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Draft Guidance on Letrozole

August 2021

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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 We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Letrozole

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: 2.5 mg
   Subjects: Females not of reproductive potential
   Additional comments: Due to potential for impairment of male and female fertility and embryo-fetal toxicity, exclude males and females of reproductive potential. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of letrozole. Alternatively, a parallel study design may be considered.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 2.5 mg
Subjects: Females not of reproductive potential
Additional comments: See comments above.

Analyte to measure: Letrozole in plasma

Bioequivalence based on (90% CI): Letrozole

Waiver request of in vivo testing: Not applicable

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 the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

Revision History: Recommended July 2008; Revised August 2021

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