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Draft Guidance on Trazodone Hydrochloride

October 2024

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Active Ingredient: Trazodone hydrochloride

Dosage Form: Tablet

Route: Oral

Strengths: 50 mg, 100 mg, 150 mg, 300 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 100 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments:
   - Exclude geriatric subjects ≥65 years of age.
   - Exclude any potential subject taking antihypertensive medications.
   - Prohibit concomitant administration of azole antifungals, barbiturates, carbamazepine, central nervous system depressants, digoxin, HIV protease inhibitors, phenothiazines, phenytoin, SSRI antidepressants, and warfarin.
   - Prohibit all herbal preparations containing substances known to affect the cytochrome enzymes.
   - Prohibit alcohol in the study.

Analyte to measure: Trazodone in plasma

Bioequivalence based on (90% CI): Trazodone

Waiver request of in vivo testing: 50 mg, 150 mg, and 300 mg strengths based on (i) an acceptable bioequivalence study on the 100 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*.