Contains Nonbinding Recommendations

Draft Guidance on Hydrochlorothiazide; Triamterene

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Hydrochlorothiazide; Triamterene

Form/Route: Capsules/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way, crossover in-vivo
   Strength: 25 mg/50 mg
   Subjects: Normal healthy males and females, general population
   Additional Comments: Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study.

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2. Type of study: Fed
   Design: Single-dose, two-way, crossover *in-vivo*
   Strength: 25 mg/50 mg
   Subjects: Normal healthy males and females, general population
   Additional comments: Please see comment above.

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 (1) acceptable bioequivalence studies on the 25 mg/50 mg strength; (2) proportional similarity across all strengths and (3) acceptable dissolution testing on all strengths.

Hydrochlorothiazide/Triamterene, 25mg/37.5 mg and 25 mg/50 mg, are the subject of two separate reference products, two separate applications must be submitted for each strength. You may request a waiver of in vivo bioequivalence testing for the 25 mg/37.5 mg strengths if you meet the criteria. Please cross-reference the in-vivo studies conducted on the higher strength along with your waiver request. Please refer to the Guidance for Industry, Variations in Drug Products that May Be Included in a Single ANDA located at: http://www.fda.gov/cder/guidance.

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at http://www.fda.gov/cder/ogd/index.htm. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.