Tofacitinib (Xeljanz®)

Tofacitinib (Xeljanz) 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. JAKs inhibitors prevent the phosphorylation and activation of Signal Transducers and Activators of Transcription (STATs) which modulate intracellular activity including gene expression. JAK enzymes transmit cytokine signaling through pairing of JAKs, with tofacitinib inhibiting the in vitro activities of JAK1/JAK2, JAK1/JAK3, and JAK2/JAK2.

Resources from Manufacturer

Patient Medication Guide

Full Prescribing Information

Xeljanz Co-pay Assistance Program

Xelsource Patient Assistance Program

Indications and Dosing in Rheumatology

Tofacitinib is indicated for:

- Adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more TNF blockers
- Adults with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to one or more TNF blockers
- Adults with active ankylosing spondylitis (AS) who have had an inadequate response or intolerance to one or more TNF blockers
- Adults with moderately to severely active ulcerative colitis (UC) who have had an inadequate response or intolerance to TNF blockers
- Pediatric patients 2 years of age and older with active polyarticular course juvenile idiopathic arthritis (pcJIA) and have had an inadequate response or intolerance to one or more TNF blockers

continued

Indications and Dosing in Rheumatology *continued*

Dosing:

For RA, PsA, and AS:

- 5 mg by mouth twice daily, or 11 mg XR by mouth once daily
- May be used in combination with nonbiologic DMARDs
- Recommended dosage is 5 mg once daily in patients with:
  - ❑ Moderate or severe renal impairment
  - ❑ Moderate hepatic impairment
  - ❑ Strong CYP3A4 inhibitors, or moderate CYP3A4 inhibitors with strong CPY2C19 inhibitors
  - ❑ For patients undergoing hemodialysis, administer dose after dialysis session

For pcJIA:

- Weight ≥ 10 kg – 20 kg: 3.2 mg (3.2 mL oral solution) twice daily
- Weight ≥ 20 kg – 40 mg: 4 mg (4 mL oral solution) twice daily
- Weight ≥ 40 kg: 5 mg (5 mg tablet or 5 mL oral solution) twice daily

Interrupt dosing if laboratory abnormalities occur in absolute neutrophil count (ANC), absolute lymphocyte count (ALC), or hemoglobin:

	Threshold	Recommendation
ANC	500-1,000 cells/mm3	Hold treatment until ANC >1,000, then resume
	<500 cells/mm3	Discontinue tofacitinib after confirmed by repeat testing
ALC	<500 cells/mm3	Discontinue tofacitinib after confirmed by repeat testing
Hemoglobin	< 8 g/dL, or Decrease of >2 g/dL	Hold treatment until hemoglobin values have normalized

Contraindications

None

continued

ACR/ARP Medication Guide

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The Interprofessional Division of the American College of Rheumatology

Black Box Warnings

- Serious Infections–Avoid use during an active serious infection, including localized infection.
- Tuberculosis–Evaluate and test for latent or active infection prior to and during administration of tofacitinib.
- Viral reactivation–Screen for hepatitis infections prior to therapy. The risk of herpes zoster increased in patients treated with tofacitinib.
- Mortality–Patients 50 years and older with at least one cardiovascular risk factor treated with tofacitinib had a higher observed rate of all-cause mortality.
- Malignancy–Lymphomas and solid cancers were observed in clinical trials.
- Major adverse cardiovascular events–Patients 50 years and older with at least one cardiovascular risk factor treated with tofacitinib had a higher rate of major adverse cardiovascular events (MACE) defined as cardiovascular death, non-fatal myocardial infarction (MI), and non-fatal stroke.
- Thrombosis–Pulmonary embolism (PE), deep venous thrombosis (DVT), and arterial thrombosis have occurred in patients treated with tofacitinib.

Warnings and Precautions

- Gastrointestinal perforation–Use with caution in patients who may be at increased risk.
- Hypersensitivity–Reactions such as angioedema and urticaria have been observed in patients receiving tofacitinib.
- Laboratory abnormalities–Monitor for potential change in lymphocytes, neutrophils, hemoglobin, liver enzymes, and lipids.
- Live vaccines–Avoid use with tofacitinib.
- Gastrointestinal obstruction with non-deformable extended-release (XR) formulation–Use XR formulation with caution in patients with pre-existing severe gastrointestinal narrowing (pathologic or iatrogenic).

Adverse Reactions

Most common adverse reactions (≥ 2%):

- Upper respiratory infections
- Nasopharyngitis
- Diarrhea
- Headache
- Elevated cholesterol levels
- Increased creatine phosphokinase
- Herpes zoster

Medication Strength and Preparations

- IR (Immediate Release) Tablets: 5 mg, 10 mg
- XR (Extended Release) Tablets: 11 mg, 22 mg
- Oral solution: 1 mg/mL

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Medication Administration and Storage

- Store in original carton to protect from light
- Store at room temperature, 20°C to 25°C (68°F to 77°F)
- For oral solution, use contents of bottle within 60 days of opening. Discard remaining solution after 60 days.

Oral Administration

- Take by mouth with or without food.
- Swallow tofacitinib XR tablets whole and intact. Do not crush, split, or chew.
- Oral solution is packaged with on press-in bottle adapter and one 5 mL oral dosing syringes with 3.2 mL, 4 mL, and 5 mL graduations. The press-in bottle adapter and oral dosing syringe are not made with natural rubber latex.

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