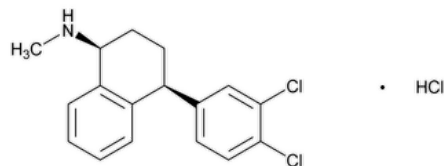


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Sertraline Hydrochloride



$C_{17}H_{17}Cl_2N \cdot HCl$ 342.69

1-Naphthalenamine, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-, hydrochloride, (1S-cis)-;

(1S,4S)-4-(3,4-Dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthylamine hydrochloride CAS RN[®]: 79559-97-0; UNII: UT18907Y6X.

DEFINITION

Sertraline Hydrochloride contains NLT 97.0% and NMT 102.0% of sertraline hydrochloride ($C_{17}H_{17}Cl_2N \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197M
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of sertraline hydrochloride from the *System suitability solution*, as obtained in the test for *Limit of (R,R) Sertraline Hydrochloride*.

Change to read:

- **C. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Chloride**

Sample solution: 1 mg/mL of Sertraline Hydrochloride in a mixture of [dehydrated alcohol](#) and [water](#)[▲](50:50),[▲] (USP 1-May-2021) prepared as follows. Dissolve 10 mg of Sertraline Hydrochloride in 5 mL of [dehydrated alcohol](#). Add 5 mL of [water](#) to the solution.

Acceptance criteria: Meets the requirements [▲][▲] (USP 1-May-2021)

ASSAY

Change to read:

• PROCEDURE

Buffer: To 28.6 mL of [glacial acetic acid](#), slowly add, while stirring, 34.8 mL of [triethylamine](#), and dilute with [water](#) to 100 mL. Dilute 10 mL of the resulting solution with [water](#) to 1 L.

Mobile phase: [Acetonitrile](#), [methanol](#), and *Buffer* (45:15:40)

Standard solution: 0.05 mg/mL of [USP Sertraline Hydrochloride RS](#) in *Mobile phase*

Sample solution: 0.05 mg/mL of Sertraline Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 15-cm; 4-μm packing [L1](#)

Column temperature: 30°

Flow rate: 1.8 mL/min

Injection volume: 20 μL

Run time: [▲]NLT[▲] (USP 1-May-2021) 2 times the retention time of sertraline

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT $\blacktriangle$ 0.73% $\blacktriangle$ (USP 1-May-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of sertraline hydrochloride ($C_{17}H_{17}Cl_2N \cdot HCl$) in the portion of Sertraline Hydrochloride taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Sertraline Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 97.0%–102.0% on the anhydrous basis

IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.3%

Change to read:

- **LIMIT OF (R,R) SERTRALINE HYDROCHLORIDE**

▲Solution A: Transfer 10.0 mL of [ammonium hydroxide](#) to a 100-mL volumetric flask. Dilute with [water](#) to volume. $\blacktriangle$ (USP 1-May-2021)

Mobile phase: $\blacktriangle$ [Chromatographic solvent hexane](#) $\blacktriangle$ (USP 1-May-2021) [2-propanol](#), and [diethylamine](#) $\blacktriangle$ (96: 4: 0.15) $\blacktriangle$ (USP 1-May-2021)

System suitability solution: Transfer 10 mg of [USP Sertraline Hydrochloride Racemic Mixture RS](#) into a 20-mL volumetric flask. Add 4 mL of $\blacktriangle$ *Solution A* $\blacktriangle$ (USP 1-May-2021) and 10 mL of $\blacktriangle$ [chromatographic solvent hexane](#) $\blacktriangle$ (USP 1-May-2021) Shake well until the organic phase is clear.

Wait for phase separation, transfer about 2.0 mL from the top layer into a 20-mL volumetric flask, and dilute with $\blacktriangle$ [chromatographic solvent hexane](#) $\blacktriangle$ (USP 1-May-2021) to volume.

Standard solution: Transfer 10 mg of [USP Sertraline Hydrochloride RS](#) into a 20-mL volumetric flask. Add 4 mL of $\blacktriangle$ *Solution A* $\blacktriangle$ (USP 1-May-2021) and 10 mL of $\blacktriangle$ [chromatographic solvent hexane](#) $\blacktriangle$ (USP 1-May-2021) Shake well until the organic phase is clear. Wait for phase separation, transfer 1.0 mL from the top layer into a 10-mL volumetric flask, and dilute with $\blacktriangle$ [chromatographic solvent hexane](#) $\blacktriangle$ (USP 1-May-2021) to volume. Further dilute quantitatively and stepwise, if necessary, to obtain a solution having a known concentration of 0.01 mg/mL.

Sample solution: Transfer 20 mg of Sertraline Hydrochloride to a 20-mL volumetric flask. Add 4 mL of $\blacktriangle$ *Solution A* $\blacktriangle$ (USP 1-May-2021) and 10 mL of $\blacktriangle$ [chromatographic solvent hexane](#) $\blacktriangle$ (USP 1-May-2021) Shake well until the organic phase is clear. Wait for phase separation, and use the top layer.

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Column: 4.6-mm $\times$ 25-cm; 5- μ m packing [L40](#)

Column temperature: 5°

Flow rate: 1 mL/min

Injection volume: 20 μ L

▲Run time: NLT 4.5 times the retention time of sertraline $\blacktriangle$ (USP 1-May-2021)

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for sertraline and (R,R) sertraline are about 1.0 and 1.16, respectively.]

Suitability requirements

Resolution: NLT 2.8 between sertraline and (R,R) sertraline

Relative standard deviation: NMT 10.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of (R,R) sertraline hydrochloride in the portion of Sertraline Hydrochloride taken:

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

r_U = peak response of (R,R) sertraline from the *Sample solution*

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

C_S = concentration of [USP Sertraline Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 1.5%

Change to read:

• **ORGANIC IMPURITIES, PROCEDURE 1**

▲ Depending on the synthetic route, perform *Organic Impurities, Procedure 2* and *Limit of Mandelic Acid*; or perform *Organic Impurities, Procedure 1*. ▲ (USP 1-May-2021) If sertraline is a known process impurity, then the tests for *Organic Impurities, Procedure 2*, and *Limit of Mandelic Acid* are recommended.

Buffer: 5.8 g/L of [monobasic ammonium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 4.2.

Mobile phase: [Methanol](#) and *Buffer* (48:52)

System suitability solution: 0.5 mg/mL each of [USP Sertraline Hydrochloride RS](#) and [USP Sertraline Hydrochloride Related Compound A RS](#) in *Mobile phase*

Standard solution: 0.5 µg/mL of [USP Sertraline Hydrochloride RS](#) in *Mobile phase*

Sample solution: 0.5 mg/mL of Sertraline Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.0-mm × 25-cm; 5-µm packing [L45](#)

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

▲ **Run time:** NLT 3 times the retention time of sertraline ▲ (USP 1-May-2021)

System suitability

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

[NOTE—See [Table 1](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 2.2 between sertraline hydrochloride related compound A (trans-R,S isomer) and sertraline, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in sertraline hydrochloride ($C_{17}H_{17}Cl_2N \cdot HCl$) in the portion of Sertraline

Hydrochloride taken:

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

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

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

C_S = concentration of [USP Sertraline Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: See [Table 1](#). ▲ The reporting threshold is 0.05%. ▲ (USP 1-May-2021)

Table 1