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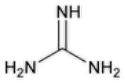
Add the following:

▲Guanidine Hydrochloride



$CH_5N_3 \cdot HCl$ 95.53

Guanidine hydrochloride (1:1);

Guanidine hydrochloride CAS RN®: 50-01-1.

DEFINITION

Guanidine Hydrochloride contains NLT 99.5% and NMT 101.0% of guanidine hydrochloride ($CH_5N_3 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K
- **B. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*:** 197U

  Sample solution: Equivalent to 572 mg/mL of anhydrous Guanidine Hydrochloride

  Analysis: Determine the absorbance of the *Sample solution* at 230, 260, and 275 nm.

  Acceptance criteria

  At 230 nm: NMT 0.2

  At 260 nm: NMT 0.03

  At 275 nm: NMT 0.03
- **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*:** Meets the requirements of test A

ASSAY

- **Procedure**

  Sample solution: 350 mg, previously dried

  Titrimetric system

  (See *Titrimetry* ⟨541⟩.)

  Mode: Direct titration

  Titrant: 0.1 N silver nitrate VS

  Endpoint detection: Potentiometric

  Blank: Mix 10 mL each of water, glacial acetic acid, and 0.2% polyvinyl alcohol and 100 mL of methanol.

  Analysis: Dissolve the *Sample* in 10 mL of water, add 10 mL of glacial acetic acid, 10 mL of 0.2% polyvinyl alcohol, and 100 mL of methanol.

  Titrate with *Titrant* to a potentiometric endpoint. Perform a blank determination.

  Calculate the percentage of guanidine hydrochloride ($CH_5N_3 \cdot HCl$) in the portion of Guanidine Hydrochloride taken:

$$\text{Result} = [(V_S - V_B) \times N_A \times F \times 100]/W$$

V_S = volume of *Titrant* consumed by the *Sample* (mL)

V_B = volume of *Titrant* consumed by the *Blank* (mL)

N_A = actual normality of the *Titrant* (mEq/mL)

F = equivalency factor, 95.53 mg/mEq

W = weight of the *Sample* (mg)

Acceptance criteria: 99.5%–101.0%

IMPURITIES

- **Residue on Ignition ⟨281⟩**

Sample: 2.0 g

Analysis: Heat a quartz crucible at 800° for 30 min, allow to cool in a desiccator, and weigh. Evenly distribute the *Sample* in the crucible and moisten the *Sample* with 0.5 mL of sulfuric acid. Volatilize the *Sample* with a Bunsen burner. Place the crucible in the furnace and ignite the residue at 800° for 15 min or until all carbon has been removed. Cool in a desiccator and weigh.

Acceptance criteria: NMT 0.05%

- **Chloride and Sulfate ⟨221⟩, *Sulfate*:** A 1.0-g portion shows no more sulfate than corresponds to 0.052 mL of 0.02 N sulfuric acid TS (0.005%).

- **Limit of Nitrate**

Standard nitrate solution and **Brucine sulfate solution:** Prepare as directed in *Reagents, Indicators, and Solutions—Buffer Solutions*.

Sample solution: Dissolve 0.40 g in 3.0 mL of water, and add *Brucine sulfate solution* to make 50 mL.

Control solution: To 2.0 mL of *Standard nitrate solution* and 1.0 mL of water, add 0.40 g of Guanidine Hydrochloride, then add *Brucine sulfate solution* to make 50 mL.

Blank: 50.0 mL of *Brucine sulfate solution*

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: Vis

Analytical wavelength: 410 nm

Cell: 1 cm

Analysis: Heat the *Sample solution*, *Control solution*, and *Blank* in a boiling water bath for 15 min with periodic gentle swirling, then cool rapidly in an ice bath to room temperature. Adjust a suitable spectrophotometer with the *Blank* to zero absorbance at 410 nm. Determine the absorbance of the *Sample solution* and the *Control solution*.

Calculate the percentage of nitrate in the portion of Guanidine Hydrochloride taken:

$$\text{Result} = [A_U/(A_C - A_U)] \times F$$

A_U = absorbance of the *Sample solution*

A_C = absorbance of the *Control solution*

F = limit of nitrate, 0.005%

Acceptance criteria: NMT 0.005%

SPECIFIC TESTS

- **Acidity**

Sample: 20 g

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Direct titration

Titrant: 0.1 N sodium hydroxide VS

Endpoint detection: Visual

Analysis: Dissolve the *Sample* in 200 mL of water, add 0.15 mL of phenolphthalein TS, and titrate with *Titrant* to a permanent pink endpoint.

Calculate the percentage of hydrochloric acid in the portion of Guanidine Hydrochloride taken:

$$\text{Result} = [(V_S \times N_A \times F) \times 100/W]$$

V_S = volume of *Titrant* consumed by the *Sample* (mL)

N_A = actual normality of the *Titrant* (mEq/mL)

F = equivalency factor, 0.03646 g/mEq

W = weight of the *Sample* (g)

Acceptance criteria: NMT 0.01%

- **Water-Insoluble Substances**

[NOTE—If intended for use in preparing parenteral dosage forms, it meets the requirements of the *Water-Insoluble Substances* test.]

Sample: 50.0 g

Analysis: Dissolve the *Sample* in 25 mL of ambient temperature water. Use a Teflon-encapsulated magnetic stirring bar and electric stir plate to dissolve the *Sample*, if necessary. Pass the solution through the tared filtering crucible, previously dried at 105 ± 2° for 1 h. Rinse the sample vessel and crucible filter with 50 mL of water. Dry the crucible at 105 ± 2° for 1 h.

Acceptance criteria: NMT 0.05%

• **LOSS ON DRYING** ⟨731⟩

Sample: 2.0 g

Analysis: Dry the *Sample* at 105 ± 2° for 4 h.

Acceptance criteria: NMT 0.5%

• **MELTING RANGE OR TEMPERATURE** ⟨741⟩, *Procedures, Procedure for Class I, Apparatus I*

Analysis: Proceed as directed in the chapter.

[NOTE—Finely grind with a mortar and pestle and dry over silica gel for NLT 16 h before testing.]

Acceptance criteria: 184°–188°

• **BACTERIAL ENDOTOXINS TEST** ⟨85⟩**:** If labeled for use in preparing parenteral dosage forms, it also meets the following requirements. The level of bacterial endotoxins is such that the requirement in the relevant dosage form monograph(s) in which Guanidine Hydrochloride is used can be met. Where the label states that Guanidine Hydrochloride must be subjected to further processing during the preparation of injectable dosage forms, the level of bacterial endotoxins is such that the requirement in the relevant dosage form monograph(s) in which Guanidine Hydrochloride is used can be met.

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store in a dry place and at a temperature below 30°.

• **LABELING:** Where Guanidine Hydrochloride is intended for use in the manufacture of injectable dosage forms, it is so labeled.

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Guanidine Hydrochloride RS▲ (NF 1-Aug-2023)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
GUANIDINE HYDROCHLORIDE	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 50(1)

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