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Draft Guidance on Cenobamate

December 2025

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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Active Ingredient: Cenobamate

Dosage Form: Tablet

Route: Oral

Strengths: 12.5 mg, 25 mg, 50 mg, 100 mg, 150 mg, 200 mg

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: 12.5 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   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.
   - $AUC_{(0\text{-}72h)}$ may be used in place of $AUC_{(0\text{-}t)}$ when comparing the extent of absorption, due to cenobamate's long half-life. Ensure adequate washout periods between treatments in the crossover study. Alternatively, a parallel study design may be considered.

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 strengths based on (i) an acceptable bioequivalence study 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 listed drug (RLD)[1]. Specifications will be determined upon review of the abbreviated new drug application.

Product-specific testing conditions for in vitro feeding tube studies: The approved labeling for the reference product states that the product may be administered by a nasogastric (NG) tube. Conduct the in vitro feeding tube studies, including comparative recovery testing, sedimentation volume and redispersibility testing, and in-use stability in designated dispersion media (i.e., water). For general procedures of in vitro feeding tube studies, refer to the most recent version of the FDA guidance for industry *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations.*[a]

Testing tubes: NG tube (8 FR)

Three types of tube configurations including different materials (e.g., polyvinyl chloride, silicone, polyurethane) and/or different designs (e.g., various numbers of ports and/or eyes, open or closed distal end)

Holding times of 0 and 15 minutes

Report of the pH value of the water

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[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[1] If the RLD is not available, refer to the most recent version of the guidance for industry *Referencing Approved Drug Products in ANDA Submissions.*