*Contains Nonbinding Recommendations*

*Draft – Not for Implementation*

**Draft Guidance on Bosentan**

**November 2025**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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.

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**Active Ingredient:** Bosentan

**Dosage Form:** Tablet

**Route:** Oral

**Strengths:** 62.5 mg, 125 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: 125 mg
   Subjects: Healthy males and healthy females not of reproductive potential
   Additional comments: Bosentan tablet is under a Risk Evaluation and Mitigation Strategy (REMS) with Elements to Assure Safe Use (ETASU), which restricts its use. All pertinent elements of the REMS/ETASU must be incorporated into the protocol and informed consent.

**Analyte to measure:** Bosentan in plasma

**Bioequivalence based on (90% CI):** Bosentan

**Waiver request of in vivo testing:** 62.5 mg strength based on (i) an acceptable bioequivalence study on the 125 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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**Document History:** Recommended September 2010; Revised March 2012, October 2024, November 2025

**Unique Agency Identifier:** PSG_021290

[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*.