Draft Guidance on Amlodipine Besylate; Perindopril Arginine

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo
   Strength: EQ10 mg base/ 14 mg
   Subjects: Healthy males and females (non-pregnant), general population
   Additional comments: See comments above

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 Cmax.

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

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reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).