RediTrex™ (methotrexate) – New drug approval

- On December 2, 2019, Cumberland Pharmaceuticals announced the FDA approval of RediTrex (methotrexate) injection, for the management of patients with severe, active rheumatoid arthritis (RA) and polyarticular juvenile idiopathic arthritis (pJIA), and for symptomatic control of severe, recalcitrant, disabling psoriasis in adults.
    - RediTrex is indicated in the management of selected adults with severe, active RA (American College of Rheumatology criteria), or children with active pJIA, who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents.
    - RediTrex is indicated in adults for the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultation. It is important to ensure that a psoriasis "flare" is not due to an undiagnosed concomitant disease affecting immune responses.
    - RediTrex is not indicated for the treatment of neoplastic diseases.
- Methotrexate is also available generically as a tablet and an injection; and as brand autoinjector injections (Otrexup®, Rasuvo®) and an oral solution (Xatmep®).
    - Consult individual drug labels for specific indication information.
- Clinical trials in patients with RA and pJIA were performed using other formulations of methotrexate.
- RediTrex carries a boxed warning for severe toxic reactions, including embryo-fetal toxicity and death.
- RediTrex is contraindicated in pregnancy and in patients who have alcoholism or liver disease, immunodeficiency syndromes, preexisting blood dyscrasias, and hypersensitivity to methotrexate.
- Additional warnings and precautions of RediTrex include organ system toxicity; effects on reproduction; laboratory tests; risks from improper dosing; patients with impaired renal function, ascites, or pleural effusions; dizziness and fatigue; malignant lymphomas; tumor lysis syndrome; and concomitant radiation therapy.
- The most common adverse reactions with RediTrex use were nausea, abdominal pain, dyspepsia, stomatitis/mouth sores, rash, nasopharyngitis, diarrhea, liver function test abnormalities, vomiting, headache, bronchitis, thrombocytopenia, alopecia, leucopenia, pancytopenia, dizziness, photosensitivity, and burning of skin lesions.
- The recommended starting doses of RediTrex for RA and pJIA are 7.5 mg subcutaneously (SC) once weekly and 10 mg/m^2 SC once weekly, respectively.
    - Dosages may be adjusted gradually to achieve an optimal response.
    - Limited experience shows a significant increase in the incidence and severity of serious toxic reactions, especially bone marrow suppression, at doses greater than 20 mg/week in adults.
    - Although there is experience with doses up to 30 mg/m^2/week in children, there are too few published data to assess how doses over 20 mg/m^2/week might affect the risk of serious toxicity in children. Experience does suggest, however, that children receiving 20 to 30

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mg/m^2/week (0.65 to 1.0 mg/kg/week) may have better absorption and fewer gastrointestinal side effects if methotrexate is administered either intramuscularly or SC.
    - Therapeutic response usually begins within 3 to 6 weeks and the patient may continue to improve for another 12 weeks or more. The optimal duration of therapy is unknown.

- The recommended starting dose of RediTrex for psoriasis is 10 to 25 mg SC once weekly.
    - Dosage may be gradually adjusted to achieve optimal clinical response; 30 mg/week should not ordinarily be exceeded.

- RediTrex is a prefilled syringe intended for SC use under the guidance and supervision of a physician.

- Patients may self-inject with RediTrex if a physician determines that it is appropriate, if they have received proper training in how to prepare and administer the correct dose, and if they receive medical follow-up, as necessary.

- Another formulation of methotrexate should be used for alternative dosing in patients who require oral, intramuscular, intravenous, intra-arterial, intrathecal dosing; doses less than 7.5 mg per week; doses more than 25 mg per week; high-dose regimens; or dose adjustments of less than 2.5 mg increments.

- Cumberland Pharmaceuticals' launch plans for RediTrex are pending. RediTrex will be available as a preservative-free solution in prefilled syringes in the following strengths: 7.5 mg, 10 mg, 15 mg, 17.5 mg, 20 mg, 22.5 mg, and 25 mg.