Trexoma®
Methotrexate

**Pre-filled syringe 7.5 mg/0.3 mL, 10 mg/0.4 mL,
15 mg/0.6 mL, 20 mg/0.8 mL, 25 mg/1 mL, 30 mg/0.6 mL**

Dosage Forms and Strengths

7.5 mg/0.3 mL, 10 mg/0.4 mL, 15 mg/0.6 mL, 20 mg/0.8 mL, 25 mg/1 mL, 30 mg/0.6 mL sterile pre-filled syringe for subcutaneous injection.

Contraindications

Known hypersensitivity to methotrexate or any component of the formulation; breastfeeding; females of childbearing potential (until pregnancy is excluded); severe renal impairment (including end-stage renal disease with or without dialysis); concomitant use with nitrous oxide anesthesia. Additional contraindications for patients with psoriasis, rheumatoid arthritis or polyarticular-course juvenile idiopathic arthritis: pregnancy, alcoholism, alcoholic liver disease or other chronic liver disease, immunodeficiency syndromes (overt or laboratory evidence); preexisting blood dyscrasias (e.g. bone marrow hypoplasia, leukopenia, thrombocytopenia, significant anemia).

Warnings/Precautions

Renal impairments (dosing adjustment may be required), bone marrow suppression (usually in high dose), dermatologic toxicity, pregnancy effects (effective contraception during and after treatment is advised in potentially reproductive females and males), gastrointestinal toxicity, hepatotoxicity, hypersensitivity reaction, infections, pneumonitis.

Monitoring Parameters

CBC with differential (complications of hematologic toxicity); liver and renal function tests; hepatitis B and C screening; latent TB screening; dermatologic toxicity assessment; signs and symptoms of infection (during and after treatment); signs and symptoms of pneumonitis (particularly dry, nonproductive cough; fever; dyspnea; hypoxemia; or pulmonary infiltrate); evaluate pregnancy status prior to use in patients who could become pregnant.

Storage and Handling

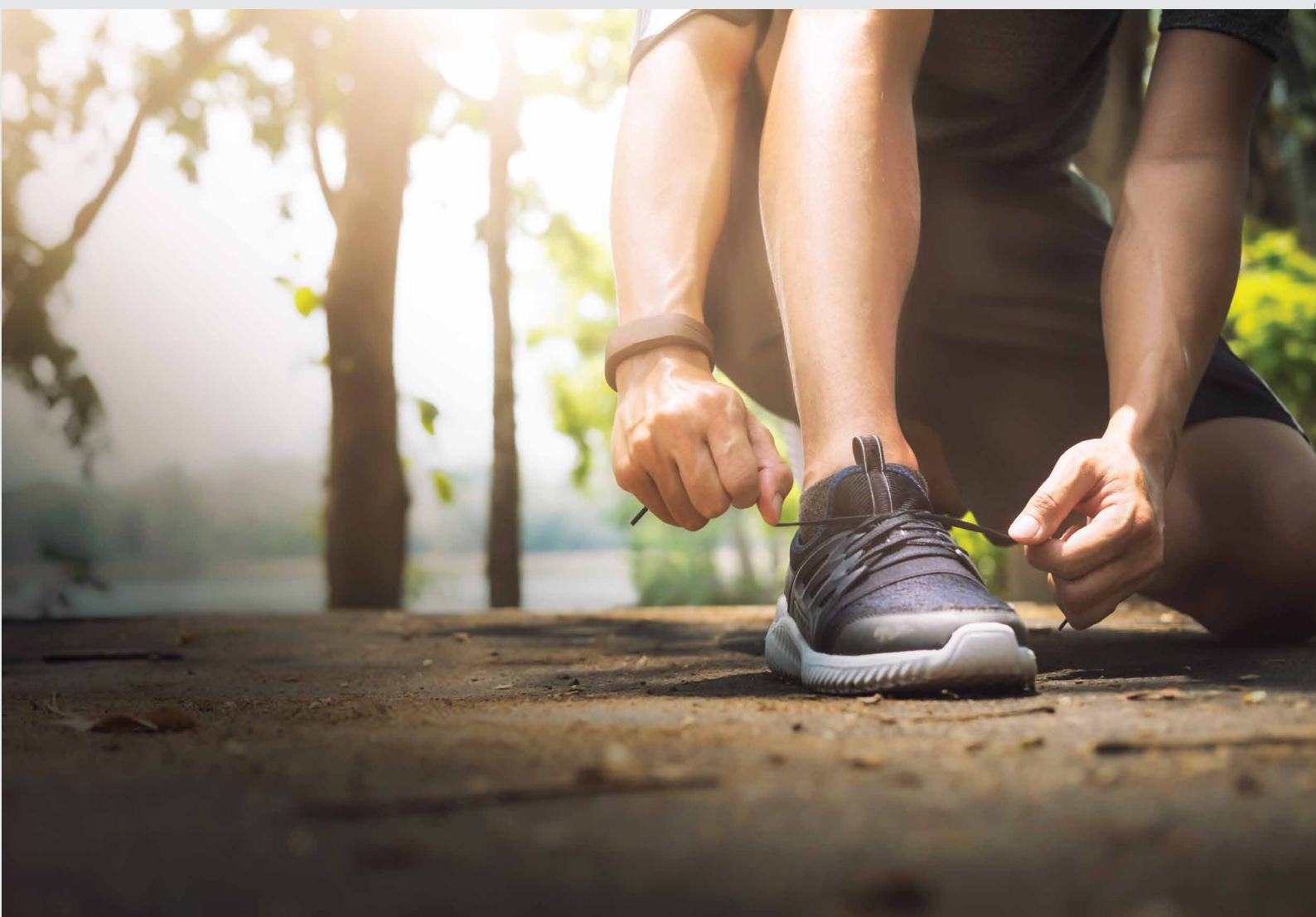
Store TREXOMA® below 25°C. Keep the pre-filled syringe in the outer carton in order to protect it from light. TREXOMA® solution should be yellow in color. Handle and dispose of TREXOMA® is consistent with recommendations for handling and disposal of cytotoxic drugs. Pregnant healthcare personnel should not handle and/or administer TREXOMA®. Methotrexate should not come into contact with the skin or mucosa. In the event of contamination, the affected area must be rinsed immediately with an ample amount of water.

Description

TREXOMA® injection contains methotrexate as an active substance, in a sterile, preservative-free, un-buffered solution. Inactive ingredients include sodium chloride and water for injection. Hydrochloric acid and additional sodium hydroxide may have been added, if necessary, to adjust the pH.

Indications

Along with oncology uses, methotrexate is indicated for symptomatic control of psoriasis (severe, recalcitrant, disabling) that is not adequately responsive to other therapies; severe, active rheumatoid arthritis (RA) that is unresponsive to or intolerant of first-line therapy including full dose nonsteroidal anti-inflammatory agents (NSAIDS), active polyarticular-course juvenile idiopathic arthritis (pJIA) that is unresponsive to or intolerant of first-line therapy including full dose NSAIDs.
Some off-label uses of methotrexate include: Atopic dermatitis (moderate to severe), Crohn's disease (moderate to severe; induction or maintenance of remission), Dermatomyositis/Polymyositis, Eosinophilic granulomatosis with polyangiitis, Giant cell arteritis, acute GVHD, Granulomatosis with polyangiitis, Microscopic polyangiitis, Localized scleroderma, Sarcoidosis (pulmonary), Still disease (moderate to severe), Systemic lupus erythematosus, Systemic sclerosis,Takayasu arteritis.



Adverse reactions

Note: Adverse reactions vary by route, dosage and indication.
The most frequently reported adverse reactions are:
Gastrointestinal: Diarrhea (16%), nausea (31%), oral mucosal ulcer (11%), vomiting (≤11%); Hepatic: Hepatic cirrhosis (chronic therapy; <1% to ≥10%), hepatotoxicity (in patients treated with 1, 2, or 5 g/m^2, grades ≥3: ≥10%), increased liver enzymes (14% to 15%; increased serum alanine aminotransferase: >1×ULN: 20%; >2×ULN: 4%); Nervous system: Dizziness (13%), fatigue (31%), headache (19%); Respiratory: Cough (16%).

Reproductive, Pregnancy and Breastfeeding Considerations

Reproduction

Patients who could become pregnant:
Patients treated for inflammatory bowel disease, psoriasis, or rheumatic and musculoskeletal diseases should discontinue methotrexate at least 3 months prior to becoming pregnant.

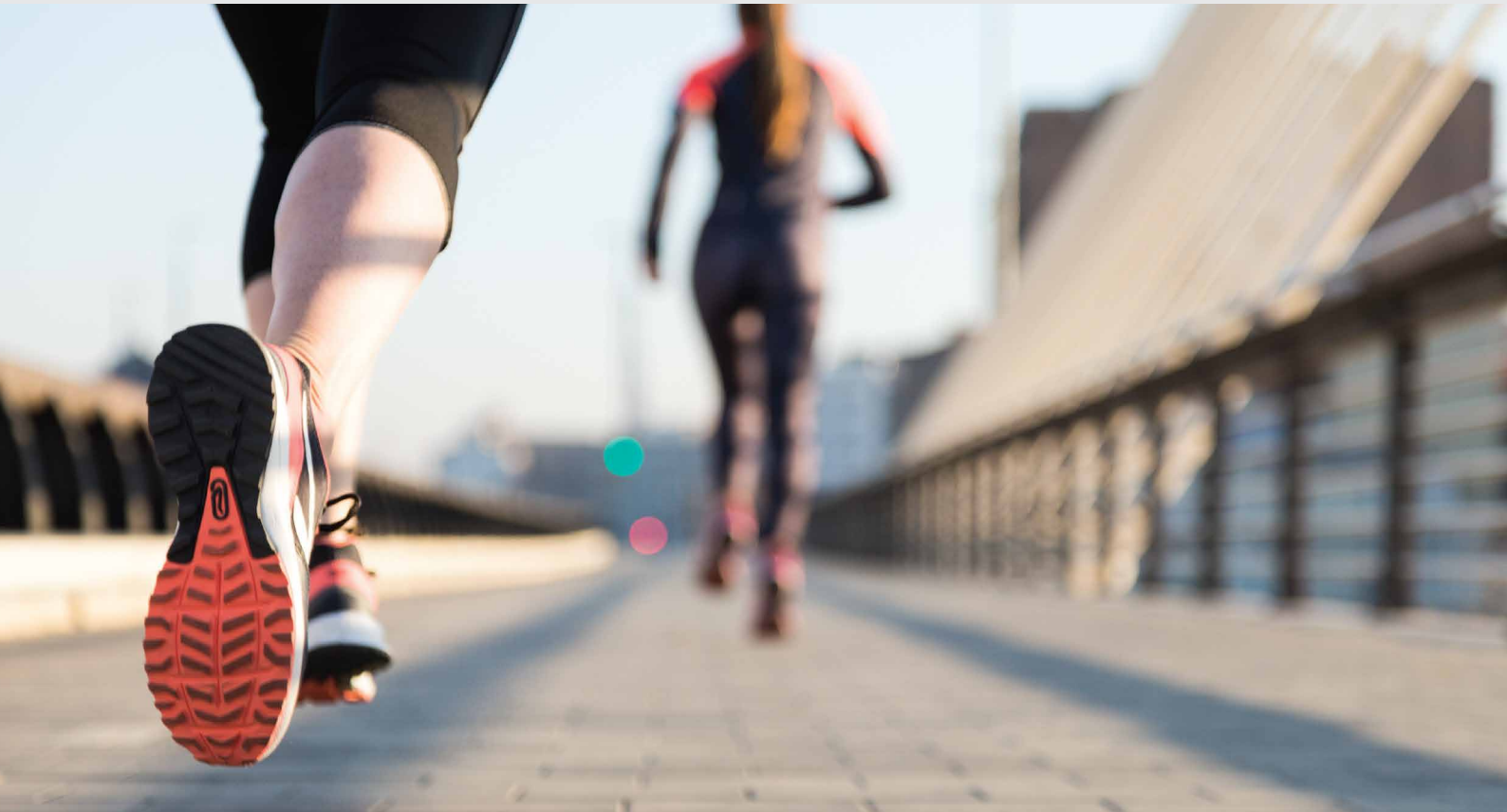
Patients who could father a child:
Use of methotrexate may be considered for patients with rheumatic and musculoskeletal diseases or psoriasis who are planning to father a child (recommendation based on limited human data)

Pregnancy

The use of methotrexate for the treatment of non-neoplastic indications including RA, pJIA, and psoriasis, is contraindicated in pregnancy.

Breastfeeding

Use of methotrexate is not recommended in breastfeeding patients when used for the treatment of inflammatory bowel disease, rheumatic and musculoskeletal diseases or psoriasis.



Mechanism of Action

Methotrexate is a folate antimetabolite that inhibits DNA synthesis, repair, and cellular replication. Methotrexate irreversibly binds to and inhibits dihydrofolate reductase, inhibiting the formation of reduced folates, and thymidylate synthetase, resulting in inhibition of purine and thymidylic acid synthesis, thus interfering with DNA synthesis, repair, and cellular replication. Methotrexate is cell cycle specific for the S phase of the cycle. Actively proliferative tissues are more susceptible to the effects of methotrexate. The mechanism in the treatment of rheumatoid arthritis and polyarticular juvenile idiopathic arthritis is unknown but may affect immune function. In psoriasis, methotrexate is thought to target rapidly proliferating epithelial cells in the skin. In Crohn's disease, it may have immune modulator and anti-inflammatory activity.

Dosing

Note: During chronic therapy, treat with folic acid to reduce the risk of adverse effects; leucovorin may be considered in patients who do not respond to folic acid.

Psoriasis

Initial: 10 to 15 mg given once weekly; Adjust dose gradually (e.g. every 4 to 8 weeks) if needed based on response (usual dosage range: 7.5 to 25mg/week)

Rheumatoid arthritis

Initial: 7.5 to 15 mg once weekly. Increase dose by 2.5 to 5 mg/week every 4 to 12 weeks if needed based on response (maximum: 25 mg/week); current guidelines suggest titrating to a target dose of ≥15 mg/week within 4 to 6 weeks of initiation. Once disease remission is achieved, may gradually reduce dose (e.g. by 2.5 mg/week every 1 to 2 months) to 15 mg/week to limit adverse effects.

Polyarticular juvenile idiopathic arthritis

BSA-directed dosing: children and adolescents: **Initial:** 10 to 15 mg/m² once weekly, adjust gradually up to 20 to 30 mg/m² once weekly; maximum dose: 25 mg/dose.
Weight-directed dosing: children and adolescents: **Initial:** 0.5 mg/kg once weekly; maximum initial dose: 15 mg/dose; if symptoms worsen or are unchanged after 4 weeks, may increase to SUBQ: 1 mg/kg; maximum dose: 25 mg/dose

Crohn's disease

Moderate to severe, induction or maintenance of remission (off-label use)
Initial: 15 to 25 mg once weekly; an initial dose of 12.5 to 15 mg/week may be used when adding to biologic therapy. For lower initial doses, may gradually increase dose (e.g. by 5 mg/week every month) if needed (maximum: 25 mg/week). If remission is sustained after 4 months, may reduce dose to 15 mg/week.

Administration

TREXOMA® is a single-dose pre-filled syringe for once-weekly subcutaneous use in the abdomen or thigh. Patient may self-administer after appropriate training on preparation and administration and appropriate follow-up monitoring. Do not inject within 2 inches of the navel or in areas where the skin is tender, bruised, red, scaly, hard or has scars or stretch marks.

Reference: Methotrexate Drug Information; UpToDate Database; Accessed in October 2023.

Orchid Pharmed
Sky's the Limit

NANOALVAND