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Draft Guidance on Sacubitril; Valsartan

November 2025

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In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredients: Sacubitril; Valsartan

Dosage Form: Capsule, pellets

Route: Oral

Strengths: 6 mg; 6 mg, 15 mg; 16 mg

Recommended Study: Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 15 mg; 16 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. Follow the approved drug labeling for the method of administration of this drug product.

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 15 mg; 16 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: See comments above.

Analytes to measure: Sacubitril and valsartan in plasma

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

Waiver request of in vivo testing: 6 mg; 6 mg strength based on (i) acceptable bioequivalence studies on the 15 mg; 16 mg strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both 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 both 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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Unique Agency Identifier: PSG_218591

[1] If the RLD is not available, refer to the most recent version of the guidance for industry *Referencing Approved Drug Products in ANDA Submissions.*