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Draft Guidance on Ramipril

October 2024

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Active Ingredient: Ramipril

Dosage Form: Capsule

Route: Oral

Strengths: 1.25 mg, 2.5 mg, 5 mg, 10 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 10 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Females of reproductive potential should use effective contraception during the study.

Analytes to measure: Ramipril and the metabolite, ramiprilat in plasma

Bioequivalence based on (90% CI): Ramipril

If ramipril can be reliably measured, a confidence interval approach for bioequivalence determination should be used for ramipril. If ramipril cannot be reliably measured, a confidence interval approach for bioequivalence determination should be used for ramiprilat.

Waiver request of in vivo testing: 1.25 mg, 2.5 mg, and 5 mg strengths based on (i) acceptable bioequivalence study on the 10 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 in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units for each of all strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.