

Draft Guidance on Esomeprazole Magnesium

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

1. **Type of study:** Fasting
Design: Single-dose, two-way crossover in vivo
Strength: EQ 20 mg base
Subjects: Healthy males, nonpregnant females, general population
Additional Comments: Applicants may consider using a reference-scaled average bioequivalence approach for esomeprazole. 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-way crossover in vivo
Strength: EQ 20 mg base
Subjects: Healthy males, nonpregnant females, general population
Additional Comments: See comments above.
-

Analytes to measure (in appropriate biological fluid): Esomeprazole in plasma using an achiral assay.

Bioequivalence based on (90% CI): Esomeprazole

Waiver request of *in vivo* testing: If 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 base.¹ The deemed bioequivalence may be based on (i) approval of Esomeprazole Magnesium DR Capsule 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).

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website available to the public at the following location: <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 ANDA.

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).