Draft Guidance on Hydrochlorothiazide; Triamterene

October 2024

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Active Ingredients: Hydrochlorothiazide; Triamterene

Dosage Form: Capsule

Route: Oral

Strengths: 25 mg; 50 mg, 25 mg; 37.5 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: 25 mg; 50 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: None

Analytes to measure: Hydrochlorothiazide and triamterene in plasma

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

Waiver request of in vivo testing: 25 mg; 37.5 mg strength based on (i) acceptable bioequivalence study on the 25 mg; 50 mg strength; (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both strengths

Hydrochlorothiazide; triamterene, 25 mg; 37.5 mg and 25 mg; 50 mg are the subject of two separate reference listed drug (RLD) products, two separate applications must be submitted for each strength. Applicants may request a waiver of in vivo bioequivalence testing for the 25 mg; 37.5 mg strengths if applicants meet the criteria. Cross-reference the in vivo studies conducted on the higher strength along with your waiver request. Refer to the most recent version of the FDA guidance for industry on *Variations in Drug Products that May Be Included in a Single ANDA*.[a]

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 both strengths of the test product and RLD.[1] Specifications will be determined upon review of the abbreviated new drug application.

Document History:	Recommended October 2008; Finalized August 2017; Revised October 2024
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[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[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*.