tacitinib (toe-fa-sye-ti-nib)

Scleroderma

Therapeutic: antirheumatics
Pharmacologic: kinase inhibitors

Pregnancy Category C

Indications

Treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate. Can be used as monotherapy or with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs). Not be used with biologic DMARDs or potent immunosuppressants including azathioprine and cyclosporine.

Action

Acts as a Janus kinase (JAK) inhibitor. Some results of inhibition include decreased hematopoiesis and immune cell function. Decreases circulating killer cells, increases in B cell count and decreases serum C-reactive protein (CRP). Therapeutic Effects: Improvement in clinical and symptomatic parameters of rheumatoid arthritis.

Pharmacokinetics

Absorption: Well absorbed following oral administration (74%).
Distribution: Distributes equally between red blood cells and plasma.
Metabolism and Excretion: 70% metabolized by the liver (primarily CYP3A4 with some contribution from CYP2C19). 30% renal excretion of the parent drug.
Half-life: 3 hr.

TIME/ACTION PROFILE (clinical improvement)

ROUTE ONSET PEAK DURATION
PO within 2 wk 3 mo unknown

Contraindications/Precautions

Contraindicated in: Active infections; administration of live vaccines; Severe hepatic impairment; Lymphocyte count < 500 cells/mm³; absolute neutrophil count (ANC) < 1000 cells/mm³; or hemoglobin levels < 9 g/dL. Lactation: Should not be used in nursing mothers.

Use Cautiously in: Patients with risk of gastric perforation; Direct: Indication risk may be 0.4% for gastric perforation. Dose: 5 mg twice daily.

Adverse Reactions/Side Effects

CNS: headache, fatigue, dizziness, tremor, confusion, pruritus, insomnia.
CV: peripheral edema.
GI: GI perforation, abdominal pain, nausea, vomiting, diarrhea, dyspepsia, gastritis, liver enzymes, vomiting.
GU: serum creatinine.
Derm: rash, pruritus, urticaria, stomatitis.
F and E: dehydration.
Metab: lipids.
MS: arthralgia, joint swelling, musculoskeletal pain, tendinitis.
Nervous system: Meningeal signs, myelopathy, seizures, peripheral neuropathy.
Other: serious infections including tuberculosis, other opportunistic pathogens, risk of malignancy.

Interactions

Drug-Drug: May increase risk of adverse reactions and rejection response to live vaccines, avoid concurrent use of JAK inhibitors and live vaccines. Blood levels and effects may be increased by strong CYP3A4 inhibitors including ketoconazole or moderate CYP3A4 inhibitors/strong CYP2C19 inhibitors including fluconazole; dose adjustments recommended. Blood levels and effectiveness may be decreased by strong CYP3A4 inducers including rifampin. Blood levels and efficacy may be decreased by concomitant use with other potent immunosuppressants including azathioprine, cyclosporine, tacrolimus, antimicrobials or radiation therapy.

PO (Adults): 5 mg twice daily; Concurrent use of strong CYP3A4 inhibitors or moderate CYP3A4 inhibitors/strong CYP2C19 inhibitors—5 mg once daily; dose adjustment recommended for neutropenia, anemia or infection.
Renal Impairment

PO (Adults): Moderate or severe renal impairment—5 mg once daily.
Hepatic Impairment

PO (Adults): Moderate hepatic impairment—5 mg once daily.

NURSING IMPLICATIONS

Assessment

Assess pain and range of motion before and periodically during therapy.
Assess for signs of infection (fever, dysuria, flu-like symptoms, frequent or painful urination, redness or swelling at the site of a wound), includ-
ing tuberculosis, prior to and periodically during therapy. Tofacitinib is contraindicated in patients with active infection. New infections should be monitored closely; most common are upper respiratory tract infections, bronchitis, and urinary tract infections. Infections may be fatal, especially in patients taking immunosuppressive therapy.

- Assess for signs and symptoms of systemic fungal infections (fever, malaise, weight loss, sweats, cough, dyspnea, pulmonary infiltrates, sepsis-like illness with or without coexistent shock). Assess if patient lives in or has traveled to areas of endemic mycoses. Consider empiric antifungal treatment for patients at risk of histoplasmosis and other invasive fungal infections until the pathogens are identified. Consult with an infectious diseases specialist. Consider stopping tofacitinib until the infection has been diagnosed and adequately treated.

- **Lab Test Considerations:** Monitor CBC prior to and periodically during therapy. Do not initiate tofacitinib in patients with lymphocyte count < 500 cells/mm³, an absolute neutrophil count (ANC) < 1000 cells/mm³, or who have hemoglobin level < 9 g/dL.

- Monitor lymphocyte count at baseline and every 3 mo thereafter. If lymphocyte count < 500 cells/mm³ maintain dose. If lymphocyte count < 500 cells/mm³ and confirmed by repeat testing, discontinue tofacitinib.

- Monitor neutrophil count at baseline, after 4–8 wks of therapy, and every 3 mo thereafter. If ANC < 1000 cells/mm³, maintain dose. If ANC 500–1000 cells/mm³, for persistent decreases in this range, interrupt dosing until ANC is > 1000 cells/mm³. If ANC < 500 cells/mm³ and confirmed by repeat testing, discontinue tofacitinib.

- Monitor hemoglobin at baseline, after 4–8 wks of therapy, and every 3 mo thereafter. If hemoglobin < 2 g/dL decrease and < 9.0 g/dL and confirmed by repeat testing, maintain dose. If hemoglobin < 2 g/dL decrease and < 8.0 g/dL, interrupt administration of tofacitinib until hemoglobin values have normalized.

- Monitor liver enzymes prior to and periodically during therapy.

- Monitor total cholesterol, LDL cholesterol, HDL cholesterol 4–8 wks following initiation of therapy.

**Potential Nursing Diagnoses**

- **Impaired physical mobility (Indications)**
- **Risk for infection (Adverse Reactions)**

**Implementation**

- Administer a tuberculosis skin test prior to administration of tofacitinib. Patients with active latent TB should be treated for TB prior to therapy.
- Immunizations should be current prior to initiation of therapy. Patients on tofacitinib should not receive the vaccines.
- PO: Administer twice daily without regard to food.

**Patient/Family Teaching**

- Instruct patient to take tofacitinib as directed. Advise patient to read Medication Guide before starting and with each Rx refill in case of changes.
- Caution patient to notify health care professional immediately if signs of infection (fever, sweating, chills, muscle aches, cough, shortness of breath, blood in phlegm, weight loss, red, or painful skin sores, diarrhea or stomach pain, burning on urination or urinating more often than normal, feeling very tired) or stomach or intestinal perforation (fever, stomach-area pain that does not go away, change in bowel habits) occur.
- Advise patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken and to consult with health care professional before taking any other medications.
- Instruct patient to notify health care professional of medication regimen prior to treatment or surgery.
- Inform patient of increased risk of lymphoma and other cancers.
- Advise female patients to notify health care professional if pregnancy is planned or suspected or if breast feeding. Encourage patient to contact the pregnancy registry by calling 1-877-311-8972 if pregnant.
- Emphasize the importance of follow-up lab tests to monitor for adverse reactions.

**Evaluation/Desired Outcomes**

- Decreased pain and swelling with improved physical functioning and decreased rate of joint destruction in patients with rheumatoid arthritis.

Why was this drug prescribed for your patient?