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Draft Guidance on Esomeprazole Magnesium

May 2026

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In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient:	Esomeprazole magnesium
Dosage Form:	For suspension, delayed release
Route:	Oral
Strengths:	EQ 2.5 mg Base/Packet | EQ 5 mg Base/Packet | EQ 10 mg Base/Packet | EQ 20 mg Base/Packet | EQ 40 mg Base/Packet
Reference Listed Drugs:	NDA 021957; NDA 022101 (EQ 10 mg Base/Packet)
Recommended Studies:	Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Class of study: Bioequivalence
   Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 40 mg Base/Packet
   Dose: EQ 40 mg Base/Packet administered as 1 packet
   Subjects: Healthy males and non-pregnant, non-lactating females

Study design recommendations:

- Applicants may consider using a reference-scaled average bioequivalence approach for esomeprazole. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability ≥30%) for the reference listed product (RLD).[1] For detailed information on this approach, refer to the guidance for industry *Bioequivalence Studies With Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA*.[a]

2. Class of study: Bioequivalence
Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 40 mg Base/Packet
Dose: EQ 40 mg Base/Packet
Subjects: Healthy males and non-pregnant, non-lactating females
Study design recommendations: See recommendations under Study #1.

Analyte to measure: Esomeprazole in plasma

Bioequivalence based on (90% CI): Esomeprazole

Additional strengths: Bioequivalence of the EQ 2.5 mg Base/Packet, EQ 5 mg Base/Packet, EQ 10 mg Base/Packet, and EQ 20 mg Base/Packet strengths to the corresponding RLD[1] may be demonstrated based on principles laid out in the guidance for industry *Bioequivalence Studies With Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA*.[a]

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 strength of the test product and RLD.[1] Specifications will be determined upon review of the abbreviated new drug application.

Alcohol dose dumping studies: None

Product-specific testing conditions for in vitro feeding tube studies: The approved labeling for the RLD states that the product may be administered by a nasogastric (NG) and gastric (G) tube. Conduct the in vitro enteral tube studies listed below. For general procedures, refer to the guidance for industry *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations*.[a]

[1] If the RLD is not available, refer to the most recent version of the guidance for industry on Referencing Approved Drug Products in ANDA Submissions.

Testing tube: NG tube (6 French), G tube (12 French)
Testing strengths: EQ 5 mg Base/Packet and EQ 40 mg Base/Packet
In vitro enteral tube testing:

1. Comparative recovery testing
    - Three different tube materials (e.g., polyvinylchloride, silicone, polyurethane) and/or designs (e.g., various numbers of ports and/or eyes, retention balloons, open or closed distal end).
        - At least one tube should be tested with an inflated balloon design.
    - Holding times: 0 and 30 minutes
    - Report pH value of the water (e.g., pH 5.5, 7.0 and 8.5)
    - Repeat administration
2. Sedimentation volume and redispersibility testing
3. In-use stability in designated dispersion media (i.e., water)
4. Particle size distribution study
5. Acid resistance stability testing

Dispersion and rinse media: For enteral administration (i.e., feeding tube), add the appropriate amount of water to a catheter-tipped syringe (5 mL for 5 mg EQ Base/packet doses, 15 mL for 40 mg EQ Base/packet doses), followed by the packet contents. Shake the mixture for 15 seconds, allow to thicken for 2-3 minutes, shake it again, and administer within 30 minutes, followed by flushing with an equal amount of water to ensure complete delivery of the medication.

Perform on samples recovered from the comparative recovery study to ensure that administration through NG or G tubes under various conditions does not compromise the acid resistance properties of the enteric-coated pellets. Conduct the testing using 300 mL of 0.1 N HCl maintained at 37 ± 0.5°C in USP Apparatus 2 at 75 rpm for 120 minutes. Measure esomeprazole and analyze the amount of esomeprazole released from the pellets (not from the dissolution medium of 0.1N HCl) at 120 minutes.

Document History: Recommended February 2010; Revised September 2015, February 2018, May 2026

[a] We update guidances periodically. For the most recent version of a guidance, refer to the FDA guidance webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.