Contains Nonbinding Recommendations

Draft Guidance on Ramipril

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way, crossover *in-vivo*
   Strength: 10 mg
   Subjects: Normal healthy males and females, general population
   Additional Comments: Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study.

---

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

Analytes to measure (in appropriate biological fluid): Ramipril and active metabolite, ramiprilat in plasma.

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 Cmax.

Bioequivalence based on (90% CI): Ramipril

Waiver request of in-vivo testing: 1.25 mg, 2.5 mg, and 5 mg based on (i) acceptable bioequivalence studies on the 10 mg strength, (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.