Contains Nonbinding Recommendations

Draft Guidance on Amoxicillin; Clarithromycin; Omeprazole

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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; Clarithromycin; Omeprazole

Dosage Forms; Route: Capsule, tablet, delayed release capsule; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 500 mg; 500 mg; 20 mg
   Subjects: Males and non-pregnant, non-lactating females, general population

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2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 500 mg; 500 mg; 20 mg
   Subjects: Males and non-pregnant, non-lactating females, general population

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Additional comments: This is a co-packaged product containing amoxicillin 500 mg capsule, clarithromycin 500 mg tablet and omeprazole 20 mg delayed release capsule. For the above studies: (1) The assay method(s) used should be free of interference for each component; (2) The sampling scheme should be adequate to accommodate each product; (3) Applicants can refer to previously conducted in vivo bioequivalence studies for the individual drug products in the co-packaged product (these can be in approved product or in an abbreviated new drug application (ANDA) that is under review for a single component product); (4) Alternatively, applicants may conduct in vivo bioequivalence studies separately for each product; (5) Applicants intending to submit separate ANDAs for individual products contained in the co-packaged product should follow the recommendations in individual product specific guidance for each product.

Analytes to measure: Amoxicillin, clarithromycin and omeprazole in plasma

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

Additional strengths: Not applicable

Dissolution test method and sampling times: Recommended studies are described below for each co-packaged product.

Amoxicillin capsule
Applicants should conduct comparative dissolution testing on 12 dosage units for each of the test and reference products using the methods specified in the current United States Pharmacopeia (USP).

Clarithromycin tablet
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 for each of the test and reference products.

Omeprazole delayed release capsule
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 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.

For all products mentioned above, specifications will be determined upon review of the ANDA.