

*Contains Nonbinding Recommendations*  
**Draft Guidance on Rabeprazole Sodium**

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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:** Rabeprazole Sodium

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

**Recommended studies:** 2 studies

1. Type of study: Fasting (sprinkle)  
Design: Single-dose, two-way crossover in vivo  
Strength: 10 mg  
Subjects: Healthy males and nonpregnant females, general population.  
Additional Comments: Applicants may consider using a reference-scaled average bioequivalence approach for this drug product. If using this approach, the applicant should provide evidence of high variability in the bioequivalence parameters AUC and/or C<sub>max</sub> (i.e., within-subject variability > 30%). Please refer to the Progesterone Capsule Draft Guidance for additional information regarding highly variable drugs.

Please administer the dose after sprinkling the entire contents of the capsule on a spoonful of applesauce in accordance with the approved labeling of the reference product.

- 
2. Type of study: Fed (sprinkle)  
Design: Single-dose, two-way crossover in vivo  
Strength: 10 mg  
Subjects: Healthy males and nonpregnant females, general population.  
Additional Comments: Please see comments above.

---

**Analytes to measure (in appropriate biological fluid):** Rabeprazole in plasma

**Bioequivalence based on (90% CI):** Rabeprazole

**Waiver request of in vivo testing:** 5 mg based on (i) acceptable bioequivalence studies on the 10 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths.

### **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.

Due to concerns of dose dumping from this drug product when taken with alcohol, please conduct additional dissolution testing using various concentrations of ethanol in the dissolution medium, as follows:

Testing Conditions: 900 mL, 0.1 N HCl, USP apparatus II (paddle) @75 rpm, with or without alcohol:

- Test 1: 12 units tested according to the proposed method (with 0.1N HCl), and data collected every 15 minutes for a total of 2 hours
- Test 2: 12 units tested by substituting 5% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours
- Test 3: 12 units tested by substituting 20% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours
- Test 4: 12 units tested by substituting 40% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours

Both test and RLD products must be tested accordingly and data must be provided on individual unit, means, range and %CV on all strengths.