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Draft Guidance on Berotralstat Hydrochloride

August 2022

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This guidance, which interprets the Agency's regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

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This is a new draft product-specific guidance for industry on generic berotralstat hydrochloride.

Active Ingredient: Berotralstat hydrochloride

Dosage Form; Route: Capsule; oral

Recommended Studies: Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 150 mg Base
   Subjects: Healthy males and non-pregnant and non-lactating females
   Additional comments: Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of berotralstat. Alternatively, a parallel study design may be considered.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 150 mg Base
Subjects: Healthy males and non-pregnant and non-lactating females
Additional comments: See comments above.

Analyte to measure: Berotralstat in plasma

Bioequivalence based on (90% CI): Berotralstat

Waiver request of in vivo testing: EQ 110 mg Base strength based on (i) acceptable bioequivalence studies on the EQ 150 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 each of both strengths of the test and reference products. Specifications will be determined upon review of the ANDA.

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