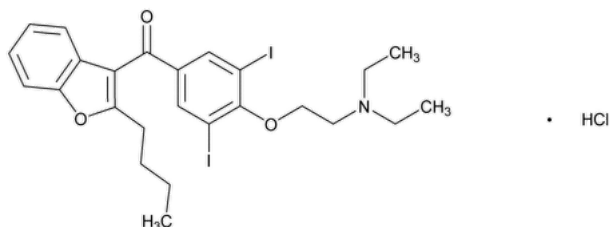


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Amiodarone Hydrochloride



$C_{25}H_{29}I_2NO_3 \cdot HCl$ 681.77

Methanone, (2-butyl-3-benzofuranyl)[4-[2-(diethyl amino)ethoxy]-3,5-diiodophenyl]- hydrochloride;

2-Butyl-3-benzofuranyl 4-[2-(diethylamino)ethoxy]-3,5-diiodophenyl ketone hydrochloride CAS RN®: 19774-82-4; UNII: 976728SY6Z.

2-Butyl-3-benzofuranyl 4-[2-(diethylamino)ethoxy]-3,5-diiodophenyl ketone CAS RN®: 1951-25-3; UNII: N3RQ532IUT.

DEFINITION

Amiodarone Hydrochloride contains NLT 98.5% and NMT 101.0% of $C_{25}H_{29}I_2NO_3 \cdot HCl$, calculated on the dried basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K
- **B. IDENTIFICATION TESTS—GENERAL, Chloride (191):** Meets the requirements

ASSAY

PROCEDURE

Buffer: Dissolve 6.80 g of monobasic potassium phosphate in 900 mL of water, and add 1.0 mL of triethylamine. Adjust with phosphoric acid to a pH of 6.00 ± 0.05 , and dilute with water to 1000 mL.

Diluent: Acetonitrile and water (1:1)

Mobile phase: Acetonitrile and *Buffer* (1:1)

Standard stock solution: 0.5 mg/mL of [USP Amiodarone Hydrochloride RS](#) in methanol

Standard solution: 0.1 mg/mL [USP Amiodarone Hydrochloride RS](#) in *Diluent* from *Standard stock solution*

Sample stock solution: 0.5 mg/mL of Amiodarone Hydrochloride in methanol

Sample solution: 0.1 mg/mL of Amiodarone Hydrochloride in *Diluent* from *Sample stock solution*

Chromatographic system

(See [Chromatography \(621\), System Suitability.](#))

Mode: LC

Detector: UV 240 nm

Column: 3.9-mm $\times$ 15-cm; 5- μ m packing L26

Flow rate: 1.5 mL/min

Injection size: 10 μ L

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 1000 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{25}H_{29}I_2NO_3 \cdot HCl$ in the portion of Amiodarone Hydrochloride taken:

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

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

r_S = peak response of amiodarone in 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: 98.5%–101.0%, on the dried basis

IMPURITIES

INORGANIC IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.1% on a 1-g sample

ORGANIC IMPURITIES

[NOTE—The product meets the requirements for both *Procedure 1* and *Procedure 2*.]

• PROCEDURE 1

Potassium iodobismuthate solution: Dissolve 100 g of tartaric acid in 400 mL of water, and add 8.5 g of bismuth subnitrate. Shake for 1 h, add 200 mL of a 400 g/L solution of potassium iodide, and shake well. Allow to stand for 24 h, filter, and protect from light.

Standard solution A: 0.02 mg/mL of [USP Amiodarone Related Compound H RS](#) in methylene chloride

Standard solution B: *Standard solution A* and *Sample solution* (1:1).

Sample solution: 100 mg/mL of Amiodarone Hydrochloride in methylene chloride

Chromatographic system

(See [Chromatography \(621\)](#), [Thin-Layer Chromatography](#).)

Mode: TLC

Adsorbent: Suitable layer of chromatographic silica gel and fluorescent indicator with maximum absorbance at 254 nm

Application volume

Standard solution A: 50 μ L

Standard solution B: 100 μ L

Sample solution: 50 μ L

Developing solvent system: Methylene chloride, methanol, and anhydrous formic acid (17:2:1)

Analysis

Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*

Develop the plate in the *Developing solvent system* until the solvent front has moved NLT two-thirds the length of the plate, and dry in a current of cold air. Spray the plate with *Potassium iodobismuthate solution* and then with 3% hydrogen peroxide solution. Examine immediately in daylight: the spot from *Standard solution B* due to amiodarone related compound H is clearly visible.

Acceptance criteria: Any spot with the same R_f as the spot due to amiodarone related compound H from the *Sample solution* is not more intense than the spot from *Standard solution A* (0.02%).

• PROCEDURE 2

Buffer: Add 3 mL of glacial acetic acid to 800 mL of water. Adjust with diluted ammonia solution to a pH of 4.9, and dilute with water to 1000 mL.

Mobile phase: Acetonitrile: methanol: *Buffer* (4:3:3 v/v/v).

Diluent: Acetonitrile and water (1:1)

Standard stock solution: Dissolve equal quantities of [USP Amiodarone Related Compound D RS](#), [USP Amiodarone Related Compound E RS](#), and [USP Amiodarone Hydrochloride RS](#) in a known amount of methanol.

Standard solution: 0.01 mg/mL each of [USP Amiodarone Related Compound D RS](#), [USP Amiodarone Related Compound E RS](#), and [USP Amiodarone Hydrochloride RS](#), in *Diluent* from *Standard stock solution*

Sample solution: 5 mg/mL of Amiodarone Hydrochloride in *Diluent*

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm $\times$ 15-cm; 5- μ m packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection size: 10 μ L

Run time: 2 times the retention time of amiodarone

System suitability

Sample: *Standard solution*

Suitability requirements

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

Analysis

[NOTE—Disregard any peak that is less than 0.05%.]

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Amiodarone Hydrochloride taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times 100$$