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Add the following:

▲Milrinone Lactate Injection

DEFINITION

Milrinone Lactate Injection is a sterile aqueous solution of Milrinone and a suitable osmolality-adjusting substance 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 milrinone ($C_{12}H_9N_3O$).

IDENTIFICATION

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

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

ASSAY

• **Procedure**

Buffer: Dissolve 3.3 g of dibasic potassium phosphate in 1 L of water and add 3 mL of triethylamine. Adjust with phosphoric acid to a pH of 7.5.

Mobile phase: Acetonitrile and *Buffer* (20:80)

Standard solution: 0.05 mg/mL of USP Milrinone RS in *Mobile phase*. Sonication may be necessary for complete dissolution.

Sample solution: Nominally equivalent to 0.05 mg/mL of milrinone prepared from a volume of Injection suitably diluted with *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.7 times the retention time of milrinone

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of milrinone ($C_{12}H_9N_3O$) in the portion of Injection taken:

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

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

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

C_S = concentration of USP Milrinone RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of milrinone in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

Change to read:

• **Organic Impurities**

Buffer and **Mobile phase:** Prepare as directed in the *Assay*.

System suitability solution: 0.5 µg/mL each of USP Milrinone RS and USP Milrinone Related Compound A RS in *Mobile phase*

Standard solution: 0.5 µg/mL of USP Milrinone RS in *Mobile phase*

Sensitivity solution: 0.1 µg/mL of USP Milrinone RS in *Mobile phase* from *Standard solution*

Sample solution: Nominally 500 µg/mL of milrinone from a volume of Injection in *Mobile phase*

Chromatographic system: Proceed as directed in the *Assay*, except for the *Run times*.

Run times

Standard solution: NLT 1.7 times the retention time of milrinone

Sample solution: NLT 4 times the retention time of milrinone

System suitability

Samples: *System suitability solution*, *Standard solution*, and *Sensitivity solution*

Suitability requirements

Resolution: NLT 5.0 between milrinone and milrinone related compound A, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 20, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \text{ ▲▲ (ERR 1-Sep-2018)} \times 100$$

r_U = peak response of each impurity from the *Sample solution*

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

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

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

▲▲ (ERR 1-Sep-2018)

Acceptance criteria: See *Table 1*. Disregard peaks below 0.01%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Milrinone related compound A[a]	0.6	—
Milrinone	1.0	—
Any unspecified degradation product	—	0.20
Total impurities[b]	—	0.5

[a] Process-related impurity; 1,6-Dihydro-2-methyl-6-oxo(3,4'-bipyridine)-5-carboxamide.

[b] Total impurities include both process-related and degradation products.

SPECIFIC TESTS

• **Content of Lactic Acid**

Mobile phase: Water adjusted with phosphoric acid to a pH of 2.1

Standard solution: 0.2 mg/mL of USP Sodium Lactate RS in *Mobile phase*

Sample solution: Nominally equivalent to 0.2 mg/mL of milrinone prepared as follows. Transfer a suitable volume of Injection into a suitable volumetric flask and add about 8% of the flask volume of 1.0 N sodium hydroxide solution. Shake well and keep for 10 min. Neutralize with an equal amount of 1.0 N sulfuric acid and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector UV 210 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

Run times

Standard solution: NLT 2.4 times the retention time of lactic acid

Sample solution: NLT 4 times the retention time of lactic acid

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lactic acid in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of lactic acid from the *Sample solution*

r_S = peak response of lactic acid from the *Standard solution*

C_S = concentration of USP Sodium Lactate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of milrinone in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of lactic acid, 90.08

M_{r2} = molecular weight of sodium lactate, 112.06

Acceptance criteria: 95.0%–129.0%

- **Bacterial Endotoxins Test ⟨85⟩:** NMT 25 USP Endotoxin Units/mg of milrinone
- **Sterility Tests ⟨71⟩:** Meets the requirements
- **pH ⟨791⟩:** 3.2–4.0
- **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections
- **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in single-dose containers. Store at controlled room temperature.
- **Labeling:** Label it to indicate that it is to be suitably diluted prior to administration.
- **USP Reference Standards ⟨11⟩**

USP Milrinone RS

USP Milrinone Related Compound A RS

1,6-Dihydro-2-methyl-6-oxo(3,4'-bipyridine)-5-carboxamide.

$C_{12}H_{11}N_3O_2$ 229.24

USP Sodium Lactate RS

Sodium 2-hydroxypropanoate.

$C_3H_5NaO_3$ 112.06▲*USP41*

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

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

Chromatographic Database Information: Chromatographic Database

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