

## Draft Guidance on Amlodipine Besylate; Perindopril Arginine

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

**Active Ingredient:** Amlodipine besylate; Perindopril arginine

**Dosage Form; Route:** Tablet; oral

**Recommended Studies:** Two studies

1. Type of study: Fasting  
Design: Single-dose, two-way crossover in vivo  
Strength: EQ 10mg base/ 14 mg  
Subjects: Healthy males and females (non-pregnant), general population.  
Additional comments: See additional warnings and precautions in the approved drug label

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2. Type of study: Fed  
Design: Single-dose, two-way crossover in vivo  
Strength: EQ 10 mg base/ 14 mg  
Subjects: Healthy males and females (non-pregnant), general population  
Additional comments: See comments above

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**Analytes to measure (in appropriate biological fluid):** Amlodipine, perindopril, and the active metabolite perindoprilat in plasma

**Bioequivalence based on (90% CI):** amlodipine and perindopril

Please submit the metabolite data (perindoprilat) 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<sub>max</sub>.

**Waiver request of in vivo testing:** EQ 5 mg base/7 mg and EQ 2.5 mg base/3.5 mg based on (i) acceptable bioequivalence studies on the EQ 10 mg base/14 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 on the FDA-Recommended Dissolution Methods Web site, available to the public at the following location: <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. 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 abbreviated new drug application (ANDA).