Contains Nonbinding Recommendations

Draft Guidance on Amlodipine Besylate; Valsartan

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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: Amlodipine Besylate; Valsartan

Form/Route: Tablets/Oral

Recommended studies: 3 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 10 mg (base); 320 mg
   Subjects: Normal healthy males and females, general population
   Additional Comments: Females should not be pregnant, and if applicable, should practice abstention or contraception during the study.
   As an option, due to the relatively long half-life of amlodipine, you may wish to conduct this study using a single dose, two-way parallel design. As an additional option for either the crossover or parallel design, you may wish to truncate the AUC at 72 hours.

2. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 10 mg (base); 320 mg
   Subjects: Normal healthy males and females, general population
   Additional Comments: Please see comment above.

3. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 10 mg (base); 160 mg
   Subjects: Normal healthy males and females, general population
   Additional Comments: Please see comment above.

Analytes to measure (in appropriate biological fluid): Amlodipine and valsartan in plasma.

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

Waiver request of in-vivo testing: 5 mg (base);160 mg and 5 mg (base);320 mg based on (i) acceptable bioequivalence studies on the 10 mg (base);160 mg and 10 mg (base);320 mg strengths, (ii) acceptable dissolution testing across all strengths, and (iii) proportional similarity in 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.fda.gov/cder/ogd/index.htm. 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.