

Draft Guidance on Cysteamine Bitartrate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Delayed-released capsules; oral

Recommended Studies: Four in vivo studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: EQ 75 MG BASE at a dose of 600 mg (8xEQ 75 MG BASE)
Subjects: Males and nonpregnant females, general population
Additional comments: Female subjects should not be pregnant or lactating, and, if applicable, should practice abstinence or contraception during the study
2. Type of study: Fed
Design: Single-dose, two-way crossover in vivo
Strength: EQ 75 MG BASE at a dose of 600 mg (8xEQ 75 MG BASE)
Subjects: Males and nonpregnant females, general population
Additional comments: Same as comments above
3. Type of study: Sprinkle
Design: Single-dose, two-way crossover in vivo
Strength: EQ 75 MG BASE at a dose of 600 mg (8xEQ 75 MG BASE)
Subjects: Males and nonpregnant females, general population
Additional comments: a. See comments above. b. Fasting study, with content sprinkled over 4 ounces (1/2 cup) of applesauce in accordance with the approved labeling of the reference listed drug (RLD)
4. Type of study: Sprinkle
Design: Single-dose, two-way crossover in vivo
Strength: EQ 75 MG BASE at a dose of 600 mg (8xEQ 75 MG BASE)
Subjects: Males and nonpregnant females, general population
Additional comments: a. See comments above. b. Fasting study, with content sprinkled in 4 ounces (1/2 cup) of either orange juice or apple juice in accordance with the approved labeling of the RLD

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

Bioequivalence based on (90% CI): Cysteamine

Waiver request of in vivo testing: EQ 25 MG BASE strength based on (i) acceptable bioequivalence studies on the EQ 75 MG BASE strength, (ii) proportional similarity between both strengths, and (iii) acceptable in vitro dissolution testing of both 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 both strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).

Alcohol dose dumping studies:

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: Volume: 1000 mL 0.1N HCl, apparatus 1 (Basket)@75 rpm, with and without the alcohol;

Test 1: Twelve units tested according to the proposed method, with data collected every 15 minutes for a total of 2 hours

Test 2: Twelve 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: Twelve 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: Twelve 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 all strengths.

Product-specific testing conditions for in vitro feeding tube studies:

The approved labeling for the reference product states that the product may be administered by a gastric (G) tube (14 French or larger). Conduct in vitro feeding tube studies including comparative recovery testing with three repeated administrations and particle size distribution study. Refer to the Lansoprazole Delayed-Release Orally Disintegrating Tablet Draft Guidance for additional information regarding procedures of in vitro feeding tube studies.

Testing tube: G tube (14 French)

Testing strength: EQ 75 MG BASE at a dose of 600 mg (8xEQ 75 MG BASE)

Incubation medium: Disperse the capsule contents in 4 ounces of applesauce, followed by flushing 10 mL of fruit juice (except grapefruit juice)

Incubation time: 0 and 30 minutes