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Draft – Not for Implementation

Draft Guidance on Dasatinib

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Active Ingredient: Dasatinib

Dosage Form: Tablet

Route: Oral

Strengths: 20 mg, 50 mg, 70 mg, 80 mg, 100 mg, 140 mg

Recommended Study: Three in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 100 mg
   Subjects: Healthy males and healthy females not of reproductive potential
   Additional comments:
   - Females not of reproductive potential are recommended due to the risk of embryo-fetal toxicity. Males with female partners of reproductive potential should use effective contraception during the study and for 30 days after the last dose.
   - Applicants may consider using a reference-scaled average bioequivalence approach. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability $\geqslant$30%) for the reference listed drug (RLD).

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 100 mg
Subjects: Healthy males and healthy females not of reproductive potential
Additional comments: See comments above.

3. Type of study: Fasting, in presence of an acid-reducing agent
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 100 mg
Subjects: Healthy males and healthy females not of reproductive potential
Additional comments:
    - A proton pump inhibitor (e.g., rabeprazole) is recommended for the selection of acid-reducing agents to compare gastric pH-dependent pharmacokinetics between the test product and RLD. The elevating effect of a proton pump inhibitor on gastric pH (e.g., mean pH over 24 hours, percentage of the time when the pH ≥4.0 in a 24-hour interval) is dependent on the individual proton pump inhibitor and its dose. Select a proton pump inhibitor that has minimal effect on pharmacokinetics of dasatinib via other interacting mechanisms and a dose that is expected to provide a near maximum effect on gastric acid suppression (i.e., pH elevation). Subjects should be pre-treated with a proton pump inhibitor for several days (e.g., 4 to 5 days) to reach its pharmacodynamic steady-state before administering the test product or RLD.
    - Other additional comments are the same as the fasting study above.

Analyte to measure: Dasatinib in plasma

Bioequivalence based on (90% CI): Dasatinib

Waiver request of in vivo testing: 20 mg, 50 mg, 70 mg, 80 mg, and 140 mg strengths based on (i) acceptable bioequivalence studies on the 100 mg strength, (ii) acceptable in vitro dissolution testing of all the 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 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 all strengths of the test product and RLD.[1] Specifications will be determined upon evaluation of the abbreviated new drug application (ANDA).

[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.*

Alternative approach to establish bioequivalence:
Dasatinib is a biopharmaceutics classification system low solubility drug with pH-dependent solubility. The RLD is formulated to minimize pH-dependent absorption. Therefore, three studies (fasting, fed, and acid-reducing agent study) are recommended.

However, applicants are recommended to discuss their development program with the FDA via the pre-abbreviated new drug application meeting pathway. For additional information, refer to the most recent versions of the guidance for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA*.[a]

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[a] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.