

## Draft Guidance on Amoxicillin; Omeprazole Magnesium; Rifabutin

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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 Ingredients:** Amoxicillin; Omeprazole magnesium; Rifabutin

**Dosage Form; Route:** Delayed release capsule; oral

**Recommended Studies:** Two studies

1. Type of study: Fasting  
Design: Single-dose, two-treatment, two-period crossover in vivo  
Strength: 250 mg; EQ 10 mg Base; 12.5 mg [recommended dose: 4 capsules (total dose: 1000 mg; EQ 40 mg Base; 50 mg)]  
Subjects: Males and non-pregnant, non-lactating females, general population  
Additional comments: None

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2. Type of study: Fed  
Design: Single-dose, two-treatment, two-period crossover in vivo  
Strength: 250 mg; EQ 10 mg Base; 12.5 mg [recommended dose: 4 capsules (total dose: 1000 mg; EQ 40 mg Base; 50 mg)]  
Subjects: Males and non-pregnant, non-lactating females, general population  
Additional comments: None

**Analytes to measure:** Amoxicillin, omeprazole, and rifabutin in plasma

**Bioequivalence based on (90% CI):** Amoxicillin, omeprazole, and rifabutin

**Additional strengths:** Not applicable

### 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 (available at <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 of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

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

Testing conditions: 900 mL, 0.1 N HCl, USP apparatus 1 (basket) at 100 rpm, with or without alcohol;

Test 1: 12 units tested according to the proposed method (with 0.1N HCl), with data collected every 15 minutes for a total of 2 hours

Test 2: 12 units analyzed 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 analyzed 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 analyzed by substituting 40% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Conduct testing on both test and reference listed drug products accordingly and provide data on individual unit, means, range and %CV.

Omeprazole is acid-labile. Dissolved omeprazole in acidic media can be quickly degraded. Therefore, in the in vitro alcohol dose dumping study, applicants should quantify the remaining amount of omeprazole in the test and reference product after 2 hours of testing for each testing condition specified above (Test 1, Test 2, Test 3 and Test 4).