Contains Nonbinding Recommendations

Draft Guidance on Bosentan

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Active Ingredient: Bosentan

Dosage Form; Route: Tablet, for suspension; Oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 32 mg
   Subjects: Heathy adult males
   Additional comments: Due to the risk of teratogenicity of bosentan, the study should be conducted in healthy male volunteers. Tracleer® (bosentan) Tablets for Oral Suspension 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.

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2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 32 mg
   Subjects: Heathy adult males
   Additional comments: See comments above.

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

Bioequivalence based on (90% CI): Bosentan

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. 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 abbreviated new drug application (ANDA).

For additional information on the evaluation of scored tablets, refer to the FDA Guidance on Tablet Scoring[1].

[1] FDA Guidance for Industry – Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation. March 2013. Available at: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm269921.pdf