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Draft – Not for Implementation

Draft Guidance on Amlodipine Besylate; Hydrochlorothiazide; Valsartan

October 2024

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Active Ingredients: Amlodipine besylate; Hydrochlorothiazide; Valsartan

Dosage Form: Tablet

Route: Oral

Strengths: EQ 5 mg Base; 12.5 mg; 160 mg, EQ 5 mg Base; 25 mg; 160 mg, EQ 10 mg Base; 12.5 mg; 160 mg, EQ 10 mg Base; 25 mg; 160 mg, EQ 10 mg Base; 25 mg; 320 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; 25 mg; 320 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: 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.

Analytes to measure: Amlodipine, hydrochlorothiazide, and valsartan in plasma

Bioequivalence based on (90% CI): Amlodipine, hydrochlorothiazide, and valsartan

Waiver request of in vivo testing: EQ 5 mg Base; 12.5 mg; 160 mg, EQ 10 mg Base; 12.5 mg; 160 mg, EQ 5 mg Base; 25 mg; 160 mg, and EQ 10 mg Base; 25 mg; 160 mg strengths based on (i) acceptable bioequivalence study on the EQ 10 mg Base; 25 mg; 320 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*.