

Draft Guidance on Esomeprazole Magnesium

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Active Ingredient: Esomeprazole magnesium

Dosage Form; Route: Delayed release capsule; 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: Applicants may consider using a reference-scaled average bioequivalence approach. If using this approach, provide evidence of high variability in the bioequivalence parameters of AUC and/or C_{max} (i.e., within-subject variability $\geq 30\%$). Refer to the Progesterone Capsule Guidance for additional information regarding highly variable drugs.

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

Waiver request of in vivo testing: Since the Over-the-Counter (OTC) Referenced List Drug (RLD) Esomeprazole Magnesium Delayed Release (DR) Capsule (NDA 204655) is identical to the prescription (Rx) version of RLD (NDA 021153) at the same strength of EQ 20 mg Base, the FDA may deem the bioequivalence between the OTC test and OTC RLD Esomeprazole Magnesium DR Capsules at the same strength of EQ 20 mg Base by cross-referencing the acceptable in vivo bioequivalence studies conducted on the Rx test product and the Rx RLD (NDA 021153) at the same strength of EQ 40 mg Base¹. The deemed bioequivalence may be

¹ See Memorandum to Division of Dockets Management fr. J. Woodcock, Dir., CDER re Docket No. FDA-2011-P-0840, at 1-2 (Jan. 20, 2013).

based on (i) approval of Esomeprazole Magnesium DR capsules for Rx use (EQ 20 mg and 40 mg Base), (ii) both Rx and OTC products have the same formulation composition, are manufactured with the same manufacturing process and process controls, and conform to the same quality standards, and (iii) comparable in vitro dissolution testing of the Rx and OTC capsules. Two separate Abbreviated New Drug Applications (ANDAs) must be submitted since they are the subject of two separate New Drug Applications (NDAs).

The reference product of Esomeprazole Magnesium DR capsules (NDA 204655) has two presentations with a different capsule size (capsule shell size 4 and 5). If applicants develop both presentations of Esomeprazole Magnesium DR capsules under one ANDA, these two presentations should have formulations that are qualitatively and quantitatively the same with an exception of a color and/or capsule shell size. Bioequivalence for the drug product with one presentation may be demonstrated based on the acceptable bioequivalence studies of the drug product with another presentation. In addition, comparable in vitro dissolution should be demonstrated between the two presentations.

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 (available at <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 ANDA.