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Draft Guidance on Vorasidenib

November 2025

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Active Ingredient: Vorasidenib

Dosage Form: Tablet

Route: Oral

Strengths: 10 mg, 40 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: 40 mg
   Subjects: Healthy males and healthy females not of reproductive potential
   Additional comments:
   - Exclude subjects with abnormal liver function tests due to potential hepatotoxicity. Exclude current or recent smokers (i.e., user of nicotine-containing products within 3 months prior to dosing) due to potential impact of smoking on pharmacokinetics of vorasidenib. Male subjects with female partners of reproductive potential should use effective contraception during the study and for 3 months after the last dose.
   - Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of vorasidenib. Alternatively, a parallel study design may be considered.

Analyte to measure: Vorasidenib in plasma

Bioequivalence based on (90% CI): Vorasidenib

Waiver request of in vivo testing: 10 mg strength based on (i) an acceptable bioequivalence study on the 40 mg strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both 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 both strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon evaluation 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.*