

Guidance on Verapamil Hydrochloride

This guidance represents 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: Verapamil hydrochloride

Dosage Form; Route: Tablets; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 120 mg
Subjects: Normal healthy males and females, general population
Additional Comments: Females should not be pregnant, and if applicable, should practice abstinence or contraception during the study.

2. Type of study: Fed
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 120 mg
Subjects: Normal healthy males and females, general population
Additional comments: Please see comment above

Analytes to measure: Verapamil and its active metabolite, norverapamil 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 C_{max}.

Bioequivalence based on (90% CI): Verapamil

Waiver request of in-vivo testing: 40 mg and 80 mg based on (i) acceptable bioequivalence studies on the 120 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: 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).