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Amiodarone Hydrochloride Injection

DEFINITION

Amiodarone Hydrochloride Injection is a sterile solution of Amiodarone Hydrochloride. It contains NLT 90.0% and NMT 110.0% of the labeled amount of amiodarone hydrochloride ($C_{25}H_{29}I_2NO_3 \cdot HCl$). It may contain suitable preservatives.

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* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Buffer: 1.36 g/L of potassium phosphate, monobasic in water prepared as follows. To 1.36 g of potassium phosphate, monobasic in a 1-L volumetric flask add about 900 mL of water and 1 mL of triethylamine. Adjust with phosphoric acid to a pH of 6.0. Dilute with water to volume.

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

Diluent: Acetonitrile and water (60:40)

Standard solution: 0.025 mg/mL of USP Amiodarone Hydrochloride RS in *Diluent*

Sample solution: Nominally 0.025 mg/mL of amiodarone hydrochloride in *Diluent* from a suitable volume of Injection

Chromatographic system

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

Mode: LC

Detector: UV 240 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 10-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of amiodarone

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 amiodarone hydrochloride ($C_{25}H_{29}I_2NO_3 \cdot HCl$) in the portion of Injection taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

- **Content of Benzyl Alcohol** (if present)

Internal standard solution: 1 mg/mL of phenol in isopropyl alcohol

Standard stock solution: 1.6 of mg/mL of USP Benzyl Alcohol RS in isopropyl alcohol

Standard solution: 0.2 mg/mL of phenol and 0.19 mg/mL of USP Benzyl Alcohol RS in isopropyl alcohol from the *Internal standard solution* and the *Standard stock solution*

Sample stock solution: Nominally 1.6 mg/mL of benzyl alcohol in isopropyl alcohol from Injection

Sample solution: Nominally 0.2 mg/mL of phenol and 0.19 mg/mL of benzyl alcohol in isopropyl alcohol from the *Internal standard solution* and the *Sample stock solution*

Blank: 0.2 mg/mL of phenol in isopropyl alcohol from the *Internal standard solution*

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 30-m fused silica capillary; coated with 1-µm film of phase G16

Temperatures

Injection port: 200°

Column: 150°

Detector: 200°

Carrier gas: Nitrogen

Flow rate: 10 mL/min

Injection volume: 1 µL

Injection type: Split; split ratio, 10:1

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0% for the peak response ratio of benzyl alcohol to phenol

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of benzyl alcohol in the portion of Injection taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of benzyl alcohol to phenol from the *Sample solution*

R_S = peak response ratio of benzyl alcohol to phenol from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

IMPURITIES

Change to read:

• **Limit of Iodide**

Use freshly prepared solutions in amber glassware.

Amiodarone stock solution: Nominally 5 mg/mL of amiodarone hydrochloride in water from Injection

Potassium iodide solution: 88.2 µg/mL of potassium iodide in water

Potassium iodate solution: 10.7 g/L of ▲potassium iodate▲ (ERR 1-Jul-2021) in water

Standard solution: 4.41 µg/mL of potassium iodide prepared as follows. Into a suitable flask pipet 15.0 mL of *Amiodarone stock solution*, 1.0 mL of 0.1 N hydrochloric acid, 1.0 mL of *Potassium iodide solution*, 1.0 mL of *Potassium iodate solution*, and 2.0 mL of water. Mix, and allow to stand for 4 h. Protect from light.

Sample solution: Nominally 3.75 mg/mL of amiodarone hydrochloride prepared as follows. Into a suitable flask pipet 15.0 mL of *Amiodarone stock solution*, 1.0 mL of 0.1 N hydrochloric acid, 1.0 mL of *Potassium iodate solution*, and 3.0 mL of water. Mix, and allow to stand for 4 h. Protect from light.

Blank: Into a suitable flask pipet 15.0 mL of *Amiodarone stock solution*, 1.0 mL of 0.1 N hydrochloric acid, and 4.0 mL of water. Mix, and allow to stand for 4 h. Protect from light.

Instrumental conditions

Mode: Vis

Analytical wavelength: 420 nm

Cell: 1 cm

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Calculate the amount of iodide, in ppm, in the portion of Injection taken:

$$\text{Result} = (A_U - A_B)/[(A_S - A_B) - (A_U - A_B)] \times (C_S/C_U) \times (M_{r1}/M_{r2})$$

A_U = absorbance of the *Sample solution*

A_B = absorbance of the *Blank*

A_S = absorbance of the *Standard solution*

C_S = concentration of potassium iodide in the *Standard solution* (µg/mL)

C_U = nominal concentration of amiodarone hydrochloride in the *Sample solution* (g/mL)

M_{r1} = molecular weight of iodide, 126.90

M_{r2} = molecular weight of potassium iodide, 166.00

Acceptance criteria: NMT 250 ppm

- **Organic Impurities**

Buffer: Add 3 mL of acetic acid, glacial to 800 mL of water. Adjust with ammonia TS to a pH of 4.9. Dilute with water to 1000 mL.

Mobile phase: Acetonitrile, methanol, and *Buffer* (40:30:30)

Diluent: Acetonitrile, methanol, and water (50:30:20)

Standard stock solution A: 0.2 mg/mL of USP Amiodarone Hydrochloride RS in *Diluent*

Standard stock solution B: 0.4 mg/mL of USP Amiodarone Related Compound E RS in *Diluent*

Standard solution: 1 µg/mL of USP Amiodarone Hydrochloride RS, 30 µg/mL of USP Amiodarone Related Compound D RS, and 2 µg/mL of USP Amiodarone Related Compound E RS in *Diluent* prepared as follows. Transfer a suitable quantity of USP Amiodarone Related Compound D RS to a suitable volumetric flask, and add a suitable amount of *Standard stock solution A* and *Standard stock solution B*. Dilute with *Diluent* to volume.

Sample solution: Nominally 1 mg/mL of amiodarone hydrochloride in *Diluent* from a suitable volume of Injection

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Temperatures

Autosampler: 2°–8°

Column: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention time of amiodarone for the *Standard solution*, and NLT 2 times the retention time of amiodarone for the *Sample solution*

System suitability

Sample: *Standard solution*

[Note—See *Table 1* for relative retention times.]

Suitability requirements

Resolution: NLT 3.5 between the amiodarone related compound E and amiodarone related compound D peaks

Tailing factor: NMT 2.0 for the amiodarone, amiodarone related compound D, and amiodarone related compound E peaks

Relative standard deviation: NMT 5.0% for the amiodarone, amiodarone related compound D, and amiodarone related compound E peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amiodarone related compound D or amiodarone related compound E in the portion of Injection taken:

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

r_U = peak response of amiodarone related compound D or amiodarone related compound E from the *Sample solution*

r_S = peak response of amiodarone related compound D or amiodarone related compound E from the *Standard solution*

C_S = concentration of USP Amiodarone Related Compound D RS or USP Amiodarone Related Compound E RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any unspecified degradation product in the portion of Injection taken:

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

r_U = peak response of any unspecified degradation product from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Amiodarone related compound E	0.39	0.2
Amiodarone related compound D	0.55	3.0
Amiodarone	1.00	—
Any unspecified degradation product	—	0.20
Total degradation products	—	3.5

SPECIFIC TESTS

- **Bacterial Endotoxins Test ⟨85⟩:** Meets the requirements
- **Sterility Tests ⟨71⟩:** Meets the requirements
- **pH ⟨791⟩:** 3.0–5.0
- **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 or multiple-dose glass containers, protected from light and excessive heat. Store at controlled room temperature.
- **Labeling:** Label it to indicate that it is to be diluted to the appropriate strength with a suitable parenteral vehicle prior to administration. Label it to indicate the type and amount of preservative used. Label it to indicate that it is preservative free, if no preservative is present.
- **USP Reference Standards ⟨11⟩**

USP Amiodarone Hydrochloride RS

USP Amiodarone Related Compound D RS
(2-Butylbenzofuran-3-yl)(4-hydroxy-3,5-diiodophenyl)methanone.
$C_{19}H_{16}I_2O_3$ 546.14

USP Amiodarone Related Compound E RS
(2-Butylbenzofuran-3-yl)(4-hydroxyphenyl)methanone.
$C_{19}H_{18}O_3$ 294.34

USP Benzyl Alcohol RS

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

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

Chromatographic Database Information: Chromatographic Database

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