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Draft Guidance on Rizatriptan Benzoate

November 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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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 April 2013, FDA issued a draft product-specific guidance for industry on generic rizatriptan benzoate. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Rizatriptan benzoate

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: EQ 10 mg Base
   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. Exclude geriatric subjects due to the greater susceptibility of cardiovascular events and subjects with multiple cardiac risk factors (e.g., diabetes, smoking, obesity). Exclude subjects taking monoamine oxidase-A inhibitors and other medications that may increase the risk for serotonin syndrome.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 10 mg Base
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: See comments above

Analyte to measure: Rizatriptan in plasma

Bioequivalence based on (90% CI): Rizatriptan

Waiver request of in vivo testing: EQ 5 mg Base based on (i) acceptable bioequivalence studies on the EQ 10 mg Base strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both 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 both strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

Revision History: Recommended April 2013; Revised November 2021

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