Contains Nonbinding Recommendations

Draft Guidance on Larotrectinib Sulfate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Active Ingredient: Larotrectinib sulfate

Dosage Form; Route: Capsule; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 100 mg Base
   Subjects: Males and non-pregnant, non-lactating females, general population
   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. 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.

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2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 100 mg Base
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: See comments above

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 studies on the EQ 100 mg Base strength, (ii) proportional similarity of the formulations between both strengths, and (iii) acceptable in vitro dissolution testing of both strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units for each of both strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.