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Draft Guidance on Larotrectinib Sulfate

October 2024

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Active Ingredient: Larotrectinib sulfate

Dosage Form: Capsule

Route: Oral

Strengths: EQ 25 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: Females of reproductive potential should use effective contraception during the study and for at least 1 week after the final dose of larotrectinib sulfate. Healthy males with female partners of reproductive potential should use effective contraception during the study and for 1 week after the final dose of larotrectinib sulfate.

Analyte to measure: Larotrectinib in plasma

Bioequivalence based on (90% CI): Larotrectinib

Waiver request of in vivo testing: EQ 25 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*.