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Draft Guidance on Mirtazapine

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 We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Mirtazapine

Dosage Form; Route: Tablet, orally disintegrating; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 15 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: The orally disintegrating tablet should be placed on the tongue, allowed to disintegrate, and swallowed without water. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of mirtazapine. Alternatively, a parallel study design may be considered.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 15 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: See comments above

Analyte to measure: Mirtazapine in plasma using an achiral assay

Bioequivalence based on (90% CI): Mirtazapine

Waiver request of in vivo testing: 30 mg and 45 mg based on (i) acceptable bioequivalence studies on the 15 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 each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

Revision History: Recommended May 2007; Finalized May 2008; Revised November 2021

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