Contains Nonbinding Recommendations

Draft Guidance on Propafenone Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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: Propafenone hydrochloride

Dosage Form; Route: Tablets; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in-vivo
   Strength: 300mg
   Subjects: Healthy males and non-pregnant, non-lactating 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, from the bioequivalence studies, of high variability in the bioequivalence parameters AUC and/or Cmax (i.e., within-subject variability > 30%). For general information on this approach, applicants are encouraged to refer to the Guidance on Progesterone Capsule/Oral.

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

Analytes to measure (in appropriate biological fluid): 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 Cmax.

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: 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).