

Guidance on Propafenone Hydrochloride

This guidance represents 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: Propafenone Hydrochloride

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 300 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional Comments: Applicants may consider using a reference-scaled average bioequivalence approach for this drug product. If using this approach, the applicant should provide evidence of high variability in the bioequivalence parameters AUC and/or C_{max} (i.e., within-subject variability $\geq 30\%$). For general information on this approach, please refer to Haidar et al., Bioequivalence Approaches for Highly Variable Drugs and Drug Products, Pharm. Res. 25:237-241(2008).

2. Type of study: Fed
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 300 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional comments: Please see comments above.

Analytes to measure: Propafenone and its metabolite, 5-OH propafenone 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): Propafenone

Waiver request of in-vivo testing: 150 mg and 225 mg based on (i) acceptable bioequivalence studies on the 300 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.accessdata.fda.gov/scripts/cder/dissolution/>. 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.