

Draft Guidance on Bosutinib Monohydrate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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: Bosutinib monohydrate

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover, in vivo
Strength: Eq. 100 mg base
Subjects: Healthy males and non-pregnant females, general population
Additional comments: 1) Females should practice abstinence or contraception during the study. 2) Investigators should refer to the FDA-approved labeling and apply appropriate screening and monitoring recommendations for changes in the liver function tests and blood counts along with other relevant recommendations described in the product's package insert. 3) Bioequivalence (BE) study protocols should include provisions for adequate treatment and discontinuation of subjects from the study upon development of hypersensitivity or other adverse reactions, as appropriate.

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2. Type of study: Fed
Design: Single-dose, two-way crossover, in vivo
Strength: Eq. 100 mg base
Subjects: Healthy males and non-pregnant females, general population
Additional comments: Same as above
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Analytes to measure (in appropriate biological fluid): Bosutinib in plasma

Bioequivalence based on (90% CI): Bosutinib

Waiver request of in vivo testing: Eq. 500 mg bosutinib (base) tablet, 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 website 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).