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Draft Guidance on Amoxicillin; Clarithromycin; Vonoprazan Fumarate

February 2024

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Active Ingredients: Amoxicillin; Clarithromycin; Vonoprazan fumarate

Dosage Forms: Capsule; Tablet; Tablet

Route: Oral

Strength: 500 mg; 500 mg; EQ 20 mg Base

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: 500 mg; 500 mg; EQ 20 mg Base
   Subject: Healthy males and non-pregnant, non-lactating females
   Additional comments: Exclude subjects with risk factors for prolonged QTc interval and Torsades de Pointes.

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 500 mg; 500 mg; EQ 20 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: See comments above.

Analytes to measure: Amoxicillin, clarithromycin, and vonoprazan in plasma

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

Waiver request of in vivo testing: Not applicable

Additional comments regarding the pharmacokinetic endpoint bioequivalence studies: Since this drug product is co-packaged with amoxicillin capsules, clarithromycin tablets, and vonoprazan fumarate tablets, abbreviated new drug application (ANDA) applicants may: (1) conduct a total of two bioequivalence studies, one under fasting and one under fed conditions, by co-administering amoxicillin capsules, clarithromycin tablets, and vonoprazan fumarate tablets; (2) conduct a total of six bioequivalence studies, separately for amoxicillin capsules, clarithromycin tablets, and vonoprazan fumarate tablets under both fasting and fed conditions; or (3) cross-reference approved applications, such as new drug application or ANDA for the individual components of this co-packaged drug product.

Dissolution test method and sampling times: The dissolution information for each component of this co-packaged 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 the test and reference products. Specifications will be determined upon evaluation of the ANDA.

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