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Draft – Not for Implementation

Draft Guidance on Brigatinib

December 2025

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Active Ingredient: Brigatinib

Dosage Form: Tablet

Route: Oral

Strengths: 30 mg, 90 mg, 180 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 90 mg
   Subjects: Healthy males and healthy females not of reproductive potential
   Additional comments:
   - Exclude geriatric subjects due to potentially increased risk of early onset pulmonary events (EOPEs). Males with female partners of reproductive potential should use effective contraception during the study and for three months after the last dose. Monitor for signs and symptoms of EOPEs (e.g., dyspnea, hypoxia, cough, chest tightness, pneumonia, and pneumonitis) and implement management protocol as needed. Monitor subjects until resolution of events.
   - Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of brigatinib. Alternatively, a parallel study design may be considered.

Analyte to measure: Brigatinib in plasma

Bioequivalence based on (90% CI): Brigatinib

Waiver request of in vivo testing: 30 mg and 180 mg strengths based on (i) an acceptable BE study on the 90 mg 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 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 reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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[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*.