

Contains Nonbinding Recommendations

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Draft Guidance on Lamotrigine

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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In May 2008, FDA issued a finalized product-specific guidance for industry on generic lamotrigine. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Lamotrigine

Dosage Form; Route: Tablet, for suspension; 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: 25 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: Subjects should swallow the tablet whole with water and should not chew the tablet. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of lamotrigine. Alternatively, a parallel study design may be considered.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 25 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: See comments above.

Analyte to measure: Lamotrigine in plasma

Bioequivalence based on (90% CI): Lamotrigine

Waiver request of in vivo testing: 2 mg and 5 mg strengths based on (i) acceptable bioequivalence studies on the 25 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (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 for each of all strengths of the test and reference products. Specifications will be determined upon evaluation of the ANDA.

Revision History: Finalized May 2008; Revised August 2022

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