Contains Nonbinding Recommendations

Draft Guidance on Sacubitril; Valsartan

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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: Sacubitril; Valsartan

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: 97 mg; 103 mg
   Subjects: Healthy males and females (nonpregnant), general population.
   Comments: Female subjects should not be pregnant or lactating, and if applicable, should practice abstinence or contraception during the study.

2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo
   Strength: 97 mg; 103 mg
   Subjects: Healthy males and females (nonpregnant), general population.
   Comments: See comments above.

Analytes to measure (in appropriate biological fluid): Sacubitril and valsartan in plasma

Bioequivalence based on (90% CI): Sacubitril and valsartan

Waiver request of in vivo testing: 24 mg; 26 mg and 49 mg; 51 mg strengths based on (i) acceptable BE studies on the 97 mg; 103 mg strength, (ii) comparable dissolution testing on all strengths, and (iii) proportional similarity in the formulations 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 website 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.