

Guidance on Amlodipine Besylate; Benazepril Hydrochloride

This guidance represents 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; Benazepril Hydrochloride

Form/Route: Capsules/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover *in-vivo*
Strength: 10 mg/40 mg
Subjects: Normal healthy males and females, general population.
Additional Comments: Female subjects should be excluded from the bioequivalence studies if they are pregnant.

2. Type of study: Fed
Design: Single-dose, two-way crossover *in-vivo*
Strength: 10 mg/40 mg
Subjects: Normal healthy males and females, general population.
Additional comments: Please see comment above.

Analytes to measure: Amlodipine, Benazepril, and active metabolite Benazeprilat in plasma.

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

Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}.

Waiver request of in-vivo testing: 2.5 mg/10 mg, 5 mg/10 mg, 5 mg/20 mg, 5 mg/40 mg and 10 mg/20 mg, based on (i) acceptable bioequivalence studies on the 10 mg/40 mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of 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.