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Draft Guidance on Hydrochlorothiazide; Irbesartan

October 2024

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Active Ingredients: Hydrochlorothiazide; Irbesartan

Dosage Form: Tablet

Route: Oral

Strengths: 12.5 mg; 150 mg, 12.5 mg; 300 mg, 25 mg; 300 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: 12.5 mg; 300 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: None

Analytes to measure: Hydrochlorothiazide and irbesartan in plasma

Bioequivalence based on (90% CI): Hydrochlorothiazide and irbesartan

Waiver request of in vivo testing: 12.5 mg; 150 mg based on (i) acceptable bioequivalence study on the 12.5 mg; 300 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

Note that per Docket No. FDA-2011-P-0822, the FDA determined that the 25 mg; 300 mg strength of the reference listed drug (RLD) was not withdrawn from sale for safety or effectiveness reasons. Should a sponsor choose to pursue approval of the 25 mg; 300 mg strength, the above fasting bioequivalence study should be performed using two tablets of the RLD (2 × 12.5; 150 mg) vs. one tablet of the test product (1 × 25 mg; 300 mg). The 12.5 mg; 150 mg strengths and 12.5 mg; 300 mg are then eligible for a waiver of in vivo testing as outlined above.

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 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*.