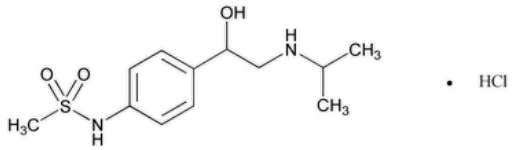
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Aug-2024
Document Type: USP Monographs
DocId: GUID-B8DC3EC2-0C67-4124-A222-50DEB8715EC1_8_en-US
DOI: https://doi.org/10.31003/USPNF_M77676_08_01
DOI Ref: f80l0

Sotalol Hydrochloride

Change to read:



$C_{12}H_{20}N_2O_3S \cdot HCl$ ▲308.82▲ (CN 1-Aug-2024)

Methanesulfonamide, *N*-[4-[1-hydroxy-2-[(1-methylethyl)amino]ethyl]phenyl]-, monohydrochloride;
4'-[1-Hydroxy-2-(isopropylamino)ethyl]methanesulfonanilide monohydrochloride CAS RN®: 959-24-0; UNII: HEC37C70XX.

DEFINITION

Sotalol Hydrochloride contains NLT 98.5% and NMT 101.5% of sotalol hydrochloride ($C_{12}H_{20}N_2O_3S \cdot HCl$).

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**
- **B.** The retention time of the sotalol peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Mobile phase: Transfer about 1.08 g of sodium 1-octanesulfonate to a 1000-mL volumetric flask. Dissolve in 10 mL of glacial acetic acid and about 70 mL of water. Add 720 mL of water and dilute with acetonitrile to volume.

Diluent: Acetonitrile and water (1:4)

Internal standard solution: 4.5 mg/mL of caffeine in *Diluent*

Standard stock solution: 2 mg/mL of USP Sotalol Hydrochloride RS in *Diluent*

Standard solution: 0.2 mg/mL of USP Sotalol Hydrochloride RS prepared as follows. Transfer 10.0 mL of *Standard stock solution* and 5.0 mL of *Internal standard solution* to a 100-mL volumetric flask. Dilute with *Diluent* to volume.

Sample stock solution: 2 mg/mL of Sotalol Hydrochloride in *Diluent*

Sample solution: 0.2 mg/mL of Sotalol Hydrochloride prepared as follows. Transfer 10 mL of *Sample stock solution* and 5.0 mL of *Internal standard solution* to a 100-mL volumetric flask. Dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 238 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 25 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for caffeine and sotalol are 0.39 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 8.5 between caffeine and sotalol

Relative standard deviation: NMT 0.55%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of sotalol hydrochloride ($C_{12}H_{20}N_2O_3S \cdot HCl$) in the portion of Sotalol Hydrochloride taken:

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

R_U = peak area ratio of sotalol to caffeine from the *Sample solution*

R_S = peak area ratio of sotalol to caffeine from the *Standard solution*

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

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

Acceptance criteria: 98.5%–101.5%

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.5%
- **Organic Impurities**

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 6 µg/mL each of USP Sotalol Hydrochloride RS, USP Sotalol Related Compound A RS, USP Sotalol Related Compound B RS, and USP Sotalol Related Compound C RS in *Mobile phase*

Sample solution: 2 mg/mL of Sotalol Hydrochloride in *Mobile phase*

System suitability

Sample: *Standard solution*

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

Suitability requirements

Resolution: NLT 2.0 between sotalol related compound A and sotalol

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each sotalol related compound in the portion of Sotalol Hydrochloride taken:

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

r_U = peak response of the corresponding sotalol related compound from the *Sample solution*

r_S = peak response of the corresponding sotalol related compound from the *Standard solution*

C_S = concentration of the corresponding Reference Standard in the *Standard solution* (µg/mL)

C_U = concentration of Sotalol Hydrochloride in the *Sample solution* (µg/mL)

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

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

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

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

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

C_U = concentration of Sotalol Hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Sotalol related compound B	0.65	0.3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Sotalol	1.0	—
Sotalol related compound A	1.2	0.3
Sotalol related compound C	1.4	0.4
Any unspecified impurity	—	0.10
Total impurities	—	0.5

SPECIFIC TESTS

• **Content of Chloride**

Sample: 310 mg

Titrimetric system

Mode: Direct titration

Titrant: 0.1 N silver nitrate VS

Endpoint detection: Potentiometric

Analysis: Transfer the *Sample* to a glass beaker, and dissolve in 100 mL of water and 10 mL of glacial acetic acid. Titrate with *Titrant*, and determine the endpoint potentiometrically. Each milliliter of *Titrant* is equivalent to 3.545 mg of chloride (Cl).

Acceptance criteria: 11.1%–11.9%

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 125 mg/mL in methanol

Acceptance criteria: −0.7° to +0.7°

• **Water Determination** ⟨921⟩, *Method I*: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Sotalol Hydrochloride RS

USP Sotalol Related Compound A RS

N-[4-(Isopropylglycyl)phenyl]methanesulfonamide hydrochloride.

$C_{12}H_{18}N_2O_3S \cdot HCl$ 306.81

USP Sotalol Related Compound B RS

N-(4-Formylphenyl)methanesulfonamide.

$C_8H_9NO_3S$ 199.22

USP Sotalol Related Compound C RS

▲*N*-{4-[2-(Isopropylamino)ethyl]phenyl}methanesulfonamide hydrochloride.

$C_{12}H_{20}N_2O_2S \cdot HCl$ 292.82▲ (CN 1-Aug-2024)

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

Topic/Question	Contact	Expert Committee
SOTALOL HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(5)

Current DocID: GUID-B8DC3EC2-0C67-4124-A222-50DEB8715EC1_8_en-US

DOI: https://doi.org/10.31003/USPNF_M77676_08_01

DOI ref: f80l0