Psoriatic arthritis, a chronic inflammatory disease that affects the immune system, is characterized by swelling, stiffness, and joint or tendon pain that is often accompanied by skin and nail psoriasis.\(^1\,^2\) Although psoriatic arthritis most often affects the distal joints in the fingers and toes, the disease can also affect the lower back, wrists, knees, and ankles.\(^3\)

Approximately 2.4 million people in the United States have psoriatic arthritis.\(^1\) More than 30% of patients with psoriasis have psoriatic arthritis, and more than 15% of those with psoriasis may have undiagnosed psoriatic arthritis.\(^1\)

Psoriatic arthritis is associated with pain, itching, fatigue, limitations in physical function, and work disability—factors that can have a substantial impact on the patient’s quality of life.\(^4\) The disease is also associated with emotional duress that stems from frustration, embarrassment, and self-consciousness.\(^4\)

Therapies for psoriatic arthritis include nonsteroidal anti-inflammatory drugs; immunosuppressant drugs; traditional disease-modifying antirheumatic drugs (DMARDs); an oral phosphodiesterase-4 inhibitor; and biologic drugs, including a T-cell inhibitor, tumor necrosis factor-alpha inhibitors, interleukin (IL)-17 antagonists, and an IL-12/23 antagonist.\(^2\,^5\) Recently, the first oral Janus kinase (JAK) inhibitor was added to the treatment options for patients with psoriatic arthritis.\(^6\)

**Mechanism of Action**

Tofacitinib/tofacitinib XR inhibits the action of JAKs, which are intracellular enzymes that transmit signals from multiple cytokines or growth factor receptor interactions involved in the pathogenesis of psoriatic arthritis.\(^9\,^10\) These signals are implicated in immune-cell function and hematopoiesis. JAKs activate and phosphorylate Signal Transducers and Activators of Transcription (STATs), a process that affects intracellular activity, including gene expression.\(^9\) Tofacitinib inhibits the JAK-signaling pathway, thereby preventing the activation and phosphorylation of STATs.\(^9\) Furthermore, tofacitinib may regulate multiple pathways associated with the stimulation and proliferation of inflammatory cells in psoriatic arthritis.\(^9\,^10\,^11\)

**Dosing and Administration**

For patients with psoriatic arthritis, the recommended dose of tofacitinib is 5 mg twice daily, and the recommended dose of tofacitinib XR is 11 mg once daily, both used in combination with nonbiologic DMARDs.\(^9\)

Tofacitinib is available as a 5-mg tablet, and tofacitinib XR is available as an 11-mg tablet.\(^9\)

**Pivotal Clinical Trials**

The safety and efficacy of tofacitinib were evaluated in 2 randomized, double-blind, placebo-controlled trials—OPAL Broaden and OPAL Beyond—that included 816 adult patients.\(^9\,^10\,^12\) Eligible patients had active psoriatic arthritis for at least 6 months and had received a stable dose of a nonbiologic DMARD at baseline.\(^9\) The primary end points in both studies were the American College of Rheumatology (ACR)20 response rate (20% improve-
ment from baseline across several specific measures) and the change from baseline in the Health Assessment Questionnaire-Disability Index (HAQ-DI) at month 3.9

At 3 months in the OPAL Broaden study, patients who received tofacitinib had significantly greater (P ≤.05) ACR20, ACR50, and ACR70 response rates compared with placebo (Table 1).9 In the OPAL Beyond study, the difference between tofacitinib and placebo was significant (P ≤.05) in ACR20 and ACR50 responses, but not significant (P >.5) in ACR70 responses (Table 2).9

In both studies, patients who received tofacitinib 5 mg or 10 mg twice daily achieved a significantly greater (P ≤.05) improvement in physical functioning (as measured by HAQ-DI score) versus placebo at 3 months.9

### Adverse Reactions

The most common (≥2%) of patients who received tofacitinib monotherapy or in combination with DMARDs) adverse reactions reported during the first 3 months of treatment with tofacitinib 5 mg twice daily or tofacitinib 10 mg twice daily were upper respiratory tract infections, headache, diarrhea, and nasopharyngitis.9 The most common serious adverse reactions reported with tofacitinib were infections. Overall, 4% of patients who received tofacitinib and 3% of patients who received placebo discontinued treatment because of adverse reactions in the double-blind, placebo-controlled clinical trials.9 Tofacitinib has no contraindications.9

### Drug Interactions

Tofacitinib/tofacitinib XR is not recommended for use in combination with biologic DMARDs or with potent immunosuppressant drugs, such as azathioprine and cyclosporine.9

The co-administration of potent cytochrome (CYP) P450 CYP3A4 inhibitors (eg, ketoconazole) with tofacitinib increases the exposure of tofacitinib. For patients who receive a potent CYP3A4 inhibitor, the recommended dose of tofacitinib is 5 mg once daily.9

For patients who receive ≥1 concomitant drugs that result in moderate inhibition of CYP3A4 and potent inhibition of CYP2C19 (eg, fluconazole), the recommended dose of tofacitinib is 5 mg once daily.9

The co-administration of potent inducers of CYP3A4 (eg, rifampin) with tofacitinib may result in a reduction or a loss of clinical response to tofacitinib. The co-administration of CYP3A4 inducers with tofacitinib is not recommended.9

### Use in Specific Populations

Women of reproductive potential should use contraception during tofacitinib therapy and for at least 4 weeks after the last dose.9

### Warnings and Precautions

Tofacitinib was approved with a boxed warning about the risk for serious infections and malignancies, including lymphoma. Serious infections, including tuberculosis and bacterial, invasive fungal, viral, and other opportu-
nistic infections, have been reported with tofacitinib.\textsuperscript{9}

Lymphoma and other malignancies have been reported with tofacitinib, as well as an increased Epstein-Barr virus–associated posttransplant lymphoproliferative disorder in patients who received tofacitinib plus immunosuppressive drugs.\textsuperscript{9}

Tofacitinib should be used with caution in patients at risk for gastrointestinal perforations.\textsuperscript{9}

Patients should be monitored for changes in lymphocytes, neutrophils, hemoglobin, liver enzymes, and lipid levels.\textsuperscript{9}

Immunizations should be updated before starting treatment with tofacitinib. Live vaccines should not be administered with tofacitinib.\textsuperscript{9}

Conclusion

The FDA approval of a new indication for tofacitinib and tofacitinib XR marks the availability of a novel oral option for appropriate patients with active psoriatic arthritis. In 2 clinical trials, tofacitinib demonstrated greater response rates in ACR20, ACR50, and ACR70 and in physical functionality, based on HAQ-DI assessment, compared with placebo.\hfill

References


