Contains Nonbinding Recommendations

Guidance on Methotrexate Sodium

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Methotrexate Sodium

Form/Route: Tablet/Oral

Recommended studies: 1 study

Type of study: Fasting
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 15 mg
Subjects: Patients with mild to severe psoriasis or RA, who are already on established regimens of 15 mg once a week.
Additional Comments: Pregnant RA or psoriasis patients should not receive methotrexate. RA patients should not receive weekly doses greater than 15 mg. Psoriasis patients should not receive weekly doses exceeding 30 mg. Investigators should refer to the Black Box Warnings, Precautions, Contraindications, Adverse Reactions in the FDA-approved labeling, and follow the directions closely.

Submission of an Investigational New Drug Application (IND) is required prior to the conduct of a bioequivalence study for a cytotoxic drug product. (See 21 C.F.R § 320.31).

Analytes to measure: Methotrexate in plasma

Bioequivalence based on (90% CI): Methotrexate

Waiver request of in-vivo testing: 5 mg, 7.5 mg, and 10 mg based on (i) acceptable bioequivalence studies on the 15 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at http://www.accessdata.fda.gov/scripts/cder/dissolution/. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.