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Draft Guidance on Enasidenib Mesylate

October 2024

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Active Ingredient: Enasidenib mesylate

Dosage Form: Tablet

Route: Oral

Strengths: EQ 50 mg Base, EQ 100 mg Base

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: EQ 100 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments:
   a. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during the bioequivalence study for at least 1 month after the last dose of enasidenib mesylate tablet.
   b. Enasidenib has a long terminal half-life. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of enasidenib. Alternatively, a parallel study design may be considered.

Analyte to measure: Enasidenib in plasma

Bioequivalence based on (90% CI): Enasidenib

Waiver request of in vivo testing: EQ 50 mg Base strength based on (i) acceptable bioequivalence study on the EQ 100 mg Base 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 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 FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.