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Dronedarone Tablets

DEFINITION

Dronedarone Tablets contain an amount of dronedarone hydrochloride equivalent to NLT 95.0% and NMT 105.0% of the labeled amount of dronedarone free base ($C_{31}H_{44}N_2O_5S$).

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 absorption spectra of the dronedarone peak in the *Sample solution* exhibit 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: Combine 2.0 mL of triethylamine with 1 L of water and adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Acetonitrile and *Buffer* (50:50)

System suitability stock solution: 0.2 mg/mL each of USP Dronedarone Hydrochloride RS and USP Dronedarone Related Compound A RS in methanol

System suitability solution: 0.01 mg/mL each of USP Dronedarone Hydrochloride RS and USP Dronedarone Related Compound A RS in *Mobile phase* from the *System suitability stock solution*

Standard stock solution: 2.13 mg/mL of USP Dronedarone Hydrochloride RS in methanol

Standard solution: 0.11 mg/mL of USP Dronedarone Hydrochloride RS in *Mobile phase* from the *Standard stock solution*

Sample stock solution: Nominally equivalent to 4 mg/mL of dronedarone in methanol prepared as follows. Dissolve and dilute in methanol to volume, an amount equivalent to 400 mg of dronedarone from NLT 20 finely powdered Tablets, taken in a 100-mL volumetric flask. Sonicate for about 5 min and allow to settle at room temperature.

Sample solution: Nominally equivalent to 0.1 mg/mL of dronedarone in *Mobile phase* from the *Sample stock solution*. Pass through a suitable filter of 0.45-µm pore size and discard the first 3 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detectors

Assay: UV 288 nm

Identification test B: UV diode array

Column: 4.6-mm × 25-cm; 5-µm packing L10

Flow rate: 0.8 mL/min

Injection volume: 20 µL

Run time: NLT 2.15 times the retention time of dronedarone

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for dronedarone related compound A and dronedarone are 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 8 between dronedarone and dronedarone related compound A

Tailing factor: 0.8–2.1 for dronedarone

Relative standard deviation: NMT 1.5%, for dronedarone

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of dronedarone free base ($C_{31}H_{44}N_2O_5S$) in the portion of Tablets taken:

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

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

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

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

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

M_{r1} = molecular weight of dronedarone free base, 556.76

M_{r2} = molecular weight of dronedarone hydrochloride, 593.22

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: 13.61 g/L of monobasic potassium phosphate in water. Adjust with 0.1 M hydrochloric acid or 0.1 M sodium hydroxide as needed to a pH of 4.5; 1000 mL

Apparatus 2: 75 rpm, with sinker ring

Times: 30 and 90 min

Standard solution: 0.43 mg/mL of USP Dronedarone Hydrochloride RS prepared as follows. Dissolve a suitable amount of USP Dronedarone Hydrochloride RS in 2% of the total volume of methanol and dilute with *Medium* to volume.

Sample solution: Pass a portion of sample under test through a suitable filter.

Instrumental conditions

Analytical wavelength: UV 288 nm

Cell: 1 mm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of dronedarone dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

A_U = absorbance from the *Sample solution*

A_S = absorbance from the *Standard solution*

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

V = volume of *Medium*, 1000 mL

L = label claim (mg/Tablet)

M_{r1} = molecular weight of dronedarone free base, 556.76

M_{r2} = molecular weight of dronedarone hydrochloride, 593.22

Tolerances

30 min: 20.0%–60.0% ▲▲ (ERR 1-Jun-2019) of the labeled amount of dronedarone free base ($C_{31}H_{44}N_2O_5S$) is dissolved.

90 min: NLT 80% (*Q*) of the labeled amount of dronedarone free base ($C_{31}H_{44}N_2O_5S$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Buffer, Mobile phase, and **System suitability stock solution:** Proceed as directed in the *Assay*.

System suitability solution: 0.01 mg/mL each of USP Dronedarone Hydrochloride RS and USP Dronedarone Related Compound A RS prepared as follows. To a suitable amount of *System suitability stock solution*, add 20% of the total volume of methanol and dilute with *Mobile phase* to volume.

Standard stock solution: 0.4 mg/mL of USP Dronedarone Hydrochloride RS in methanol

Standard solution: 0.002 mg/mL of USP Dronedarone Hydrochloride RS prepared as follows. To a suitable amount of *Standard stock solution*, add 25% of the total volume of methanol and dilute with *Mobile phase* to volume.

Sensitivity solution: 0.0005 mg/mL of USP Dronedarone Hydrochloride RS prepared as follows. To a suitable amount of the *Standard solution*, add 20% of the total volume of methanol and dilute with *Mobile phase* to volume.

Sample stock solution: Nominally equivalent to 4 mg/mL of dronedarone in methanol prepared as follows. Dissolve and dilute in methanol to volume, an amount equivalent to 400 mg of dronedarone from NLT 20 finely powdered Tablets, taken in a 100-mL volumetric flask. Sonicate for about 5 min and allow to settle at room temperature.

Sample solution: Nominally equivalent to 1 mg/mL of dronedarone in *Mobile phase* from *Sample stock solution*. Pass through a suitable filter of 0.45-µm pore size and discard the first 3 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 246 nm

Column: 4.6-mm × 25-cm; 5-µm packing L10

Flow rate: 0.8 mL/min

Injection volume: 20 µL

Run time: NLT 3.6 times the retention time of dronedarone

System suitability

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

[NOTE—The relative retention times for dronedarone related compound A and dronedarone are 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 8 between dronedarone and dronedarone related compound A, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

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

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

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

M_{r1} = molecular weight of dronedarone free base, 556.76

M_{r2} = molecular weight of dronedarone hydrochloride, 593.22

Acceptance criteria: Disregard peaks less than 0.05%.

Any unspecified impurity: NMT 0.20%

Total impurities: NMT 0.4%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Store at controlled room temperature.
- **USP REFERENCE STANDARDS ⟨11⟩**

USP Dronedarone Hydrochloride RS

USP Dronedarone Related Compound A RS

N-(2-Butyl-3-{4-[3-(butylamino)propoxy]benzoyl}benzofuran-5-yl)methanesulfonamide.

$C_{27}H_{36}N_2O_5S$ 500.65

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

Topic/Question	Contact	Expert Committee
DRONEDARONE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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