Contains Nonbinding Recommendations

Draft Guidance on Esomeprazole Magnesium

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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: Powder for delayed-release suspension; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 40 mg
   Subjects: Males and non-pregnant females, general population
   Additional comments: Applicants may consider using a reference-scaled average bioequivalence (BE) approach for esomeprazole. If using this approach, provide evidence of high variability in the BE parameters of AUC and/or Cmax (i.e., within-subject variability ≥ 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: 40 mg
   Subjects: Healthy males and non-pregnant 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: EQ 2.5 mg, 5 mg, 10 mg, and 20 mg Base/packet strengths based on (i) acceptable BE studies on the 40 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity in the formulations across all strengths.

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, 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 all strengths of the test and

reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).

Product-specific testing conditions for in vitro feeding tube studies:
The approved labeling for the reference product states that the product may be administered by a nasogastric (NG) or gastric (G) tube. Conduct the in vitro feeding tube studies including comparative recovery testing, particle size distribution, comparative acid resistance stability testing, and sedimentation volume testing (risk assessment). Refer to the Lansoprazole Delayed-Release Orally Disintegrating Tablet Draft Guidance for additional information regarding procedures of in vitro feeding tube studies.

Testing tube: NG tube (6 French), G tube (12 French)

Testing strength: 5 mg, 40 mg

Dispersion medium: 40 mg strength in 15 mL and 5 mg strength in 5 mL water with different pH values (e.g., pH 5.5, 7.0 and 8.5)

Incubation time: 0 and 30 minutes

Testing conditions for acid resistance stability testing**:** 300 mL of 0.1 N HCl maintained at 37 ± 0.5°C; USP Apparatus II at 75 rpm. Measure esomeprazole and analyze the amount of esomeprazole released from the pellets (not from the dissolution medium of 0.1N HCl) at 120 minutes.