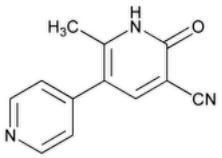
Status: Currently Official on 18-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-8588DD93-F191-4EF8-A881-55BA98A9BE9B_5_en-US
DOI: https://doi.org/10.31003/USPNF_M54072_05_01
DOI Ref: t5lq2

Milrinone



$C_{12}H_9N_3O$ 211.22

[3,4'-Bipyridine]-5-carbonitrile, 1,6-dihydro-2-methyl-6-oxo-;

1,6-Dihydro-2-methyl-6-oxo[3,4'-bipyridine]-5-carbonitrile CAS RN®: 78415-72-2; UNII: JU9YAX04C7.

DEFINITION

Milrinone contains NLT 98.0% and NMT 102.0% of milrinone ($C_{12}H_9N_3O$), calculated on the anhydrous basis.

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

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

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

ASSAY

Change to read:

• **Procedure**

Buffer: To 72.44 g of sodium tetraborate, ▲anhydrous▲ (ERR 1-Jun-2019) add 900 mL of water. Adjust with hydrochloric acid to a pH of 6.5. The solution should become nearly transparent after adjustment. Dilute with water to 1 L.

Mobile phase: Methanol, *Buffer*, and water (320:40:640)

Diluent: Methanol, water, and lactic acid (320: 679: 1.2)

Standard solution: 0.1 mg/mL of USP Milrinone RS in *Diluent*. Sonicate until dissolved.

Sample solution: 0.1 mg/mL of Milrinone in *Diluent*. Sonicate until dissolved.

Chromatographic system

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

Mode: LC

Detector: UV 268 nm

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

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of milrinone ($C_{12}H_9N_3O$) in the portion of Milrinone 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 = concentration of Milrinone in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.2%

• **Organic Impurities**

Buffer: To 2.7 g of dibasic potassium phosphate in 800 mL of water add 2.4 mL of triethylamine, and adjust with phosphoric acid to a pH of 7.5.

Mobile phase: Acetonitrile and *Buffer* (200:800)

System suitability stock solution: 0.2 mg/mL of USP Milrinone Related Compound A RS in *Mobile phase*. Heat in a water bath at approximately 80°, and/or sonicate if necessary to dissolve.

Standard stock solution: 2 mg/mL of USP Milrinone RS in *Mobile phase*. Heat in a water bath at approximately 80°, and/or sonicate if necessary to dissolve.

System suitability solution: 10.0 mL of *System suitability stock solution* and 1.0 mL of *Standard stock solution* in a 100-mL volumetric flask. Dilute with *Mobile phase* to volume.

Standard solution: 0.006 mg/mL of USP Milrinone RS, from the *Standard stock solution,* in *Mobile phase*

Sample solution: 2 mg/mL of Milrinone in *Mobile phase*. Heat in a water bath at approximately 80°, if necessary to dissolve.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; packing L7

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for milrinone related compound A and milrinone are 0.6 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 4.0 between milrinone related compound A and milrinone

Relative standard deviation: NMT 5.0% from the milrinone peak

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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* (mg/mL)

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

Acceptance criteria

Any individual impurity: NMT 0.3%

Total impurities: NMT 1.0%

SPECIFIC TESTS

• **Water Determination, *Method I* ⟨921⟩:** NMT 2.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.

• **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.

$C_{12}H_{11}N_3O_2$ 229.23

Topic/Question	Contact	Expert Committee
MILRINONE	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 40(3)

Current DocID: GUID-8588DD93-F191-4EF8-A881-55BA98A9BE9B_5_en-US

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