

Draft Guidance on Clomipramine Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Capsule; oral

Recommended Studies: Two in vivo studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 25 mg
Subjects: Normal healthy males and nonpregnant females, general population
Additional comments: The study design (e.g., inclusion/exclusion criteria), procedures (e.g., safety monitoring), and concomitant medications (drug interactions) should address all of the elements related to subject safety specified in the RLD label

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 25 mg
Subjects: Normal healthy males and nonpregnant females, general population
Additional comments: Same as comments above

Analytes to measure (in appropriate biological fluid): Clomipramine and its active metabolite desmethyl clomipramine in plasma

Bioequivalence based on (90% CI): Clomipramine

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 (AUC, C_{max} and T_{max}); and geometric means and ratios of means for AUC and C_{max}

Waiver request of in vivo testing: 50 mg and 75 mg strength capsules based on i) acceptable bioequivalence studies on the 25 mg strength, ii) proportional similarity of formulations across all strengths, and iii) acceptable dissolution among 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).