

Draft Guidance on Bosentan

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind the FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Bosentan

Form/Route: Tablet/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way, crossover in vivo
Strength: 125 mg
Subjects: Healthy males, general population.
Additional comments: Due to the risk of teratogenicity of bosentan, the study should be conducted in healthy male volunteers. Tracleer® (bosentan) Tablets was approved with a Risk Evaluation and Mitigation Strategy (REMS), which restricts its use. All pertinent elements of the REMS must be incorporated into the protocol and informed consent.

2. Type of study: Fed
Design: Single-dose, two-way, crossover in vivo
Strength: 125 mg
Subjects: Healthy males, general population.
Additional Comments: Please see comment above. Please refer to the Amantadine Hydrochloride Tablet Draft Guidance for additional information regarding fed studies.

Analytes to measure (in appropriate biological fluid): Bosentan in plasma

Bioequivalence based on (90% CI): Bosentan

Waiver request of in vivo testing: 62.5 mg based on (i) acceptable bioequivalence studies on the 125 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths. Please refer to the Mirtazapine Tablet Draft Guidance for additional information regarding waivers of in-vivo testing

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information for this product at this website. Please 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 application