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Draft Guidance on Sacubitril; Valsartan

February 2026

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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: Tablet

Route: Oral

Strengths: 24 mg; 26 mg, 49 mg; 51 mg, 97 mg; 103 mg

Recommended Studies: Two in vivo bioequivalence studies 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 comment: Females of reproductive potential should use effective contraception during the study.

2. Type of study: Fed
   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 comment: See comment above.

Analytes to measure: Sacubitril and valsartan in plasma

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

Waiver request of in vivo testing of additional strengths: Justification based on (i) acceptable bioequivalence studies on the 97 mg; 103 mg strength, (ii) acceptable comparative in vitro dissolution studies between additional strengths and the 97 mg; 103 mg strength using 12 units per strength, and (iii) proportional similarity of the formulations across all strengths

Dissolution: Dissolution test(s) should be included for quality control and to support waiver request of in vivo testing of additional strengths.

Dissolution test method and sampling times: Provide a dissolution method development report for the test product containing information and data that demonstrate appropriateness of the selected dissolution method[1] and sampling times, such as the discriminating ability to detect changes in critical quality attributes that could potentially impact drug product performance.

Document History: Recommended April 2016; Revised October 2024, February 2026

Unique Agency Identifier: PSG_207620

[1] Applicant-developed, United States Pharmacopeia drug product monograph or Dissolution Methods database, https://www.accessdata.fda.gov/scripts/cder/dissolution/index.cfm