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Draft Guidance on Cenobamate

November 2021

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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 cenobamate.

Active Ingredient: Cenobamate

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 12.5 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: Exclude subjects with risk factors for shortened QTc interval (e.g., Familial Short QT syndrome). Exclude subjects with a history of drug allergic reactions (e.g., drug rash). If a subject develops a rash, the subject should be discontinued from the study. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of cenobamate. Alternatively, a parallel study design may be considered.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 12.5 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: See comments above

Analyte to measure: Cenobamate in plasma

Bioequivalence based on (90% CI): Cenobamate

Waiver request of in vivo testing: 25 mg, 50 mg, 100 mg, 150 mg, and 200 mg based on (i) acceptable bioequivalence studies on the 12.5 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, (iii) proportional similarity of the formulations across all 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 all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

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