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Draft Guidance on Olanzapine

October 2024

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Active ingredient: Olanzapine

Dosage Form: Tablet

Route: Oral

Strengths: 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 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: Exclude geriatric subjects (aged 65 years and over) due to higher incidences of orthostatic hypotension and central nervous system adverse events (e.g., cognitive impairment). Monitor vital signs and adverse events associated with orthostatic hypotension during the study. Subjects should be evaluated prior to discharge for cognitive impairment and instructed not to drive or operate machinery until their cognitive function returns to baseline level. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half- life of olanzapine. Alternatively, a parallel study design may be considered.

Analyte to measure: Olanzapine in plasma

Bioequivalence based on (90% CI): Olanzapine

Waiver request of in-vivo testing: 2.5 mg, 7.5 mg, 10 mg, 15 mg, and 20 mg strengths, based on (i) acceptable bioequivalence study on the 5 mg strength, (ii) acceptable dissolution testing across 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*.