

## Draft Guidance on Esomeprazole Magnesium; Naproxen

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

**Active ingredient:** Esomeprazole Magnesium; Naproxen

**Form/Route:** Delayed Release Tablet/Oral

**Recommended study:** 2 studies

1. Type of study: Fasting  
Design: Single-dose, two-way crossover in-vivo  
Strength: EQ 20 mg base/500 mg  
Subjects: Healthy males and nonpregnant females, general population  
Additional comments: Applicants may consider using a reference-scaled average bioequivalence approach for esomeprazole. If using this approach, please provide evidence of high variability in the bioequivalence parameters of AUC and/or C<sub>max</sub> (i.e., within-subject variability  $\geq 30\%$ ). Please 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/500 mg  
Subjects: Healthy males and nonpregnant females, general population  
Additional Comments: Please refer to the Amantadine Hydrochloride Tablet Draft Guidance for additional information regarding fed studies.

---

**Analytes to measure (in appropriate biological fluid):** Esomeprazole in plasma using an achiral assay, and naproxen in plasma

**Bioequivalence based on (90% CI):** Esomeprazole and Naproxen

**Waiver request of in-vivo testing:** EQ 20 mg base/375 mg based on (i) acceptable bioequivalence studies on the EQ 20 mg base/500 mg strength, (ii) acceptable in-vitro dissolution testing of all strengths, and (iii) proportional similarity in the formulations across all strengths. Please refer to the Mirtazapine Tablet Draft Guidance for additional information regarding waivers of in-vivo testing.

**Dissolution test method and sampling times:**

**Please note that a Dissolution Methods Database** is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information for this product at this website. Please 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 application.