, or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Atopic dermatitis: Treatment of refractory, moderate to severe atopic dermatitis in pediatric patients ≥12 years of age and adults who had an inadequate response or intolerance to other systemic drug products, including biologics, or when use of those therapies is inadvisable.

Limitation of use: Use of upadacitinib in combination with other Janus-associated kinase inhibitors, biologic immunomodulators, or with other immunosuppressants is not recommended.

Crohn disease: Treatment of moderate to severe Crohn disease in adults who have had an inadequate response or intolerance to one or more TNF blockers.

Limitation of use: Use of upadacitinib in combination with other Janus-associated kinase inhibitors, biologic therapies for Crohn disease, or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Juvenile idiopathic arthritis: Treatment of active polyarticular juvenile idiopathic arthritis in patients ≥2 years of age who have had an inadequate response or intolerance to one or more TNF blockers.

> Limitation of use: Use of upadacitinib in combination with other Janus-associated kinase inhibitors, biologic disease-modifying antirheumatic drugs, or with potent immunosuppressants, such as azathioprine and cyclosporine, is not recommended.

Nonradiographic axial spondyloarthritis: Treatment of active nonradiographic axial spondyloarthritis in adults with objective signs of inflammation who had an inadequate response or intolerance to TNF blockers.

> Limitation of use: Use of upadacitinib in combination with other Janus-associated kinase inhibitors, biologic disease-modifying antirheumatic drugs, or with potent immunosuppressants, such as azathioprine and cyclosporine, is not recommended.

Psoriatic arthritis: Treatment of active psoriatic arthritis in adults and pediatric patients ≥2 years of age who have had an inadequate response or intolerance to one or more TNF blockers.

> Limitation of use: Use of upadacitinib in combination with other Janus-associated kinase inhibitors, biologic disease-modifying antirheumatic drugs, or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Rheumatoid arthritis: Treatment of moderately to severely active rheumatoid arthritis in adults who have had an inadequate response or intolerance to one or more TNF blockers.

> Limitation of use: Use of upadacitinib in combination with other Janus-associated kinase inhibitors, biologic disease-modifying antirheumatic drugs, or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Ulcerative colitis: Treatment of moderately to severely active ulcerative colitis in adults who have had an inadequate response or intolerance to 1 or more TNF blockers.

> Limitation of use: Use of upadacitinib in combination with other Janus-associated kinase inhibitors, biological therapies for ulcerative colitis, or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Metabolism/Transport Effects

Substrate of CYP2D6 (minor), CYP3A4 (major); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential; **Induces** BCRP/ABCG2, CYP3A4 (weak), OATP1B1/1B3 (SLCO1B1/1B3)

Drug Interactions

(For additional information: Launch drug interactions program)

Note: Interacting drugs may **not be individually listed below** if they are part of a group interaction (eg, individual drugs within "CYP3A4 Inducers [Strong]" are NOT listed). For a complete list of drug interactions by individual drug name and detailed management recommendations, use the drug interactions program by clicking on the "Launch drug interactions program" link above.

Abrocitinib: May enhance the immunosuppressive effect of Immunosuppressants (Therapeutic Immunosuppressant Agents). *Risk X: Avoid combination*

Anifrolumab: Biologic Disease-Modifying Antirheumatic Drugs (DMARDs) may enhance the immunosuppressive effect of Anifrolumab. *Risk X: Avoid combination*

Atogepant: CYP3A4 Inducers (Weak) may decrease the serum concentration of Atogepant. Management: For treatment of episodic migraine, the recommended dose of atogepant is 30 mg once daily or 60 mg once daily when combined with CYP3A4 inducers. When used for treatment of chronic migraine, use of atogepant with CYP3A4 inducers should be avoided. *Risk D: Consider therapy modification*

Baricitinib: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the immunosuppressive effect of Baricitinib. *Risk X: Avoid combination*

BCG Products: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the adverse/toxic effect of BCG Products. Specifically, the risk of vaccine-associated infection may be increased. Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of BCG Products. *Risk X: Avoid combination*

Brincidofovir: Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Brincidofovir. *Risk C: Monitor therapy*

Brivudine: May enhance the adverse/toxic effect of Immunosuppressants (Therapeutic Immunosuppressant Agents). *Risk X: Avoid combination*

Chikungunya Vaccine (Live): Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the adverse/toxic effect of Chikungunya Vaccine (Live). Specifically, the risk of vaccine-associated infection may be increased. Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Chikungunya Vaccine (Live). *Risk X: Avoid combination*

Cladribine: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the immunosuppressive effect of Cladribine. *Risk X: Avoid combination*

Clofazimine: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

CloZAPine: CYP3A4 Inducers (Weak) may decrease the serum concentration of CloZAPine. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the diagnostic effect of Coccidioides immitis Skin Test. Management: Consider discontinuing therapeutic immunosuppressants several weeks prior to coccidioides immitis skin antigen testing to increase the likelihood of accurate diagnostic results. *Risk D: Consider therapy modification*

Corticosteroids (Systemic): May enhance the immunosuppressive effect of Upadacitinib. Management: Coadministration of upadacitinib with systemic corticosteroids at doses equivalent to greater than 2 mg/kg or 20 mg/day of prednisone (for persons over 10 kg) administered for 2 or more weeks is not recommended. *Risk D: Consider therapy modification*

COVID-19 Vaccines: Upadacitinib may diminish the therapeutic effect of COVID-19 Vaccines. Management: Rheumatology guidelines recommend holding baricitinib, tofactinib, or upadacitinib for 1 to 2 weeks after vaccine administration as permitted by the underlying disease. *Risk D: Consider therapy modification*

CYP2D6 Substrates (Narrow Therapeutic Index/Sensitive): Upadacitinib may increase the serum concentration of CYP2D6 Substrates (Narrow Therapeutic Index/Sensitive). *Risk C: Monitor therapy*

CYP3A4 Inducers (Moderate): May decrease the serum concentration of Upadacitinib. *Risk C: Monitor therapy*

CYP3A4 Inducers (Strong): May decrease the serum concentration of Upadacitinib. *Risk X: Avoid combination*

CYP3A4 Inhibitors (Strong): May increase the serum concentration of Upadacitinib. Management: Upadacitinib dose adjustments are often needed when combined with strong CYP3A4 inhibitors. Specific adjustments vary based on upadacitinib indication. See full interact monograph for details. *Risk D: Consider therapy modification*

Dengue Tetravalent Vaccine (Live): Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the adverse/toxic effect of Dengue Tetravalent Vaccine (Live). Specifically, the risk of vaccine-associated infection may be increased. Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Dengue Tetravalent Vaccine (Live). *Risk X: Avoid combination*

Denosumab: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the immunosuppressive effect of Denosumab. Management: Consider the risk of serious infections versus the potential benefits of coadministration of denosumab and immunosuppressants. If combined, monitor for signs/symptoms of serious infections. *Risk D: Consider therapy modification*

Deucravacitinib: May enhance the immunosuppressive effect of Immunosuppressants (Therapeutic Immunosuppressant Agents). *Risk X: Avoid combination*

Etrasimod: May enhance the immunosuppressive effect of Immunosuppressants (Therapeutic Immunosuppressant Agents). *Risk X: Avoid combination*

Filgotinib: May enhance the immunosuppressive effect of Immunosuppressants (Therapeutic Immunosuppressant Agents). *Risk X: Avoid combination*

Fusidic Acid (Systemic): May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). Management: Consider avoiding this combination if possible. If required, monitor patients closely for increased adverse effects of the CYP3A4 substrate. *Risk D: Consider therapy modification*

Grapefruit Juice: May increase the serum concentration of Upadacitinib. *Risk X: Avoid combination*

Immunosuppressants (Cytotoxic Chemotherapy): May enhance the immunosuppressive effect of Upadacitinib. *Risk X: Avoid combination*

Immunosuppressants (Miscellaneous Oncologic Agents): May enhance the immunosuppressive effect of Upadacitinib. *Risk X: Avoid combination*

Immunosuppressants (Therapeutic Immunosuppressant Agents): May enhance the immunosuppressive effect of Upadacitinib. *Risk X: Avoid combination*

Influenza Virus Vaccines: Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Influenza Virus Vaccines. Management: Administer influenza vaccines at least 2 weeks prior to initiating immunosuppressants if possible. If vaccination occurs less than 2 weeks prior to or during therapy, revaccinate 2 to 3 months after therapy discontinued if immune competence restored. *Risk D: Consider therapy modification*

Methotrexate: May enhance the immunosuppressive effect of Upadacitinib. Management: Concomitant use of upadacitinib with high-dose or IV methotrexate is not recommended. Use with antirheumatic doses of methotrexate is permitted, and if combined, patients should be monitored for infection. *Risk D: Consider therapy modification*

Mumps- Rubella- or Varicella-Containing Live Vaccines: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the adverse/toxic effect of Mumps- Rubella- or Varicella-Containing Live Vaccines. Specifically, the risk of vaccine-associated infection may be increased. Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Mumps- Rubella- or Varicella-Containing Live Vaccines. *Risk X: Avoid combination*

Nadofaragene Firadenovec: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the adverse/toxic effect of Nadofaragene Firadenovec. Specifically, the risk of disseminated adenovirus infection may be increased. *Risk X: Avoid combination*

Natalizumab: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the immunosuppressive effect of Natalizumab. *Risk X: Avoid combination*

NiMODipine: CYP3A4 Inducers (Weak) may decrease the serum concentration of NiMODipine. *Risk C: Monitor therapy*

Pidotimod: Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Pidotimod. *Risk C: Monitor therapy*

Pimecrolimus: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the immunosuppressive effect of Pimecrolimus. *Risk X: Avoid combination*

Pneumococcal Vaccines: Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Pneumococcal Vaccines. *Risk C: Monitor therapy*

Poliovirus Vaccine (Live/Trivalent/Oral): Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the adverse/toxic effect of Poliovirus Vaccine (Live/Trivalent/Oral). Specifically, the risk of vaccine-associated infection may be increased. Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Poliovirus Vaccine (Live/Trivalent/Oral). *Risk X: Avoid combination*

Polymethylmethacrylate: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the potential for allergic or hypersensitivity reactions to Polymethylmethacrylate. Management: Use caution when considering use of bovine collagen-containing implants such as the polymethylmethacrylate-based Bellafill brand implant in patients who are receiving immunosuppressants. Consider use of additional skin tests prior to administration. *Risk D: Consider therapy modification*

Rabies Vaccine: Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Rabies Vaccine. Management: Complete rabies vaccination at least 2 weeks before initiation of immunosuppressant therapy if possible. If combined, check for rabies antibody titers, and if vaccination is for post exposure prophylaxis, administer a 5th dose of the vaccine. *Risk D: Consider therapy modification*

Ritlecitinib: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the immunosuppressive effect of Ritlecitinib. *Risk X: Avoid combination*

Ruxolitinib (Topical): Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the immunosuppressive effect of Ruxolitinib (Topical). *Risk X: Avoid combination*

Selpercatinib: CYP3A4 Inducers (Weak) may decrease the serum concentration of Selpercatinib. *Risk C: Monitor therapy*

Sipuleucel-T: Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Sipuleucel-T. Management: Consider reducing the dose or discontinuing the use of immunosuppressants prior to initiating sipuleucel-T therapy. *Risk D: Consider therapy modification*

Tacrolimus (Topical): Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the immunosuppressive effect of Tacrolimus (Topical). *Risk X: Avoid combination*

Talimogene Laherparepvec: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the adverse/toxic effect of Talimogene Laherparepvec. Specifically, the risk of infection from the live, attenuated herpes simplex virus contained in talimogene laherparepvec may be increased. *Risk X: Avoid combination*

Tertomotide: Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Tertomotide. *Risk X: Avoid combination*

Tofacitinib: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the immunosuppressive effect of Tofacitinib. Management: Coadministration of tofacitinib with potent immunosuppressants is not recommended. Use with non-biologic disease-modifying antirheumatic drugs (DMARDs) was permitted in psoriatic arthritis clinical trials. *Risk X: Avoid combination*

Typhoid Vaccine: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the adverse/toxic effect of Typhoid Vaccine. Specifically, the risk of vaccine-associated infection may be increased. Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Typhoid Vaccine. *Risk X: Avoid combination*

Ubrogepant: CYP3A4 Inducers (Weak) may decrease the serum concentration of Ubrogepant. Management: Use an initial ubrogepant dose of 100 mg and second dose (if needed) of 100 mg when used with a weak CYP3A4 inducer. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the adverse/toxic effect of Vaccines (Live). Specifically, the risk of vaccine-associated infection may be increased. Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Vaccines (Live). *Risk X: Avoid combination*

Vaccines (Non-Live/Inactivated/Non-Replicating): Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Vaccines (Non-Live/Inactivated/Non-Replicating). Management: Give non-live/inactivated/non-replicating vaccines at least 2 weeks prior to starting immunosuppressants when possible. Patients vaccinated less than 14 days before or during therapy should be revaccinated at least 2 to 3 months after therapy is complete. *Risk D: Consider therapy modification*

Yellow Fever Vaccine: Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the adverse/toxic effect of Yellow Fever Vaccine. Specifically, the risk of vaccine-associated infection may be increased. Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Yellow Fever Vaccine. *Risk X: Avoid combination*

Zavegepant: OATP1B1/1B3 (SLCO1B1/1B3) Inducers may decrease the serum concentration of Zavegepant. *Risk X: Avoid combination*

Zoster Vaccine (Live/Attenuated): Immunosuppressants (Therapeutic Immunosuppressant Agents) may enhance the adverse/toxic effect of Zoster Vaccine (Live/Attenuated). Specifically,

the risk of vaccine-associated infection may be increased. Immunosuppressants (Therapeutic Immunosuppressant Agents) may diminish the therapeutic effect of Zoster Vaccine (Live/Attenuated). *Risk X: Avoid combination*

Food Interactions

Grapefruit increases exposure to upadacitinib. Management: Avoid grapefruit during therapy.

Reproductive Considerations

Verify pregnancy status prior to use in patients who could become pregnant. Patients who could become pregnant should use effective contraception during treatment and for 4 weeks following the last dose of upadacitinib.

Agents other than upadacitinib are preferred to treat inflammatory bowel disease in patients planning to become pregnant. Disease management should be optimized prior to pregnancy (Ref).

Pregnancy Considerations

Based on data from animal reproduction studies, in utero exposure to upadacitinib may cause fetal harm.

Outcome data following maternal use of upadacitinib during pregnancy are available (Ref).

Agents other than upadacitinib are preferred to treat inflammatory bowel disease in pregnant patients (Ref). Janus kinase inhibitors, such as upadactinib, are not recommended for the treatment of atopic dermatitis during pregnancy (Ref).

Data collection to monitor pregnancy and infant outcomes following exposure to upadacitinib is ongoing. Health care providers should report patients exposed to upadacitinib during pregnancy by calling 1-800-633-9110.

Breastfeeding Considerations

It is not known if upadacitinib is present in breast milk.

Janus kinase inhibitors, such as upadacitinib, are not recommended for the treatment of atopic dermatitis in breastfeeding patients (Ref). Due to the potential for serious adverse reactions in the breastfed infant, breastfeeding is not recommended by the manufacturer during treatment and for 6 days following the last dose of upadacitinib.

Dietary Considerations

Avoid grapefruit juice.

Monitoring Parameters

Lymphocyte count, neutrophil count, hemoglobin, and LFTs (baseline and periodically thereafter); lipids (12 weeks after therapy initiation and periodically thereafter); viral hepatitis (prior to initiating therapy and periodically thereafter); tuberculosis (TB) infection and disease (latent and active TB) screen at baseline; verify pregnancy status (prior to initiating therapy); signs/symptoms of infection (including TB) during and after therapy; skin examinations (periodically, in patients at increased risk for skin cancer); symptoms of thrombosis.

Mechanism of Action

Upadacitinib inhibits Janus kinase (JAK) enzymes, which are intracellular enzymes involved in stimulating hematopoiesis and immune cell function through a signaling pathway. JAKs activate signal transducers and activators of transcription (STATs), which regulate gene expression and intracellular activity. The inhibition of JAKs prevents the activation of STATs.

Pharmacokinetics (Adult Data Unless Noted)

Protein binding: 52% (plasma proteins)

Metabolism: Hepatic, primarily via CYP3A4

Half-life elimination: Terminal: 8 to 14 hours

Time to peak: ER tablets: 2 to 4 hours; oral solution: 1 hour.

Excretion: Urine (24% as unchanged drug); feces (38% as unchanged drug)

Pharmacokinetics: Additional Considerations (Adult Data Unless Noted)

Altered kidney function: AUC_{inf} 18%, 33%, and 44% higher in mild, moderate, and severe renal impairment, respectively, compared to subjects with normal renal function. C_{max} similar in subjects with normal and impaired renal function.

Hepatic function impairment: AUC_{inf} 28% and 24% higher in mild and moderate hepatic impairment, respectively, compared to subjects with normal hepatic function. C_{max} unchanged in mild hepatic impairment and 43% higher in moderate hepatic impairment compared to subjects with normal hepatic function. Not studied in patients with severe hepatic impairment (Child-Pugh C).

Brand Names: International

International Brand Names by Country

REFERENCES

1. *Adam DN, Gooderham MJ, Beecker JR, et al. Expert consensus on the systemic treatment of atopic dermatitis in special populations. J Eur Acad Dermatol Venereol. 2023;37(6):1135-1148. doi:10.1111/jdv.18922 [PubMed 36695072]*
2. *Ahlfors CE. Benzyl alcohol, kernicterus, and unbound bilirubin. J Pediatr. 2001;139(2):317-319. [PubMed 11487763]*
3. *Alves C, Penedones A, Mendes D, Marques FB. The risk of infections associated with JAK inhibitors in rheumatoid arthritis: a systematic review and network meta-analysis. J Clin Rheumatol. 2022;28(2):e407-e414. doi:10.1097/RHU.0000000000001749 [PubMed 33902098]*
4. *American Academy of Pediatrics (AAP) Committee on Drugs. "Inactive" ingredients in pharmaceutical products: update (subject review). Pediatrics. 1997;99(2):268-278. [PubMed 9024461]*
5. *Bechman K, Subesinghe S, Norton S, et al. A systematic review and meta-analysis of infection risk with small molecule JAK inhibitors in rheumatoid arthritis. Rheumatology (Oxford). 2019;58(10):1755-1766. doi:10.1093/rheumatology/kez087 [PubMed 30982883]*
6. *Burmester GR, Cohen SB, Winthrop KL, et al. Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis. RMD Open. 2023;9(1):e002735. doi:10.1136/rmdopen-2022-002735 [PubMed 36754548]*
7. *Cantini F, Blandizzi C, Niccoli L, Petrone L, Goletti D. Systematic review on tuberculosis risk in patients with rheumatoid arthritis receiving inhibitors of Janus kinases. Expert Opin Drug Saf. 2020;19(7):861-872. doi:10.1080/14740338.2020.1774550 [PubMed 32552289]*

8. *Centers for Disease Control (CDC). Neonatal deaths associated with use of benzyl alcohol—United States. MMWR Morb Mortal Wkly Rep. 1982;31(22):290-291. http://www.cdc.gov/mmwr/preview/mmwrhtml/00001109.htm [PubMed 6810084]*

9. *Charles-Schoeman C, Choy E, McInnes IB, et al. MACE and VTE across upadacitinib clinical trial programmes in rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis. RMD Open. 2023;9(4):e003392. doi:10.1136/rmdopen-2023-003392 [PubMed 37945286]*

10. *Charles-Schoeman C, Giles JT, Lane NE, et al. Impact of upadacitinib on laboratory parameters and related adverse events in patients with RA: integrated data up to 6.5 years. Rheumatol Ther. 2024;11(1):157-175. doi:10.1007/s40744-023-00624-3 [PubMed 38180720]*

11. *Cohen SB, van Vollenhoven RF, Winthrop KL, et al. Safety profile of upadacitinib in rheumatoid arthritis: integrated analysis from the SELECT phase III clinical programme. Ann Rheum Dis. 2021;80(3):304-311. doi:10.1136/annrheumdis-2020-218510 [PubMed 33115760]*

12. *Ertus C, Scailteux LM, Lescoat A, et al. Major adverse cardiovascular events in patients with atopic dermatitis treated with oral Janus kinase inhibitors: a systematic review and meta-analysis. Br J Dermatol. 2023;189(4):368-380. doi:10.1093/bjd/ljad229 [PubMed 37410552]*

13. *Fleischmann R, Curtis JR, Charles-Schoeman C, et al. Safety profile of upadacitinib in patients at risk of cardiovascular disease: integrated post hoc analysis of the SELECT phase III rheumatoid arthritis clinical programme. Ann Rheum Dis. 2023;82(9):1130-1141. doi:10.1136/ard-2023-223916 [PubMed 37308218]*

14. *Fleischmann R, Mysler E, Bessette L, et al. Long-term safety and efficacy of upadacitinib or adalimumab in patients with rheumatoid arthritis: results through 3 years from the SELECT-COMPARE study. RMD Open. 2022;8(1):e002012. doi:10.1136/rmdopen-2021-002012 [PubMed 35121639]*

15. *Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Care Res (Hoboken). 2021;73(7):924-939. doi:10.1002/acr.24596 [PubMed 34101387]*

16. *Gargiulo L, Ibba L, Fiorillo G, et al. Pregnancy outcome of a patient treated with upadacitinib for severe atopic dermatitis. J Eur Acad Dermatol Venereol. 2024;38(3):e252-e253. doi:10.1111/jdv.19557 [PubMed 37795665]*

17. *Goodman SM, Springer BD, Chen AF, et al. 2022 American College of Rheumatology/American Association of Hip and Knee Surgeons guideline for the perioperative management of antirheumatic medication in patients with rheumatic diseases undergoing elective total hip or total knee arthroplasty. Arthritis Care Res (Hoboken). 2022;74(9):1399-1408. doi:10.1002/acr.24893 [PubMed 35718887]*

18. *Guttman-Yassky E, Teixeira HD, Simpson EL, et al. Once-daily upadacitinib versus placebo in adolescents and adults with moderate-to-severe atopic dermatitis (Measure Up 1 and Measure Up 2): results from two replicate double-blind, randomised controlled phase 3 trials. Lancet. 2021;397(10290):2151-2168. doi:10.1016/S0140-6736(21)00588-2 [PubMed 34023008]*

19. *Guttman-Yassky E, Thyssen JP, Silverberg JI, et al. Safety of upadacitinib in moderate-to-severe atopic dermatitis: an integrated analysis of phase 3 studies. J Allergy Clin Immunol. 2023;151(1):172-181. doi:10.1016/j.jaci.2022.09.023 [PubMed 36195170]*

20. *Hodson L, Ovesen J, Couch J, et al; US Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. Managing hazardous drug exposures: information for healthcare settings, 2023. https://doi.org/10.26616/NIOSHPUB2023130. Updated April 2023. Accessed December 27, 2024.*

21. *Hoisnard L, Meyer A, Dray-Spira R, Weill A, Zureik M, Sbidian E. Risk of gastrointestinal perforation in patients with rheumatic diseases exposed to Janus kinase inhibitors versus adalimumab: a nationwide cohort study. Arthritis Rheumatol. 2024;76(9):1364-1376. doi:10.1002/art.42862 [PubMed 38699822]*

22. *Ji X, Hu L, Wang Y, et al. Risk of tuberculosis in patients with rheumatoid arthritis treated with biological and targeted drugs: meta-analysis of randomized clinical trials. Chin Med J (Engl). 2022;135(4):409-415. doi:10.1097/CM9.0000000000001948 [PubMed 35194004]*

23. *Katoh N, Ohya Y, Murota H, et al. A phase 3 randomized, multicenter, double-blind study to evaluate the safety of upadacitinib in combination with topical corticosteroids in adolescent and adult patients with moderate-to-severe atopic dermatitis in Japan (Rising Up): An interim 24-week analysis. JAAD Int. 2021;6:27-36. doi:10.1016/j.jdin.2021.11.001 [PubMed 34988493]*

24. *Kotyla PJ, Engelmann M, Giemza-Stoklosa J, Wnuk B, Islam MA. Thromboembolic adverse drug reactions in Janus kinase (JAK) inhibitors: does the inhibitor specificity play a role? Int J Mol Sci. 2021;22(5):2449. doi:10.3390/ijms22052449 [PubMed 33671049]*

25. *Liu-Yan N, Kun Z, Cheng X, Ming-Hao L, Xue-Xiao J, Yong-Mei H. Impact of upadacitinib on the risk of digestive events in patients with rheumatoid arthritis: a systematic review and meta-analysis of randomized controlled trials. Heliyon. 2023;9(6):e17002. doi:10.1016/j.heliyon.2023.e17002 [PubMed 37484342]*

26. *Mahadevan U, Levy G, Gensler L, et al. Pregnancy outcomes in patients treated with upadacitinib: analysis of data from clinical trials and postmarketing reports. Drug Saf. 2024;47(10):1039-1049. doi:10.1007/s40264-024-01454-0 [PubMed 39008024]*

27. *Mahadevan U, Robinson C, Bernasko N, et al. Inflammatory bowel disease in pregnancy clinical care pathway: a report from the American Gastroenterological Association IBD Parenthood Project Working Group. Am J Obstet Gynecol. 2019;220(4):308-323. doi:10.1016/j.ajog.2019.02.027 [PubMed 30948039]*

28. *Olivera PA, Lasa JS, Bonovas S, Danese S, Peyrin-Biroulet L. Safety of Janus kinase inhibitors in patients with inflammatory bowel diseases or other immune-mediated diseases: a systematic review and meta-analysis. Gastroenterology. 2020;158(6):1554-1573.e12. doi:10.1053/j.gastro.2020.01.001 [PubMed 31926171]*

29. *Ouranos K, Avila DV, Mylona EK, et al. Cumulative incidence and risk of infection in patients with rheumatoid arthritis treated with Janus kinase inhibitors: a systematic review and meta-analysis. PLoS One. 2024;19(7):e0306548. doi:10.1371/journal.pone.0306548 [PubMed 39083492]*

30. *Ovesen JL, Sammons D, Connor TH, et al; US Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. NIOSH list of hazardous drugs in healthcare settings, 2024. https://doi.org/10.26616/NIOSHPUB2025103. Updated December 18, 2024. Accessed December 20, 2024.*

31. *Reich K, Teixeira HD, de Bruin-Weller M, et al. Safety and efficacy of upadacitinib in combination with topical corticosteroids in adolescents and adults with moderate-to-severe atopic dermatitis (AD Up): results from a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2021;397(10290):2169-2181. doi:10.1016/S0140-6736(21)00589-4 [PubMed 34023009]*

32. *Rinvoq and Rinvoq LQ (upadacitinib) [prescribing information]. North Chicago, IL: AbbVie Inc; April 2024.*

33. *Silverberg JI, de Bruin-Weller M, Bieber T, et al. Upadacitinib plus topical corticosteroids in atopic dermatitis: Week 52 AD Up study results. J Allergy Clin Immunol. Published online August 14, 2021. doi:10.1016/j.jaci.2021.07.036 [PubMed 34403658]*

34. *Thanigaimani S, Phie J, Krishna SM, Moxon J, Golledge J. Effect of disease modifying anti-rheumatic drugs on major cardiovascular events: a meta-analysis of randomized controlled trials. Sci Rep. 2021;11(1):6627. doi:10.1038/s41598-021-86128-y [PubMed 33758292]*

35. *Trueman S, Mohamed MF, Feng T, Lacerda AP, Marbury T, Othman AA. Characterization of the effect of hepatic impairment on upadacitinib pharmacokinetics. J Clin Pharmacol. 2019;59(9):1188-1194. doi:10.1002/jcph.1414 [PubMed 30973649]*

36. *Urquhart SA, Chedid VG, Kane SV. Use of upadacitinib as salvage therapy for ulcerative colitis in pregnancy: a case report. Inflamm Bowel Dis. Published online July 5, 2024. doi:10.1093/ibd/izae146 [PubMed 38970379]*

37. *United States Pharmacopeia. <800> Hazardous Drugs—Handling in Healthcare Settings. In: USP-NF. United States Pharmacopeia; July 1, 2020. Accessed January 16, 2025. doi:10.31003/USPNF_M7808_07_01*

38. *US Food and Drug Administration (FDA). FDA Safety Alert. MedWatch. Xeljanz, Xeljanz XR (tofacitinib): FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions. https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-warnings-about-increased-risk-serious-heart-related-events-cancer-blood-clots-and-death. Accessed September 2, 2021*

39. *Valor-Méndez L, Manger B, Wacker J, Kleyer A, Schett G. Lymph node and pulmonary tuberculosis during upadacitinib treatment in a psoriatic arthritis patient. Rheumatol Adv Pract. 2022;6(2):rkac032. doi:10.1093/rap/rkac032 [PubMed 35601270]*

40. *Wang F, Sun L, Wang S, et al. Efficacy and safety of tofacitinib, baricitinib, and upadacitinib for rheumatoid arthritis: a systematic review and meta-analysis. Mayo Clin Proc. 2020;95(7):1404-1419. doi:10.1016/j.mayocp.2020.01.039 [PubMed 32499126]*

41. *Winthrop KL, Nash P, Yamaoka K, et al. Incidence and risk factors for herpes zoster in patients with rheumatoid arthritis receiving upadacitinib: a pooled analysis of six phase III clinical trials. Ann Rheum Dis. 2022;81(2):206-213. doi:10.1136/annrheumdis-2021-220822 [PubMed 34615638]*

42. *Yamaoka K, Tanaka Y, Kameda H, et al. The safety profile of upadacitinib in patients with rheumatoid arthritis in Japan. Drug Saf. 2021;44(6):711-722. doi:10.1007/s40264-021-01067-x [PubMed 34041702]*

43. *Ytterberg SR, Bhatt DL, Mikuls TR, et al. Cardiovascular and cancer risk with tofacitinib in rheumatoid arthritis. N Engl J Med. 2022;386(4):316-326. doi:10.1056/NEJMoa2109927 [PubMed 35081280]*

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