

Draft Guidance on Thiothixene

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Thiothixene

Dosage Form; Route: Capsule; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 5 mg
Subjects: Healthy males and non-pregnant, non-lactating females

Additional comments: To prevent severe dystonia, subjects should be pre-medicated with benztropine tablets, 1 mg every 10 to 12 hours beginning 4 to 6 hours before dosing with thiothixene and continuing for a total of 4 doses to provide coverage during periods of substantial thiothixene levels. In the event of breakthrough acute dystonia, diphenhydramine injection 50 mg could be administered intramuscular (IM) or intravenous (IV).

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2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 5 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: Same as above

Analytes to measure (in appropriate biological fluid): Thiothixene in plasma

Bioequivalence based on (90% CI): Thiothixene

Waiver request of in vivo testing: 1 mg, 2 mg, 10 mg and 20 mg based on (i) acceptable bioequivalence studies on the 5 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: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. 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 abbreviated new drug application (ANDA).