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Draft Guidance on Amoxicillin; Clavulanate Potassium

August 2022

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

This guidance, which interprets the Agency's regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

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In January 2008, FDA issued a draft product-specific guidance for industry on generic amoxicillin; clavulanate potassium. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredients: Amoxicillin; Clavulanate potassium

Dosage Form; Route: Tablet, chewable; oral

Recommended Studies: Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 400 mg; EQ 57 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comment: The tablet should be chewed, then swallowed without water.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 400 mg; EQ 57 mg Base
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comment: See comment above.

Analytes to measure: Amoxicillin and clavulanic acid in plasma

Bioequivalence based on (90% CI): Amoxicillin and clavulanic acid

Waiver request of in vivo testing: 200 mg; EQ 28.5 mg Base strength based on (i) acceptable bioequivalence studies on the 400 mg; EQ 57 mg Base strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units for each of both strengths of the test and reference products. Specifications will be determined upon review of the ANDA.

Revision History: Recommended January 2008; Revised August 2022

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