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Inamrinone Injection

DEFINITION

Inamrinone Injection is a sterile solution of Inamrinone in Water for Injection, prepared with the aid of Lactic Acid. It contains NLT 90.0% and NMT 110.0% of the labeled amount of inamrinone ($C_{10}H_9N_3O$).

[**Caution—**Inamrinone is a cardiotonic agent.]

IDENTIFICATION

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

• **B.** The UV spectrum of the major peak of the *Sample solution* exhibits maxima and minima at the same wavelengths as that of the *Standard solution*, as obtained in the *Assay*.

Change to read:

• **C.**

Indicator solution: Freshly prepare. Dissolve 250 mg of sodium nitroferricyanide in sufficient water to make 9 mL and mix with 1 mL of morpholine.

Sample solution: Transfer a volume of Injection, equivalent to about 50 mg of inamrinone, to a glass-stoppered container. Add about 2 g of 50–100 mesh sulfonic acid cation-exchange resin, and shake for about 2 min or until the supernatant becomes essentially colorless. Filter, and collect the filtrate in an arsine generator flask (see ▲*Arsenic ⟨211⟩, Procedures, Procedure 1, Apparatus*▲ (CN 1-Jun-2023)).

Analysis: Add 5 mL of diluted sulfuric acid to the *Sample solution*, and boil gently on a hot plate for 5–10 min. Cool to room temperature. Add 10 mL of 0.1 N potassium permanganate VS, attach the scrubber unit and absorber tube, and place the apparatus on a warm hot plate. Add 1 mL of *Indicator solution* to the absorber tube. Heat gently, allowing the vapors to bubble through the indicator solution.

Acceptance criteria: The indicator solution turns blue within 5 min (presence of lactate).

ASSAY

• **Procedure**

Freshly prepare all inamrinone-containing solutions before injection.

Solution A: 0.5 M of borate buffer prepared as follows. Transfer 31 g of boric acid to a beaker containing approximately 800 mL of water. Slowly add 5 N sodium hydroxide in small quantities, stirring well after each addition, until all the boric acid is dissolved and the pH is constant at 7.0 ± 0.3. Transfer this solution to a 1000-mL volumetric flask, and dilute with water to volume.

Mobile phase: Methanol, *Solution A*, and water (48:2:50)

System suitability solution: 50 µg/mL each of USP Inamrinone RS and USP Inamrinone Related Compound C RS in *Mobile phase*

Standard solution: 50 µg/mL of USP Inamrinone RS in *Mobile phase*

Sample solution: Nominally 50 µg/mL of inamrinone prepared as follows. Transfer a volume of Injection, equivalent to about 5 mg of inamrinone, to a 100-mL volumetric flask, and dilute with *Mobile phase* to volume.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution* and *Standard solution*

[Note—The relative retention times for inamrinone related compound C and inamrinone are about 0.6 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3 between inamrinone related compound C and inamrinone, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of inamrinone ($C_{10}H_9N_3O$) in the portion of the Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of inamrinone from the *Sample solution*

r_S = peak response of inamrinone from the *Standard solution*

C_S = concentration of USP Inamrinone RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of inamrinone in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Lactic Acid Content**

Ion–exchange column: Place a small pledget of glass wool at the bottom of a 100- × 6-mm glass column equipped with a stopcock and a 25-mL reservoir. Soak a suitable quantity of 50- to 100-mesh sulfonic acid cation-exchange resin in 6 N hydrochloric acid for several minutes. Wash with water until the wash is neutral to wide-range pH indicator paper. Fill the column with the prepared resin to the base of the reservoir. Wash the column with 50 mL of water in several portions, draining each wash to the top of the resin before adding the next portion. Discard the washes.

Sample solution: Place a 125-mL conical flask below the ion-exchange column. Pipet a volume of Injection equivalent to about 50 mg of inamrinone onto the column. Allow the specimen to pass through the column at the rate of about 0.5–1 mL/min, draining the specimen to the top of the column and collecting the eluate in the flask. Wash the column with five 5-mL portions of water, collecting the washings in the flask. Add several small glass beads to the solution in the flask, and boil on a hot plate for 10 min.

Blank: Proceed as in *Sample solution*, substituting the volume of Injection used with the same volume of water.

Titrimetric system

(See *Titrimetry ⟨541⟩, Residual Titrations*.)

Mode: Residual titration

Titrant: 0.1 N sodium hydroxide VS

Back-titrant: 0.1 N hydrochloric acid VS

Endpoint detection: Visual

Analysis: Add 10.0 mL of the *Titrant* to the *Sample solution*, and boil for 20 min. Add phenolphthalein TS, and titrate the warm solution with the *Back-titrant*. Perform a blank determination with the *Blank*.

Calculate the content of lactic acid ($C_3H_6O_3$) in the portion of the Injection taken:

$$\text{Result} = (V_B - V_S) \times M \times F \times (1/V)$$

V_B = volume of the *Back-titrant* consumed by the *Blank* (mL)

V_S = volume of the *Back-titrant* consumed by the *Sample solution* (mL)

M = actual molarity of the *Back-titrant* (mM/mL)

F = equivalency factor, 90.08 mg/mM

V = volume of Injection taken from the *Sample solution* (mL)

Acceptance criteria: 5.0–7.5 mg/mL of Injection

• **Organic Impurities**

Freshly prepare all inamrinone-containing solutions before injection.

Solution A: Phosphoric acid and water (11.4:978.6)

Mobile phase: Acetonitrile and *Solution A* (1:99)

Lactic acid solution: 11.8 mg/mL of lactic acid in water

Standard stock solution: 0.1 mg/mL of USP Inamrinone RS and 0.25 mg/mL of USP Inamrinone Related Compound B RS, prepared as follows. Transfer suitable quantities of USP Inamrinone RS and USP Inamrinone Related Compound B RS to a suitable volumetric flask. Add 60% of the flask volume of *Lactic acid solution*, and sonicate for 2 min to effect solution. Cool, and dilute with *Lactic acid solution* to volume.

Standard solution: 4 µg/mL of USP Inamrinone RS and 10 µg/mL of USP Inamrinone Related Compound B RS, prepared as follows. Transfer a volume of *Standard stock solution* into a suitable volumetric flask. Dilute with *Mobile phase* to volume.

Sample solution: Nominally 2 mg/mL of inamrinone prepared as follows. Transfer a volume of Injection, equivalent to about 100 mg of inamrinone into a 50-mL volumetric flask, and dilute with *Mobile phase* to volume.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 313 nm

Column: 4.6-mm × 15-cm; 5-µm base-deactivated packing L7

Column temperature: 30°–35°

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 10 between inamrinone and inamrinone related compound B

Relative standard deviation: NMT 10% for inamrinone related compound B

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of inamrinone related compound B and any unspecified impurity in the volume of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response for inamrinone related compound B or any unspecified impurity from the *Sample solution*

r_S = peak response for inamrinone related compound B RS from the *Standard solution*

C_S = concentration of USP Inamrinone Related Compound B RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of inamrinone in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Inamrinone	1.0	—
Inamrinone related compound B	3.7	2.0
Any unspecified impurity	—	0.5
Total impurities	—	3.0

SPECIFIC TESTS

- **Bacterial Endotoxins Test ⟨85⟩:** NMT 0.5 USP Endotoxin Unit/mg of inamrinone
- **pH ⟨791⟩:** 3.2–4.0
- **Other Requirements:** Meets the requirements under *Injections and Implanted Drug Products ⟨1⟩*

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in single-dose containers, preferably of Type I glass, protected from light. Store at room temperature.
- **USP Reference standards ⟨11⟩**

USP Inamrinone RS

USP Inamrinone Related Compound B RS
2-Hydroxy-*N*-(6-oxo-1,6-dihydro-[3,4'-bipyridin]-5-yl)propanamide.
$C_{13}H_{13}N_3O_3$ 259.27

USP Inamrinone Related Compound C RS
6-Oxo-1,6-dihydro-[3,4'-bipyridine]-5-carbonitrile.
$C_{11}H_7N_3O$ 197.20

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

Topic/Question	Contact	Expert Committee
INAMRINONE INJECTION	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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