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Draft Guidance on Esomeprazole Magnesium

August 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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This is a new draft product-specific guidance for industry on generic esomeprazole magnesium.

Active Ingredient: Esomeprazole magnesium

Dosage Form; Route: Tablet, orally disintegrating, delayed release; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 20 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.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 20 mg Base
Subjects: Males and non-pregnant, non-lactating females, general population

Additional comments: See comments above.

Analyte to measure: Esomeprazole in plasma using an achiral assay

Bioequivalence based on (90% CI): Esomeprazole

Additional strengths: Not applicable

Dissolution test method and sampling times:

For modified release drug products, applicants should develop specific discriminating dissolution methods. Alternatively, applicants may use the dissolution method set forth in any related official United States Pharmacopeia (USP) drug product monograph, or in the FDA's database, <http://www.accessdata.fda.gov/scripts/cder/dissolution/>, provided that applicants submit adequate dissolution data supporting the discriminating ability of such a method. If a new dissolution method is developed, submit the dissolution method development and validation report with the complete information/data supporting the proposed method. Conduct comparative dissolution testing on 12 dosage units for each of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

Alcohol dose dumping studies:

Due to concerns of dose dumping of drug from this product when taken with alcohol, conduct additional dissolution testing using various concentrations of ethanol in the dissolution medium as follows:

Testing Conditions: 300 mL, 0.1N HCl, USP Apparatus 2 (paddle) at 100 rpm, with or without alcohol;

Test 1: 12 units tested according to the proposed method (with 0.1 N HCl) with data collected every 15 minutes for a total of 2 hours

Test 2: 12 units analyzed by substituting 5% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Test 3: 12 units analyzed by substituting 20% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Test 4: 12 units analyzed by substituting 40% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Conduct testing on both test and reference products accordingly, and provide data on individual unit, means, range and %CV.

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