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Draft Guidance on Thiothixene

October 2024

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Active Ingredient: Thiothixene

Dosage Form: Capsule

Route: Oral

Strengths: 1 mg, 2 mg, 5 mg 10 mg, 20 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

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 concentrations. In the event of breakthrough acute dystonia, diphenhydramine injection 50 mg could be administered intramuscular or intravenous.

Analyte to measure: Thiothixene in plasma

Bioequivalence based on (90% CI): Thiothixene

Waiver request of in vivo testing: 1 mg, 2 mg, 10 mg and 20 mg strengths based on (i) acceptable bioequivalence study on the 5 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution. Conduct comparative dissolution testing on 12 dosage units for each of all strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions.*