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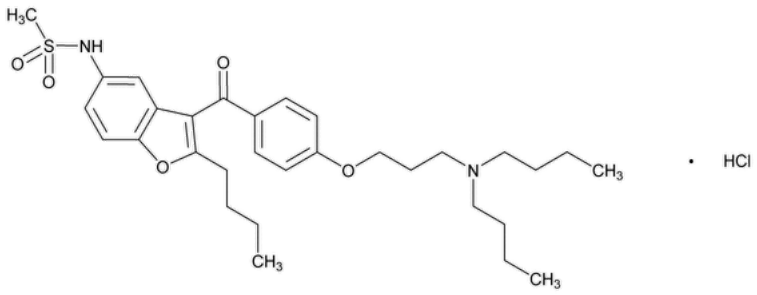
Dronedarone Hydrochloride



$C_{31}H_{44}N_2O_5S \cdot HCl$ 593.2

N-{2-Butyl-3-[4-(3-dibutylaminopropoxy)benzoyl] benzofuran-5-yl}methanesulfonamide, hydrochloride;

Methanesulfonamide, *N*-[2-butyl-3-[4-[3-(dibutylamino)propoxy]benzoyl]-5-benzofuranyl]-, monohydrochloride CAS RN®: 141625-93-6; UNII: FA36DV299Q.

DEFINITION

Dronedarone Hydrochloride contains NLT 98.0% and NMT 101.5% of dronedarone hydrochloride, calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

- **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020) **:** Meets the requirements
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay*.
- **C.** Identification Tests—General, *Chloride* ⟨191⟩

Sample solution: Dissolve 100 mg of Dronedarone Hydrochloride in 8 mL of methanol and dilute with water to 10.0 mL. Use 2.0 mL for the analysis.

Acceptance criteria: Meets the requirements

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: 1 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 *System suitability stock solution*

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

Sample solution: 0.1 mg/mL of Dronedarone Hydrochloride in *Mobile phase*

Chromatographic system

Mode: LC

Detector: UV 288 nm

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

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times for dronedarone related compound A and dronedarone are 0.71 and 1.0, respectively.]

Suitability requirements

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

Tailing factor: 0.8–2.2 for dronedarone, *System suitability solution*

Relative standard deviation: NMT 0.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dronedarone hydrochloride ($C_{31}H_{44}N_2O_5S \cdot HCl$) in the portion of Dronedarone Hydrochloride taken:

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

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 = concentration of Dronedarone Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–101.5% on the anhydrous and solvent-free basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Solution A: Combine 2 mL of triethylamine with 950 mL of water. Adjust with phosphoric acid to a pH of 4.0 and then dilute with water to 1 L.

Solution B: Acetonitrile

Mobile phase: See *Table 1*. [Note—Collect data for 58 min.]

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	70	30
15	60	40
25	60	40
40	50	50
45	40	60
58	40	60
60	70	30
70	70	30

Diluent: Acetonitrile and *Solution A*, 50:50

Standard stock solution: 0.2 mg/mL of USP Dronedarone Hydrochloride RS and 0.4 mg/mL of USP Dronedarone Related Compound A RS, respectively, in methanol

Standard solution: 2 µg/mL of USP Dronedarone Hydrochloride RS and 4 µg/mL of USP Dronedarone Related Compound A RS, respectively, in *Diluent* from the *Standard stock solution*

Sensitivity solution: 1 µg/mL of USP Dronedarone Hydrochloride RS and 2 µg/mL of USP Dronedarone Related Compound A RS in *Diluent* from the *Standard solution*

Sample solution: 2 mg/mL of Dronedarone Hydrochloride in *Diluent*. Sonicate for 5 min to dissolve completely. Pass through a suitable filter of 0.45-µm pore size.

Chromatographic system

Mode: LC

Detector: UV 246 nm

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

Flow rate: 0.8 mL/min

Injection volume: 25 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

[Note—The relative retention times for dronedarone related compound A and dronedarone are 0.58 and 1.00, respectively.]

Suitability requirements

Resolution: NLT 25 between dronedarone and dronedarone related compound A, *Standard solution*

Signal-to-noise ratio: NLT 10 for dronedarone and NLT 20 for dronedarone related compound A, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dronedarone related compound A in the portion of Dronedarone Hydrochloride taken:

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

r_U = peak response of dronedarone related compound A from the *Sample solution*

r_S = peak response of dronedarone related compound A from the *Standard solution*

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

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

Calculate the percentage of any unspecified impurity in the portion of Dronedarone Hydrochloride taken:

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

r_U = peak response of any unspecified 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 = concentration of Dronedarone Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: Disregard peaks below 0.05%.

Dronedarone related compound A: NMT 0.15%

Any unspecified impurity: NMT 0.10%

Total impurities: NMT 0.3%

SPECIFIC TESTS

• **Water Determination,** *Method Ia*⟨921⟩**:** NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Protect from light and store at 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 HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 41(2)

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