Ciproheptadine Hydrochloride Tablets

Ciproheptadine Hydrochloride Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of \( \text{C}_{21}\text{H}_{21}\text{N} \cdot \text{HCl} \).

Packaging and storage—Preserve in well-closed containers.

USP Reference standards (11)—
USP Ciproheptadine Hydrochloride RS

Identification—Tablets meet the requirements under Identification—Organic Nitrogenous Bases (181).

Dissolution (711)—
Medium: 0.1 N hydrochloric acid; 900 mL.
Apparatus 2: 50 rpm.
Time: 30 minutes.

Procedure—Determine the amount of \( \text{C}_{21}\text{H}_{21}\text{N} \cdot \text{HCl} \) dissolved by employing UV absorption at the wavelength of maximum absorbance at about 285 nm on filtered portions of the solution under test, suitably diluted with Dissolution Medium, if necessary, in comparison with a Standard solution having a known concentration of USP Ciproheptadine Hydrochloride RS in the same Medium.

Tolerances—Not less than 80% \((Q)\) of the labeled amount of \( \text{C}_{21}\text{H}_{21}\text{N} \cdot \text{HCl} \) is dissolved in 30 minutes.

Uniformity of dosage units (905): meet the requirements.

Assay—
Methanesulfonic acid solution—Prepare a solution of methanesulfonic acid in water \( (3:1000) \).

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile, isopropyl alcohol, and Methanesulfonic acid solution \( (20:15:65) \), while mixing adjust with triethylamine to a pH of 4.0 ± 0.05. Make adjustments if necessary (see System Suitability under Chromatography (621)).

Standard preparation—Dissolve an accurately weighed quantity of USP Ciproheptadine Hydrochloride RS in Mobile phase to obtain a solution having a known concentration of about 0.08 mg per mL.

Assay preparation—Transfer a number of Tablets, accurately weighed, equivalent to 80 mg of ciproheptadine hydrochloride, to a 1-\( \text{L} \) volumetric flask, dissolve by sonication in 500 mL of Mobile phase for 15 minutes, and agitate for 30 minutes. Dilute with Mobile phase to volume, and mix. Pass through a filter having a 0.45-\( \mu \)m filter paper.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 285-nm detector and a 3.9-mm \( \times \) 15-cm column that contains packing L1. The flow rate is about 1 mL per minute. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the tailing factor is not more than 2.5; and the relative standard deviation for replicate injections is not more than 2%.

Procedure—Separately inject equal volumes (about 10 \( \mu \)L) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of ciproheptadine hydrochloride \( (\text{C}_{21}\text{H}_{21}\text{N} \cdot \text{HCl}) \) in the portion of Oral Solution taken by the formula:

\[
1000(C / r_U) / (C / r_S) / (C / r_U)
\]

in which \( C \) is the concentration, in mg per mL, of USP Ciproheptadine Hydrochloride RS in the Standard preparation; \( r_U \) and \( r_S \) are the ciproheptadine peak responses obtained from the Assay preparation and the Standard preparation, respectively.

Cyromazine

\( \text{C}_{9}\text{H}_{10}\text{N}_6 \) 166.18

N-Cyclopropyl-1,3,5-triazine-2,4,6-triamine.

2-Cyclopropylamino-4,6-diamino-s-triazine [66215-27-8].

Cyromazine contains not less than 98.0 percent and not more than 102.0 percent of \( \text{C}_{9}\text{H}_{10}\text{N}_6 \), calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

Labeling—Label it to indicate that it is for veterinary use only.

USP Reference standards (11)—
USP Cyromazine RS

Identification—
A: Infrared Absorption (197K).

B: The retention time of the major peak in the chromatogram of the Assay preparation corresponds to that in the chromatogram of the Standard preparation, as obtained in the Assay.

Melting range (741): between 219° and 226°.

Loss on drying (731): Dry it at 105° to a constant weight: it loses not more than 1.0% of its weight.

Residue on ignition (281): not more than 0.1%.

Assay—
Mobile phase—Mix 930 mL of water, 3.72 g of dibasic potassium phosphate, and \( 6.48 \) g of monobasic potassium phosphate. Add 50 mL of methanol and 20 mL of acetonitrile, and mix. Make adjustments if necessary (see System Suitability under Chromatography (621)).

Standard preparation—Dissolve an accurately weighed quantity of USP Cyromazine RS in methanol to obtain a solution having a known concentration of about 0.50 mg per mL. Dilute an aliquot of the resulting solution with Mobile phase to obtain a solution having a known concentration of about 0.10 mg per mL.

Assay preparation—Dissolve an accurately weighed quantity of Cyromazine in methanol to obtain a solution having a known concentration of about 0.50 mg per mL. Dilute an aliquot of the resulting solution with Mobile phase to obtain a solution having a known concentration of about 0.10 mg per mL.
The solution to stand for 5 min before using.

**Cysteine Hydrochloride**

C₆H₇NO₂S · HCl · H₂O 175.63

C₆H₇NO₂S · HCl 157.62

L-Cysteine hydrochloride monohydrate [7048-04-6]. Anhydrous [52-89-1].

**DEFINITION**

Cysteine Hydrochloride is L-cysteine hydrochloride monohydrate and contains NLT 98.5% and NMT 101.5% of L-cysteine hydrochloride (C₆H₇NO₂S · HCl), calculated on the dried basis.

**IDENTIFICATION**

- **A. INFRARED ABSORPTION (197K)**

**ASSAY**

**Change to read:**

- **Procedure**
  
  Sample: 250 mg of Cysteine Hydrochloride
  
  Blank: Proceed as directed in the Analysis without the Sample.
  
  **Titrimetric system (See Titrimetry (541).)**
  
  Mode: Residual titration
  
  Titrant: 0.1 N iodine VS
  
  Back titrant: 0.1 N sodium thiosulfate VS
  
  **Endpoint detection:** Visual
  
  Analysis: Transfer the Sample to an iodine flask. Add 20.0 mL of water and 4 g of potassium iodide, and mix. Cool the solution in an ice bath, and add 5 mL of 3 N hydrochloric acid and 25.0 mL of 0.1 N iodine VS. Insert the stopper, and allow to stand in the dark for 20 min, while remaining in the ice bath. Titrate the excess iodine with the Back titrant. Add 3 mL of starch TS as the endpoint is approached. Perform the Blank determination. Calculate the percentage of cysteine hydrochloride (C₆H₇NO₂S · HCl) in the Sample taken:

  \[
  \text{Result} = \left( \frac{V_b - V_s}{N} \right) \times F \times W \times 100
  \]

  \(V_b\) = Back titrant volume consumed by the Blank (mL)

  \(V_s\) = Back titrant volume consumed by the Sample (mL)

  \(N\) = actual normality of the Back titrant (mEq/mL)

  \(F\) = equivalency factor, 157.6 mg/mEq

  \(W\) = Sample weight (mg)

  **Acceptance criteria:** 98.5%–101.5% on the dried basis

**IMPURITIES**

- **Residue on Ignition (281):** NMT 0.4%
- **Chloride and Sulfate, Sulfate (221)**
  
  Standard solution: 0.10 mL of 0.020 N sulfuric acid
  
  Sample: 0.33 g of Cysteine Hydrochloride
  
  **Acceptance criteria:** NMT 0.03%.
- **Iron (241):** NMT 30 ppm
- **Heavy Metals (231):** NMT 15 ppm
- **Related Compounds**
  
  N-Ethylmaleimide solution: 40 mg/mL of N-ethylmaleimide in alcohol
  
  Standard stock solution: Dissolve 20 mg of USP L-Cysteine Hydrochloride RS in 10.0 mL of water. Add 10.0 mL of N-Ethylmaleimide solution, and mix. Allow the solution to stand for 5 min before using.
  
  **Standard solution:** 0.05 mg/mL from Standard stock solution in water. [Note—This solution has a concentration equivalent to 0.5% of that of the Sample solution.]
  
  **System suitability solution:** Transfer 10 mg of USP L-Tyrosine RS and 10 mL of the Standard stock solution to a 25-mL volumetric flask. Dilute with water to volume.
  
  **Sample stock solution:** Transfer 0.2 g of Cysteine Hydrochloride to a 10-mL volumetric flask, dissolve, and dilute with water to volume.
  
  **Sample solution:** To 5.0 mL of the Sample stock solution add 5.0 mL of N-Ethylmaleimide solution, and mix. Allow the solution to stand for 5 min before using.
  
  **Chromatographic system (See Chromatography (621), Thin-Layer Chromatography.)**
  
  **Mode:** TLC
  
  **Adsorbent:** 0.25-mm layer of chromatographic silica gel mixture
  
  **Application volume:** 5 μL
  
  **Developing solvent system:** Butyl alcohol, glacial acetic acid, and water (3:1:1)
  
  **Spray reagent:** 2 mg/mL of ninhydrin in a mixture of butyl alcohol and 2 N acetic acid (95:5)
  
  **System suitability**
  
  **Suitability requirements:** The chromatogram of the System suitability solution exhibits two clearly separated spots.
  
  **Analysis**
  
  **Samples:** Standard solution, System suitability solution, and Sample solution.
  
  After air-drying the plate, spray with Spray reagent, and heat between 100° and 105° for 15 min. Examine the plate under white light.
  
  **Acceptance criteria:** Any secondary spot of the Sample solution is not larger or more intense than the principal spot of the Standard solution.
  
  **Individual impurities:** NMT 0.5%
  
  **Total impurities:** NMT 2.0%

**SPECIFIC TESTS**

- **Optical Rotation, Specific Rotation (7815)**
  
  Sample solution: 80 mg/mL in 6 N hydrochloric acid
  
  **Acceptance criteria:** +5.7° to +6.8°
- **Loss on Drying (731):** Dry a sample at room temperature at a pressure not exceeding 5 mm of mercury for 24 h: it loses 8.0%–12.0% of its weight.