Contains Nonbinding Recommendations

Draft Guidance on Thioridazine Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: 100 mg
   Subjects: Healthy adult males
   Additional comments: Elderly subjects and subjects with risk factors for prolonged QTc interval and Torsades de Pointes should be excluded from the study. Subjects should be appropriately monitored for electrocardiogram changes during the study.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo
   Strength: 100 mg
   Subjects: Healthy adult males
   Additional comments: See comments above

Analytes to measure (in appropriate biological fluid): Thioridazine and its active metabolite, mesoridazine, 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 area under the plasma concentration time curve and peak drug concentration.

Bioequivalence based on (90% CI): Thioridazine

Waiver request of in vivo testing: 10 mg, 25 mg, and 50 mg strengths based on (i) acceptable bioequivalence studies on the 100 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of 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 the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.