Tofacitinib (Xeljanz®)

Tofacitinib is a JanusKinase (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 Xeljanz
Full Prescribing Information
Xeljanz Co-pay Assistance Program
Xelsource Patient Assistance Program

FDA-Approved Indications and Dosing in Rheumatology

Tofacitinib/Tofacitinib extended-release (XR) is indicated for:

- Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more TNF blockers.
  - ❏ Limitations of Use: Use of tofacitinib/tofacitinib XR in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.
- Adult patients with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers.
  - ❏ Limitations of Use: Use of tofacitinib/tofacitinib XR in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.
- Adult patients with active ankylosing spondylitis who have had inadequate response or intolerance to one or more TNF blockers.
  - ❏ Limitations of Use: Use of tofacitinib/tofacitinib XR in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.
- Adult patients with moderately to severely active ulcerative colitis (UC), who have had an inadequate response or intolerance to one or more TNF blockers.
  - ❏ Limitations of Use: Use of tofacitinib/tofacitinib XR in combination with biological therapies for UC or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Tofacitinib/tofacitinib oral solution is indicated for:

- Active polyarticular course juvenile idiopathic arthritis (pcJIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more TNF blockers.
  - ❏ Limitations of Use: Use of tofacitinib/tofacitinib oral solution in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

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	
	<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

Black Box Warnings

- Serious Infections–Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to hospitalization or death, including tuberculosis (TB). Interrupt treatment with tofacitinib/tofacitinib XR/tofacitinib Oral Solution if serious infection occurs until the infection is controlled. Test for latent TB before and during therapy; treat latent TB prior to use. Monitor all patients for active TB during treatment, even patients with initial negative latent TB test.
- 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.

ACR/ARP Medication Guide

American College of Rheumatology
Empowering Rheumatology Professionals

Association of Rheumatology Professionals
The Interprofessional Division of the American College of Rheumatology

Warnings and Precautions

1. Serious infections–do not administer with active infection
2. Laboratory abnormalities: Neutropenia, lymphocyte abnormalities, anemia, elevated liver enzymes, lipid abnormalities- monitor lab parameters
3. Gastrointestinal perforation–use with caution in patients who may be at an increased risk (those with diverticulitis or concomitant use of NSAIDs or steroids)
4. Hypersensitivity reactions
5. Live vaccines–avoid use
6. Active hepatic disease or impairment

Adverse Reactions

Most common adverse reactions are:

- Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis: Reported during the first 3 months in rheumatoid arthritis placebo-controlled clinical trials and occurring in ≥2% of patients treated with tofacitinib monotherapy or in combination with DMARDs: upper respiratory tract infection, nasopharyngitis, diarrhea, and headache.
- Ulcerative Colitis: Reported in ≥5% of patients treated with either 5 mg or 10 mg twice daily of tofacitinib and ≥1% greater than reported in patients receiving placebo in either the induction or maintenance clinical trials: nasopharyngitis, elevated cholesterol levels, headache, upper respiratory tract infection, increased blood creatine phosphokinase, rash, diarrhea, and herpes zoster.
- Polyarticular Course Juvenile Idiopathic Arthritis: Consistent with common adverse reactions reported in adult rheumatoid arthritis patients.

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

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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