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Draft Guidance on Sacubitril; Valsartan

October 2024

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Active Ingredients: Sacubitril; Valsartan

Dosage Form: Tablet

Route: Oral

Strengths: 24 mg; 26 mg, 49 mg; 51 mg, 97 mg; 103 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: 97 mg; 103 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Female subjects should not be pregnant or lactating, and if applicable, should practice abstinence or contraception during the study.

Analytes to measure: 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 bioequivalence study on the 97 mg; 103 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

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 all strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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[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.*