Amiodarone Hydrochloride Tablets

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Expert Committee	Chemical Medicines Monographs 2
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 2 Expert Committee has revised the Amiodarone Hydrochloride Tablets monograph. The purpose for the revision is to add *Dissolution Test 2* to accommodate FDA-approved drug products with different dissolution conditions and tolerances than the existing dissolution test. A *Labeling* section has also been added.

The Amiodarone Hydrochloride Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Edith Chang, Senior Scientific Liaison—Team Leader (301-816-8392 or yec@usp.org).

Add the following:

▲Amiodarone Hydrochloride Tablets

DEFINITION

Amiodarone Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of amiodarone hydrochloride ($C_{25}H_{29}I_2NO_3 \cdot HCl$).

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: Add 3 mL of acetic acid, glacial to 1 L of water. Adjust with ammonia water, 25 percent to a pH of 3.0.

Mobile phase: Acetonitrile and *Buffer* (40:60)

Standard solution: 0.1 mg/mL of USP Amiodarone Hydrochloride RS in *Mobile phase*

Sample stock solution: Nominally 1 mg/mL of amiodarone hydrochloride in *Mobile phase* prepared as follows. Transfer a quantity, equivalent to 100 mg of amiodarone hydrochloride, from NLT 20 finely powdered Tablets to a 100-mL volumetric flask. Add *Mobile phase* to about 50% of the final flask volume. Sonicate with occasional shaking to dissolve. Cool the solution and dilute with *Mobile phase* to volume.

Sample solution: Nominally 0.1 mg/mL of amiodarone hydrochloride in *Mobile phase* from *Sample stock solution*. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, discard the first few milliliters, and collect the filtrate.

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 × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 2.5 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 Tablets 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%

PERFORMANCE TESTS

Change to read:

- **DISSOLUTION** ⟨711⟩

▲Test 1▲ (RB 1-Dec-2019)

Medium: 1% (w/v) sodium dodecyl sulfate; 1000 mL

Apparatus 2: 100 rpm

Time: 60 min

Standard stock solution: 0.2 mg/mL of USP Amiodarone Hydrochloride RS prepared as follows. Transfer an appropriate quantity of USP Amiodarone Hydrochloride RS to a suitable volumetric flask and add methanol to 5% of the final flask volume. Sonicate to dissolve and dilute with *Medium* to volume.

Standard solution: 0.01 mg/mL of USP Amiodarone Hydrochloride RS in *Medium* from *Standard stock solution*

Sample solution: Dilute a portion of the solution under test with *Medium* to a concentration similar to that of the *Standard solution*. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, discard the first few milliliters, and collect the filtrate.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 243 nm

Cell: 1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amiodarone hydrochloride ($C_{25}H_{29}I_2NO_3 \cdot HCl$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times D \times V \times (1/L) \times 100$$

A_U = absorbance of amiodarone from the *Sample solution*

A_S = absorbance of amiodarone from the *Standard solution*

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

D = dilution factor for the *Sample solution*

V = volume of *Medium*, 1000 mL

L = label claim of amiodarone hydrochloride (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of amiodarone hydrochloride ($C_{25}H_{29}I_2NO_3 \cdot HCl$) is dissolved.

▲Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.2% (v/v) polysorbate 80 in 0.05 N hydrochloric acid prepared as follows. Add 26 mL of hydrochloric acid and 12 mL of polysorbate 80 to 6 L of deaerated water; 900 mL

Apparatus 2: 75 rpm

Time: 30 min

Standard solution: 0.22 mg/mL of USP Amiodarone Hydrochloride RS prepared as follows. Transfer an appropriate quantity of USP Amiodarone Hydrochloride RS to a suitable volumetric flask, and add methanol to 20% of the final flask volume. Sonicate to dissolve and dilute with *Medium* to volume.

Sample solution: Pass a portion of the solution through a suitable filter of 0.45-µm pore size, discard the first few milliliters, and collect the filtrate.

Instrumental conditions

Mode: UV

Analytical wavelength: 244 nm
Cell: 0.1 cm
Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amiodarone hydrochloride ($C_{25}H_{29}I_2NO_3 \cdot HCl$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of amiodarone from the *Sample solution*
A_S = absorbance of amiodarone from the *Standard solution*
C_S = concentration of USP Amiodarone Hydrochloride RS in the *Standard solution* (mg/mL)
V = volume of *Medium*, 900 mL
L = label claim of amiodarone hydrochloride (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of amiodarone hydrochloride ($C_{25}H_{29}I_2NO_3 \cdot HCl$) is dissolved. ▲ (RB 1-Dec-2019)

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Buffer: Add 3 mL of acetic acid, glacial to 800 mL of water. Adjust with 10% (v/v) ammonia hydroxide solution to a pH of 4.9. Dilute with water to 1000 mL.

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

Diluent: Acetonitrile and water (50:50)

Standard solution: 0.01 mg/mL of USP Amiodarone Hydrochloride RS in *Diluent*

Sensitivity solution: 0.3 µg/mL of USP Amiodarone Hydrochloride RS in *Diluent* from *Standard solution*

Sample solution: Nominally 1 mg/mL of amiodarone hydrochloride in *Diluent* prepared as follows. Transfer a quantity equivalent to 50 mg of amiodarone hydrochloride from NLT 20 finely powdered Tablets to a 50-mL volumetric flask. Add *Diluent* to 50% of the final flask volume. Sonicate with occasional shaking to dissolve. Cool the solution and dilute with *Diluent* to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, discard the first few milliliters, and collect the filtrate.

Chromatographic system

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

Mode: LC
Detector: UV 240 nm
Column: 4.6-mm × 15-cm; 5-µm packing L1
Column temperature: 30°
Flow rate: 1 mL/min
Injection volume: 10 µL
Run time: NLT 1.7 times the retention time of amiodarone for the *Standard solution*; NLT 3.4 times the retention time of amiodarone for the *Sample solution*

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Relative standard deviation: NMT 10.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amiodarone related compound D or any unspecified degradation product in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of amiodarone related compound D or 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)
F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.03%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Amiodarone related compound A[a, b]	0.22	—	—
Amiodarone related compound D[c]	0.29	0.90	0.5
Amiodarone related compound C[d, b]	0.52	—	—
Amiodarone	1.00	—	—
Any unspecified degradation product	—	1.00	0.2
Total degradation products	—	—	1.0

[a] (2-Butylbenzofuran-3-yl){4-[2-(diethylamino)ethoxy]phenyl}methanone.
[b] Process impurity included in the table for identification only. Process impurities are controlled in the drug substance and are not to be reported or included in the total degradation products for the drug product.
[c] (2-Butylbenzofuran-3-yl)(4-hydroxy-3,5-diiodophenyl)methanone.
[d] (2-Butylbenzofuran-3-yl){4-[2-(diethylamino)ethoxy]-3-iodophenyl}methanone.

ADDITIONAL REQUIREMENTS

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

Add the following:

▲• **Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used. ▲ (RB 1-Dec-2019)

• **USP Reference Standards** ⟨11⟩

USP Amiodarone Hydrochloride RS ▲ (USP 1-Dec-2019)