

Draft Guidance on Cyclobenzaprine Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Extended release capsules; oral

Recommended Studies: Three studies

1. Type of study: Fasting
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 30 mg
Subjects: Normal healthy males and non-pregnant, non-lactating females, general population 18 to 65 years of age.

2. Type of study: Fed
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 30 mg
Subjects: Normal healthy males and non-pregnant, non-lactating females, general population 18 to 65 years of age.

3. Type of study: Fasting sprinkle-in-applesauce
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 30 mg
Subjects: Normal healthy males and non-pregnant, non-lactating females, general population 18 to 65 years of age.

Analytes to measure (in appropriate biological fluid): Cyclobenzaprine in plasma

Bioequivalence based on (90% CI): Cyclobenzaprine

Waiver request of in-vivo testing: 15 mg based on (i) acceptable bioequivalence studies on the 30 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/>. 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 abbreviated new drug application (ANDA).

For modified release products, dissolution profiles generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5 and 6.8 buffer, water) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. The following sampling times are recommended: 1, 2, and 4 hours and every 2 hours thereafter, until at least 80% of the drug is dissolved. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for twelve tablets. Specifications will be determined upon review of the data submitted in the application.

Due to a concern of dose dumping of drug from this drug product when taken with alcohol, the Agency currently requests that additional dissolution testing be conducted using various concentrations of ethanol in the dissolution medium, as follows:

Testing Conditions: 900 mL, 0.1 N HCl, USP apparatus 2 (paddle) @50 rpm, with or without alcohol;

Test 1: 12 units tested according to the proposed method (with 0.1N HCl), with data collected every 15 minutes for a total of 2 hours.

Test 2: 12 units analyzed by substituting 5% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours.

Test 3: 12 units analyzed by substituting 20% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours.

Test 4: 12 units analyzed by substituting 40% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours.

Both test and RLD products must be tested accordingly and data must be provided on individual unit, means, range and %CV on both strengths.