

Contains Nonbinding Recommendations
Draft – Not for Implementation
Draft Guidance on Enalapril Maleate
October 2024

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Active Ingredient:	Enalapril maleate
Dosage Form:	Tablet
Route:	Oral
Strengths:	2.5 mg, 5 mg, 10 mg, 20 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: 20 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: Enalapril and active metabolite, enalaprilat in plasma

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}.

Bioequivalence based on (90% CI): Enalapril

Waiver request of in vivo testing: 2.5 mg, 5 mg, and 10 mg strengths based on (i) acceptable bioequivalence study on the 20 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*.