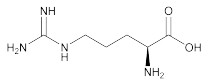
Arginine



$C_6H_{14}N_4O_2$ 174.20
L-Arginine [74-79-3].

DEFINITION
Arginine contains NLT 98.5% and NMT 101.5% of $C_6H_{14}N_4O_2$, as L-arginine, calculated on the dried basis.

IDENTIFICATION
- **INFRARED ABSORPTION ⟨197K⟩**

ASSAY
- **PROCEDURE**

Sample: 80 mg of Arginine

Titrimetric system
(See *Titrimetry* ⟨541⟩.)
Mode: Direct titration
Titrant: 0.1 N perchloric acid VS
Endpoint detection: Potentiometric
Blank: 3 mL of formic acid and 50 mL of glacial acetic acid

Analysis: Dissolve the *Sample* in a mixture of 3 mL of formic acid and 50 mL of glacial acetic acid, and titrate with Titrant. Calculate the percentage of $C_6H_{14}N_4O_2$ in the portion taken:

$$\text{Result} = [(V - B) \times N \times F \times 100]/W$$

V = *Sample* titrant volume (mL)
B = *Blank* titrant volume (mL)
N = titrant normality (mEq/mL)
F = equivalency factor: 87.10 mg/mEq
W = weight of *Sample* (mg)

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

IMPURITIES
Inorganic Impurities
- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.3%
- **CHLORIDE AND SULFATE,** *Chloride* ⟨**221**⟩**:** A 1.0-g portion shows no more chloride than corresponds to 0.70 mL of 0.020 N hydrochloric acid (0.05%).
- **CHLORIDE AND SULFATE,** *Sulfate* ⟨**221**⟩**:** A 1.0-g portion shows no more sulfate than corresponds to 0.30 mL of 0.020 N sulfuric acid (0.03%).
- **IRON ⟨241⟩:** NMT 30 ppm
- **HEAVY METALS,** *Method I* ⟨**231**⟩**:** NMT 15 ppm

Organic Impurities
- **PROCEDURE**

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture
Standard solution: 0.05 mg/mL of USP L-Arginine RS in 0.1 N hydrochloric acid. [NOTE—This solution has a concentration equivalent to 0.5% of that of the *Sample solution*.]
Sample solution: 10 mg/mL of Arginine in 2 N hydrochloric acid
System suitability solution: 0.4 mg/mL each of USP L-Arginine RS and USP L-Lysine Hydrochloride RS in 0.1 N hydrochloric acid
Spray reagent: 2 mg/mL of ninhydrin in a mixture of butyl alcohol and 2 N acetic acid (95:5)
Application volume: 5 µL
Developing solvent system: Isopropyl alcohol and ammonium hydroxide (7:3)
Analysis
Samples: *Standard solution*, *Sample solution*, and *System suitability solution*

Proceed as directed under *Chromatography* ⟨621⟩*, Thin-Layer Chromatography*. Dry the plate between 100° and 105° until the ammonia disappears completely. Spray with *Spray reagent*, and heat between 100° and 105° for about 15 min. Examine the plate under white light. The chromatogram obtained from the *System suitability solution* exhibits two clearly separated spots.

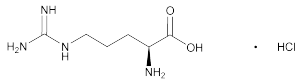
Acceptance criteria
Individual impurities: Any secondary spot from the *Sample solution* is not larger or more intense than the principal spot from the *Standard solution*, NMT 0.5%
Total impurities: NMT 2.0%

SPECIFIC TESTS
- **OPTICAL ROTATION,** *Specific Rotation* ⟨**781S**⟩**:** +26.3° to +27.7°

Sample solution: 80 mg/mL in 6 N hydrochloric acid
- **LOSS ON DRYING ⟨731⟩:** Dry a sample at 105° for 3 h: it loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in well-closed containers.
- **USP REFERENCE STANDARDS ⟨11⟩**
USP L-Arginine RS
USP L-Lysine Hydrochloride RS

Arginine Hydrochloride



$C_6H_{14}N_4O_2 \cdot HCl$ 210.66
L-Arginine monohydrochloride;
L-(+)-Arginine monohydrochloride [1119-34-2].

DEFINITION
Arginine Hydrochloride contains NLT 98.5% and NMT 101.5% of arginine hydrochloride ($C_6H_{14}N_4O_2 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION
- **A. INFRARED ABSORPTION ⟨197K⟩**

ASSAY
- **PROCEDURE**

Sample: 100 mg of Arginine Hydrochloride

Titrimetric system
(See *Titrimetry* ⟨541⟩.)
Mode: Direct titration
Titrant: 0.1 N perchloric acid VS
Endpoint detection: Potentiometric
Blank: 50 mL of glacial acetic acid and 3 mL of 98% formic acid. Add 6 mL of mercuric acetate TS.

Analysis: Dissolve the *Sample* in 3 mL of 98% formic acid and 50 mL of glacial acetic acid. Add 6 mL of mercuric acetate TS and titrate with the *Titrant*.

Calculate the percentage of arginine hydrochloride ($C_6H_{14}N_4O_2 \cdot HCl$) in the *Sample* taken:

$$\text{Result} = [(V - B) \times N \times F \times 100]/W$$

V = *Sample* titrant volume (mL)
B = *Blank* titrant volume (mL)
N = titrant normality (mEq/mL)
F = equivalency factor, 105.3 mg/mEq
W = weight of *Sample* (mg)

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

IMPURITIES

- **Residue on Ignition** ⟨**281**⟩**:** NMT 0.1%
- **Chloride and Sulfate,** *Sulfate* ⟨**221**⟩**:** A 1.6-g portion shows no more sulfate than corresponds to 0.50 mL of 0.020 N sulfuric acid (0.03%).
- **Heavy Metals,** *Method I* ⟨**231**⟩
  Test preparation: Proceed as directed in the chapter, except to dissolve 1.0 g in 20 mL of water, add 2 mL of 1 N acetic acid, and dilute with water to 25 mL.
  Acceptance criteria: NMT 20 ppm
- **Chromatographic Purity**
  System suitability solution: 0.4 mg/mL each of USP Arginine Hydrochloride RS and USP L-Lysine Hydrochloride RS in water
  Standard solution: 0.05 mg/mL of USP Arginine Hydrochloride RS in water. [NOTE—This solution has a concentration equivalent to about 0.5% of that of the *Sample solution*.]
  Sample solution: 10 mg/mL of Arginine Hydrochloride in water
  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: Isopropyl alcohol and ammonium hydroxide (70:30)
  Spray reagent: 2 mg/mL of ninhydrin in a mixture of butyl alcohol and 2 N acetic acid (95:5)
  Analysis
  Samples: *System suitability solution*, *Standard solution*, and *Sample solution*
  Proceed as directed in the chapter. Dry the plate between 100° and 105° until the ammonia disappears completely. Spray with *Spray reagent*, and heat between 100° and 105° for about 15 min. Examine the plate under white light. The *System suitability solution* exhibits two clearly separated spots.
  Acceptance criteria: Any secondary spot from the *Sample solution* is not larger or more intense than the principal spot from the *Standard solution*.
  Individual impurities: NMT 0.5%
  Total impurities: NMT 2.0%

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation* ⟨**781S**⟩**:** +21.4° to +23.6° (t = 20°)
  Sample solution: 80 mg/mL in 6 N hydrochloric acid
- **Loss on Drying** ⟨**731**⟩**:** Dry a sample at 105° for 2 h: it loses NMT 0.2% of its weight.
- **Chloride Content**
  Sample: 350 mg of Arginine Hydrochloride
  Titrimetric system
  (See *Titrimetry* ⟨541⟩.)
  Mode: Direct titration
  Titrant: 0.1 N silver nitrate VS
  Endpoint detection: Colorimetric
  Blank: 140 mL of water and 1 mL of dichlorofluorescein TS
  Analysis: Transfer the *Sample* to a porcelain casserole, and add 140 mL of water and 1 mL of dichlorofluorescein TS. Mix and titrate with the *Titrant* until the silver chloride flocculates and the mixture acquires a faint pink color.
  Calculate the percentage of chloride (Cl) in the *Sample* taken:

$$\text{Result} = [(V - B) \times N \times F \times 100]/W$$

V = *Sample* titrant volume (mL)
B = *Blank* titrant volume (mL)
N = titrant normality (mEq/mL)
F = equivalency factor, 35.45 mg/mEq
W = weight of *Sample* (mg)

Acceptance criteria: 16.5%–17.1%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards** ⟨**11**⟩
  USP Arginine Hydrochloride RS
  USP L-Lysine Hydrochloride RS

Arginine Hydrochloride Injection

» Arginine Hydrochloride Injection is a sterile solution of Arginine Hydrochloride in Water for Injection. It contains not less than 9.5 percent and not more than 10.5 percent of $C_6H_{14}N_4O_2 \cdot HCl$. It contains no antimicrobial agents.
NOTE—The chloride ion content of Arginine Hydrochloride Injection is approximately 475 mEq per L.

Packaging and storage—Preserve in single-dose containers, preferably of Type II glass.

USP Reference standards ⟨11⟩**—**
USP Arginine Hydrochloride RS
USP Endotoxin RS

Labeling—The label states the total osmolar concentration in mOsmol per L. Where the contents are less than 100 mL, or where the label states that the Injection is not for direct injection but is to be diluted before use, the label alternatively may state the total osmolar concentration in mOsmol per mL.

Identification—

A: Transfer 1 mL of the Injection to a 200-mL volumetric flask, and dilute with water to volume. To 1 mL of this dilution add 2 mL of a solution of 0.02% 8-hydroxyquinoline in 3 N sodium hydroxide, and add 1 mL of 0.1% *N*-bromosuccinimide solution: an orange color is produced.

B: It meets the requirements of the tests for *Chloride* ⟨191⟩.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 0.01 USP Endotoxin Unit per mg of arginine hydrochloride.

pH ⟨791⟩: between 5.0 and 6.5.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—

Color reagent—Dissolve 28.0 g of potassium hydroxide and 2.0 g of potassium sodium tartrate in 100 mL of water. Cool, and add, in the order named, 100 mg of 2,4-dichloro-1-naphthol, 180 mL of alcohol, and 20.0 mL of 0.475% sodium hypochlorite solution. Mix by swirling, and allow to stand at room temperature for 1 hour before using. This *Color reagent* may be stored in a glass-stoppered bottle, in a refrigerator, for 2 months.

Standard preparation—Dissolve an accurately weighed quantity of USP Arginine Hydrochloride RS in water, and dilute quantitatively and stepwise with water to obtain a solution having a known concentration of about 40 µg per mL.

Assay preparation—Pipet into a 100-mL volumetric flask a volume of Injection, equivalent to 200 mg of arginine hydrochloride, add water to volume, and mix. Pipet 5 mL of this solution into a 250-mL volumetric flask, add water to volume, and mix.

Procedure—Transfer 2.0-mL portions of the *Assay preparation* and the *Standard preparation*, respectively, to separate