Contains Nonbinding Recommendations

Draft Guidance on Bosutinib Monohydrate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 100 mg Base
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: Due to the embryo-fetal toxicity of bosutinib, females should avoid pregnancy and use effective method of contraception during the study and continue through one month following the last dose of bosutinib. Males should use effective method of contraception during the study and for at least one month following the last dose of bosutinib.

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2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 100 mg Base
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: See comments above

Analyte to measure (in appropriate biological fluid): Bosutinib in plasma

Bioequivalence based on (90% CI): Bosutinib

Waiver request of in vivo testing: EQ 500 mg Base and EQ 400 Base based on (i) acceptable bioequivalence studies on the EQ 100 mg Base strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

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.