Contains Nonbinding Recommendations

Draft Guidance on Chlorpromazine Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended studies: Three studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 100 mg
   Subjects: Healthy males and non-pregnant, non-lactating females.
   Additional Comments: None

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2. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 100 mg
   Subjects: Healthy males and non-pregnant, non-lactating females.
   Additional comments: None

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3. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 25 mg
   Subjects: Healthy males and non-pregnant, non-lactating females.
   Additional comments: None

Analytes to measure (in appropriate biological fluid): Chlorpromazine and its active metabolite, 7-hydroxychlorpromazine, 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 Cmax.

Bioequivalence based on (90% CI): Chlorpromazine

Waiver request of in-vivo testing: 50 mg and 200 mg based on (i) acceptable bioequivalence studies on the 100 mg strength, (ii) acceptable in-vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths.

Waiver request of in-vivo testing: 10 mg based on (i) acceptable bioequivalence studies on the 25 mg strength, (ii) acceptable in-vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations across both strengths.

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website 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).