Rhofanib®
Tofacitinib

Description

Rhofanib® contains Tofacitinib as an active substance.

Dosage Form & Strengths

5 mg and 10 mg film-coated immediate-release tablets

Mechanism of Action

Tofacitinib inhibits Janus kinase (JAK) enzymes, which are intracellular enzymes involved in stimulating hematopoiesis and immune cell function through a signaling pathway. In response to extracellular cytokine or growth factor signaling, JAKs activate Signal Transducers and Activators of Transcription (STATs), which regulate gene expression and intracellular activity. Inhibition of JAKs prevents cytokine- or growth factor-mediated gene expression and intracellular activity of immune cells, reduces circulating CD16/56+ natural killer cells, serum IgG, IgM, IgA, and C-reactive protein, and increases B cells.

Indications

Tofacitinib is indicated for the following conditions in patients who have had an inadequate response or intolerance to 1 or more Tumor Necrosis Factor (TNF) blockers: *Moderately to severely active Rheumatoid Arthritis*; *Active Ankylosing Spondylitis*; *Active Psoriatic Arthritis*; *Active polyarticular course Juvenile Idiopathic Arthritis*; *Moderately to severely active Ulcerative Colitis*; *Psoriasis* (off-label). Tofacitinib is also indicated for the following indications: *Alopecia Areata* (off-label); *Vitiligo* (off-label); *COVID-19, Hospitalized patients* (For use only as an alternative to baricitinib, for hospitalized patients with significant oxygen requirements (e.g., high-flow oxygen, non-invasive ventilation, mechanical ventilation, extracorporeal membrane oxygenation) and those with lower but increasing oxygen requirements and evidence of systemic inflammation) (off-label).

Limitations of use: For the above indications, the use of tofacitinib in combination with biologic DMARDs, biologic therapies (for ulcerative colitis), or with potent immunosuppressants (e.g., azathioprine, cyclosporine) is not recommended.

Dosing: Adults

- **Rheumatoid Arthritis**
  - For use as adjunctive therapy with non-biologic DMARDs 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–naïve patients with moderate to high disease activity.

  5 mg twice daily (as monotherapy or in combination with methotrexate or other non-biologic DMARDs).

- **Ankylosing Spondylitis**

  5 mg twice daily.

- **Psoriatic Arthritis**

  5 mg twice daily (in combination with non-biologic DMARDs).

- **Ulcerative Colitis**

  Induction: 10 mg twice daily for at least 8 weeks; based on therapeutic response, may continue 10 mg twice daily for a maximum of 16 weeks or transition to maintenance dose.

  - Discontinue therapy if inadequate response achieved after 16 weeks using 10 mg twice daily.

  Maintenance: 5 mg twice daily; if patient experiences loss of response on 5 mg twice daily, then use 10 mg twice daily after assessing the benefits and risks and use for the shortest duration; use lowest effective dose to maintain response.

- **Psoriasis**

  5 mg twice daily is recommended (The recommended dose can be increased up to 10 mg twice daily).

- **Alopecia Areata**

  5 mg twice daily is recommended (The recommended dose can be increased up to 10 mg twice daily).

- **Vitiligo**

  5 mg twice daily is recommended (The recommended dose can be increased up to 10 mg twice daily).

- **COVID-19, Hospitalized patients**

  10 mg twice daily, as part of an appropriate combination regimen, for 14 days or until hospital discharge, whichever is earlier.

Dosing: Pediatrics

- **Polyarticular course Juvenile Idiopathic Arthritis** (Children ≥2 years; weighing ≥10 kg and Adolescents)

  10 to <20 kg: Oral solution (1 mg/mL): 3.2 mg twice daily.
  20 to <40 kg: Oral solution (1 mg/mL): 4 mg twice daily.
  ≥40 kg: Oral solution (1 mg/mL) or immediate-release tablet: 5 mg twice daily.

Dosing in Hepatic and Renal Impairment

Hepatic impairment

- *Mild impairment:* No dosage adjustment necessary.
- *Moderate impairment:* Reduce dose to 5 mg twice daily (if taking 10 mg twice daily) or 5 mg once daily (if taking 5 mg twice daily).
- *Severe impairment:* Use is not recommended (has not been studied in patients with severe hepatic impairment or in patients with hepatitis B or hepatitis C viruses).

Renal Impairment

- *Mild impairment:* No dosage adjustment necessary.
- *Moderate to severe impairment:* Reduce dose to 5 mg twice daily (if taking 10 mg twice daily) or 5 mg once daily (if taking 5 mg twice daily).
- *End-stage renal disease requiring hemodialysis:* Reduce dose to 5 mg twice daily (if taking 10 mg twice daily) or 5 mg once daily (if taking 5 mg twice daily).

  Note: Administer after dialysis session on dialysis days; if dose given prior to dialysis, supplemental dose is not recommended after dialysis session.

Adverse Reactions

>10%: Endocrine & metabolic: Hyperlipidemia (including increased HDL cholesterol [10% to 12%], Increased LDL cholesterol [15% to 19%], Increased serum cholesterol [total: ≤9%], and Increased serum triglycerides [≤9%]); Infection: Infection (20% to 22%; including bacterial infection, BK virus, cryptococcosis, cytomegalovirus disease, fungal infection, histoplasmosis, listeriosis, mycobacterium infection, opportunistic infection, reactivation of HBV, serious infection, tuberculosis [including disseminated], Viral infection [and reactivation]); Respiratory: Nasopharyngitis (3% to 14%).

1% to 10%: Cardiovascular: Hypertension (2%); Dermatologic: Acne vulgaris (≥2%), Skin rash (6%); Gastrointestinal: Diarrhea (3% to 5%), Gastroenteritis (4%), Nausea (4%); Genitourinary: Urinary tract infection (2%); Hematologic & oncologic: Anemia (4%); Infection: Herpes zoster infection (5%; including disseminated cutaneous, meningoencephalitis, ophthalmologic); Nervous system: Headache (3% to 9%); Neuromuscular & skeletal: Increased creatine phosphokinase in blood specimen (3% to 7%); Respiratory: Upper respiratory tract infection (4% to 7%); Miscellaneous: Fever (≥2%).

Reproductive Considerations

- Recommendations for use of tofacitinib to treat rheumatic and musculoskeletal diseases in patients planning to become pregnant or who are planning to father a child are not available due to lack of data.
- Agents other than tofacitinib are preferred to treat Inflammatory Bowel Disease (IBD) in patients planning to become pregnant. Disease management should be optimized prior to pregnancy.
- Tofacitinib should be avoided or used with caution prior to a planned pregnancy; **discontinue 1 week prior to conception to limit first trimester fetal exposure.**

Pregnancy Considerations

- Outcome data following tofacitinib exposure in pregnancy are limited.
- Placental transfer may be expected based on molecular weight.
- When treatment for IBD is needed in pregnant patients, use of tofacitinib should be avoided at least during the first trimester.

Breastfeeding Considerations

- Recommendations for use of tofacitinib in breastfeeding patients with rheumatic and musculoskeletal diseases are not available due to lack of data.
- Transfer into breast milk may be expected based on molecular weight.
- Tofacitinib is not recommended to treat IBD in patients who are breastfeeding.
- Due to the potential for serious adverse reactions in the breastfed infant, the manufacturer does not recommend breastfeeding during treatment and for at least 18 hours after the last dose of immediate release tofacitinib.

Contraindications

Canadian Labeling

Hypersensitivity to tofacitinib or any component of the formulation; Severe hepatic impairment; Pregnancy; Breastfeeding.

Warnings/ Precautions

Bone marrow suppression (Do not initiate therapy in patients with an anticipated long-term duration of therapy with an absolute lymphocyte count <500 cells/mm^3, ANC <1,000 cells/mm^3, or Hb <9 g/dL); *GI perforations*: Use with caution in patients at increased risk for GI perforation (e.g., history of diverticulitis); *Hepatotoxicity*; *Hypersensitivity*; *Infections including Tuberculosis*; *Interstitial lung disease*; *Lipid abnormalities*; *Malignancy*.

Monitoring Parameters

- Lymphocyte count (baseline and every 3 months thereafter)
- Neutrophil/platelet counts (baseline, after 4 to 8 weeks, and every 3 months thereafter)
- Hemoglobin (baseline, after 4 to 8 weeks, and every 3 months thereafter)
- Lipids (4 to 8 weeks after therapy initiation and periodically)
- LFTs (baseline and periodically)
- Viral hepatitis (prior to initiating therapy in accordance with clinical guidelines)
- Signs/symptoms of infections (including tuberculosis) during and after therapy
- Abdominal symptoms
- Skin examinations (periodically, in patients at increased risk for skin cancer)
- Heart rate and blood pressure at baseline and periodically thereafter.

Storage and Handling

- Store below 30°C and in the original package in order to protect from light and moisture.
- Keep this medicine out of the sight and reach of children.
- Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, placing in storage and administration.

Reference:
Tofacitinib Drug Information, UpToDate Database, Accessed in 2022.

Orchid Pharmed
Sky's the Limit

NANOALVAND