CLINICAL UPDATE

Brand Name	RediTrex®
Generic Name	methotrexate
Drug Manufacturer	Cumberland Pharmaceuticals Inc.

Clinical Update

TYPE OF CLINICAL UPDATE

New Brand

FDA APPROVAL DATE

November 27, 2019

LAUNCH DATE

November 17, 2020

REVIEW DESIGNATION

Standard

TYPE OF REVIEW

Type 5 - New Formulation or New Manufacturer

DISPENSING RESTRICTIONS

Specialty Only

Overview

INDICATION(S) FOR USE

RediTrex® is a folate analog metabolic inhibitor indicated for the:

- Management of patients with severe, active rheumatoid arthritis (RA) and polyarticular juvenile idiopathic arthritis (pJIA), who are intolerant of or had an inadequate response to first-line therapy.
- Symptomatic control of severe, recalcitrant, disabling psoriasis in adults who are not adequately responsive to other forms of therapy.

Limitation of Use: RediTrex® is not indicated for the treatment of neoplastic diseases.

MECHANISMS OF ACTION

Methotrexate inhibits dihydrofolic acid reductase. Dihydrofolates must be reduced to tetrahydrofolates by this enzyme before they can be utilized as carriers of one-carbon groups in the synthesis of purine nucleotides and thymidylate. Therefore, methotrexate interferes with DNA synthesis, repair, and cellular replication. Actively proliferating tissues such as malignant cells, bone marrow, fetal cells, buccal and intestinal mucosa, and cells of the urinary bladder are in general more sensitive to this effect of methotrexate. The mechanism of action in rheumatoid arthritis is unknown; it may affect immune function.

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DOSAGE FORM(S) AND STRENGTH(S)

Injection: Single-dose pre-filled syringe (in a needle safety device) delivering methotrexate in the following dosage strengths: 7.5 mg, 10 mg, 12.5 mg, 15 mg, 17.5 mg, 20 mg, 22.5 mg, and 25 mg.

DOSE & ADMINISTRATION

- RediTrex® is for once weekly subcutaneous use only. Administer RediTrex® in the abdomen or thigh.
- Use another formulation of methotrexate for patients requiring oral, intramuscular, intravenous, intra-arterial, or intrathecal dosing, doses less than 7.5 mg per week, doses above 25 mg per week, high-dose regimens, or dose adjustments of less than 2.5 mg increments.
- Starting doses of methotrexate:
    - RA: 7.5 mg once weekly.
    - pJIA: 10 mg/m2 once weekly.
    - Psoriasis: 10 to 25 mg once weekly of an oral, intramuscular, subcutaneous, or intravenous formulation.
- Adjust dose gradually to achieve an optimal response.

EFFICACY

Rheumatoid Arthritis

Clinical trials in patients with rheumatoid arthritis were performed using other formulations of methotrexate. In patients with rheumatoid arthritis, effects of methotrexate on articular swelling and tenderness can be seen as early as 3 to 6 weeks. Most studies of methotrexate in patients with rheumatoid arthritis are relatively short term (3 to 6 months). Limited data from long-term studies indicate that an initial clinical improvement is maintained for at least two years with continued therapy.

Polyarticular Juvenile Idiopathic Arthritis

Clinical trials in patients with polyarticular juvenile idiopathic arthritis were performed using other formulations of methotrexate. In a 6-month double-blind, placebo-controlled trial of 127 pediatric patients with pJIA (mean age, 10.1 years; age range, 2.5 to 18 years; mean duration of disease, 5.1 years) on background nonsteroidal anti-inflammatory drugs and/or prednisone, methotrexate given weekly at an oral dose of 10 mg/m2 provided significant clinical improvement compared to placebo as measured by either the physician's global assessment, or by a patient composite (25% reduction in the articular-severity score plus improvement in parent and physician global assessments of disease activity). Over two-thirds of the patients in this trial had polyarticular-course JIA, and the numerically greatest response was seen in this subgroup treated with 10 mg/m2/wk methotrexate. The overwhelming majority of the remaining patients had systemic-course JIA. All patients were unresponsive to NSAIDs; approximately one-third were using low dose corticosteroids. Weekly methotrexate at a dose of 5 mg/m2 was not significantly more effective than placebo in this trial.