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Draft Guidance on Amlodipine Besylate; Celecoxib

October 2024

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Active Ingredients: Amlodipine besylate; Celecoxib

Dosage Form: Tablet

Route: Oral

Strengths: EQ 2.5 mg Base; 200 mg, EQ 5 mg Base; 200 mg, EQ 10 mg Base; 200 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two- treatment, two-period crossover in vivo
   Strength: EQ 10 mg Base; 200 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Exclude geriatric subjects and subjects with a prior history of gastric ulcer and bleeding as well as allergic reaction from nonsteroidal anti-inflammatory drugs and sulfonamides. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of amlodipine. Alternatively, a parallel study design may be considered. Exclude CYP2C9 poor metabolizers (i.e., CYP2C9*3/*3).

Analytes to measure: Amlodipine and celecoxib in plasma

Bioequivalence based on (90% CI): Amlodipine and celecoxib

Waiver request of in vivo testing: EQ 2.5 mg Base; 200 mg and EQ 5 mg Base; 200 mg strengths based on (i) acceptable bioequivalence study on the EQ 10 mg Base; 200 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: 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 all strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions.*