Contains Nonbinding Recommendations

Guidance on Hydrochlorothiazide; Losartan Potassium

This guidance represents 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; Losartan Potassium

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 25 mg/ 100 mg
   Subjects: Normal healthy males and females, general population.
   Additional Comments: Females should not be pregnant, 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/ 100 mg
   Subjects: Normal healthy males and females, general population.
   Additional comments: Please see comments above.

Analytes to measure: Hydrochlorothiazide, losartan, and its carboxylic metabolite* in plasma.

*For the carboxylic acid metabolite, the following data should be submitted: (1) Individual and mean concentration, (2) Individual and mean pharmacokinetic parameters, and (3) Geometric means and ratios of means for AUC and Cmax.

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

Waiver request of in-vivo testing: 12.5 mg/50 mg and 12.5 mg/ 100 mg based on (i) acceptable bioequivalence studies on the 25 mg/100 mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

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.