Contains Nonbinding Recommendations

Draft Guidance on Aliskiren Hemifumarate; Amlodipine Besylate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Aliskiren Hemifumarate; Amlodipine Besylate

Form/Route: Tablet; Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, partial or fully replicated crossover in vivo
   Strength: EQ 300mg base; EQ 10mg base
   Subjects: Normal healthy males and females, general population
   Additional comments: (1) Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. (2) Applicants may consider using a reference-scaled average bioequivalence approach for Aliskiren Hemifumarate. Provide evidence of high variability in the bioequivalence parameters, AUC and/or Cmax (i.e., within-subject variability ≥ 30%) when using this approach. For general information on this approach, please refer to the Draft Guidance on Progesterone Capsules.

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2. Type of study: Fed
   Design: Single-dose, partial or fully replicated crossover in vivo
   Strength: EQ 300mg base; EQ 10mg base
   Subjects: Normal healthy males and females, general population
   Additional comments: Please see comment above.

Analytes to measure (in appropriate biological fluid): Aliskiren and amlodipine in plasma

Bioequivalence based on (90% CI): Aliskiren and amlodipine

Waiver request of in vivo testing: EQ 300mg base; EQ5 mg base, EQ 150mg base; EQ 10mg base and EQ 150mg base; EQ 5mg base based on (i) acceptable bioequivalence studies on the 300 mg/10 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: Please note that a **Dissolution Methods Database** is available to the public at the OGD website at http://www.accessdata.fda.gov/scripts/cder/dissolution/. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.