Contains Nonbinding Recommendations

Guidance on Hydrochlorothiazide; Valsartan

This guidance represents the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Hydrochlorothiazide; Valsartan

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Randomized, single-dose, two-treatment, two-period crossover in vivo
   Strength: 25 mg/ 320 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: Randomized, single-dose, two-treatment, two-period crossover in vivo
   Strength: 25 mg/ 320 mg
   Subjects: Normal healthy males and females, general population
   Additional comments: Please see comment above.

Analytes to measure (in appropriate biological fluid): Valsartan and hydrochlorothiazide in plasma.

Bioequivalence based on (90% CI): Valsartan and hydrochlorothiazide

Waiver request of in vivo testing: 12.5 mg/ 80 mg, 12.5 mg/ 160 mg, 12.5 mg/ 320 mg, 25 mg/ 160 mg based on (i) acceptable bioequivalence studies on the 25 mg/ 320 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. 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 abbreviated new drug application (ANDA).