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Draft Guidance on Cysteamine Bitartrate

May 2026

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Active Ingredient: Cysteamine bitartrate

Dosage Form: Capsule, delayed release

Route: Oral

Strengths: EQ 25 mg Base | EQ 75 mg Base

Reference Listed Drug: NDA 203389

Recommended Studies: Two in vivo bioequivalence studies with pharmacokinetic endpoints and two in vitro characterization studies

1. Class of study: Bioequivalence
   Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 75 mg Base
   Dose: EQ 150 mg Base administered as 2 capsules
   Subjects: Healthy males and non-pregnant, non-lactating females

2. Class of study: Bioequivalence
   Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover
   Strength: EQ 75 mg Base
   Dose: EQ 150 mg Base administered as 2 capsules
   Subjects: Healthy males and non-pregnant, non-lactating females

Analyte to measure: Cysteamine in plasma

Bioequivalence based on (90% CI): Cysteamine

3.	Class of study:	Characterization
	Type of study:	In vitro dissolution after exposure to soft food and liquid vehicles
	Strength:	EQ 75 mg Base
	Testing vehicles:	120 mL of applesauce, 120 mL of orange juice
	Holding time:	30 minutes
	Dissolution conditions:	(1) Acid stage: 1000 mL, 0.1 N HCl, United States Pharmacopeia (USP) apparatus 1 (basket) at 75 rpm; (2) Buffer stage: 1000 mL, pH 6.8 sodium phosphate buffer, USP apparatus 1 at 75 rpm
	Sampling times: (1)	Acid stage: 2 hours; (2) Buffer stage: 20 and 30 minutes. Use at least 12 dosage units for each of the test product and reference listed drug (RLD).[1] Provide mass balance to account for drug substance present in the vehicles after filtrating and washing and amount present in sample for dissolution.
	Reconstitution:	Open a capsule. Sprinkle and mix capsule contents with vehicle in accordance with the approved labeling of the RLD.

For general procedures of in vitro methods for product quality assessments, refer to the guidance for industry *Use of Liquids and/or Soft Food as Vehicles for Drug Administration: General Considerations for Selection and In Vitro Methods for Product Quality Assessments*.[a]

4.	Class of study:	Characterization
	Type of study:	In vitro dissolution for products with and without capsule shell
	Strength:	EQ 75 mg Base
	Dissolution conditions:	(1) Acid stage: 1000 mL, 0.1 N HCl, USP apparatus 1 at 75 rpm; (2) Buffer stage: 1000 mL, pH 6.8 sodium phosphate buffer, USP apparatus 1 at 75 rpm)
	Sampling times:	(1) Acid stage: 2 hours; (2) Buffer stage: 20 and 30 minutes. Use at least 12 dosage units for each of the test product and RLD. Provide mass balance to account for drug substance present in the vehicles after filtrating and washing and amount present in sample for dissolution.

Bioequivalence of additional strength: Bioequivalence of the EQ 25 mg Base strength to the corresponding RLD strength may be demonstrated based on principles laid out in the guidance for industry *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an Abbreviated New Drug Application*.[a]

[1] If the RLD is not available, refer to the most recent version of the guidance for industry *Referencing Approved Drug Products in ANDA Submissions*.

Dissolution: For modified release drug products, applicants should develop specific discriminating dissolution methods. Alternatively, applicants may use the dissolution method set forth in any related official USP drug product monograph, or in the FDA's database, http://www.accessdata.fda.gov/scripts/cder/dissolution/, provided that applicants submit adequate dissolution data supporting the discriminating ability of such a method. If a new dissolution method is developed, submit the dissolution method development and validation report with the complete information/data supporting the proposed method. Conduct comparative dissolution testing on 12 dosage units for each strength of the test product and the RLD. Specifications will be determined upon review of the abbreviated new drug application.

Alcohol dose dumping studies: None

Product-specific testing conditions for in vitro enteral tube studies: The approved labeling for the RLD states that the product may be administered by a gastric (G) tube (14 French or greater). Conduct the in vitro enteral tube studies below. For general procedures, refer to the guidance for industry *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations*.[a]

Testing tube: G tube (14 French)
Testing strength: EQ 75 mg Base at a dose of EQ 600 mg Base (8 x EQ 75 mg Base)
In vitro enteral tube testing:

1. Comparative recovery testing
    - Three different configurations, defined by materials (e.g., polyvinylchloride, silicone, polyurethane) and/or designs (e.g., number of ports/eyes, open or closed distal end)
        - At least one tube should be tested with an inflated balloon design
    - Repeated administration
    - Reporting the pH value of applesauce
    - Holding times of 0 and 30 minutes
2. Sedimentation volume and redispersibility testing
3. In-use stability in designated dispersion media (i.e., applesauce)
4. Particle size distribution study
5. Conditional acid resistance testing
    - Conduct this testing if the pH of the drug-applesauce dispersion is measured to be ≥ 5.5 at any of the following time points: 0 minutes (initial mix), 30 minutes (end of the in-use holding time), or in the sample collected after it has passed through the tube

Dispersion and rinse media: Disperse the capsule contents in 120 mL of applesauce, followed by flushing 10 mL of water.

Document History: Recommended September 2015; Revised February 2018, May 2026

[a] We update guidances periodically. For the most recent version of a guidance, refer to the FDA guidance webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.