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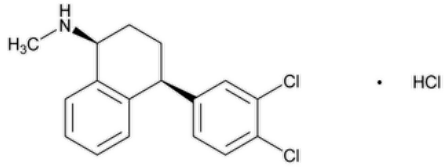
Sertraline Hydrochloride



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

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

(1*S*,4*S*)-4-(3,4-Dichlorophenyl)-1,2,3,4-tetrahydro-*N*-methyl-1-naphthylamine hydrochloride CAS RN®: 79559-97-0; UNII: UTI8907Y6X.

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 ▲0.73%▲ (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.▲ (USP 1-May-2021)

Mobile phase: ▲Chromatographic solvent hexane,▲ (USP 1-May-2021) 2-propanol, and diethylamine▲ (96: 4: 0.15)▲ (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 ▲*Solution A*▲ (USP 1-May-2021) and 10 mL of ▲chromatographic solvent hexane.▲ (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 ▲chromatographic solvent hexane▲ (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 ▲*Solution A*▲ (USP 1-May-2021) and 10 mL of ▲chromatographic solvent hexane.▲ (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 ▲chromatographic solvent hexane▲ (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 ▲*Solution A*▲ (USP 1-May-2021) and 10 mL of ▲chromatographic solvent hexane.▲ (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 × 25-cm; 5-µm packing L40

Column temperature: 5°

Flow rate: 1 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 4.5 times the retention time of sertraline▲ (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 sertralone 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

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
2,3-Isosertraline[a]	0.32	0.15
4-Deschlorosertraline[b]	0.42	0.20
3-Deschlorosertraline[c]	0.60	0.20
Mandelic acid	0.70	0.10
Sertraline	1.0	—
Sertraline related compound A (trans-*R,S* isomer)	1.19	0.10
Sertraline related compound A (trans-*S,R* isomer)	1.64	0.10
Any individual unspecified impurity	—	0.10
Total impurities	—	0.5

[a] (1*RS*,4*RS*)-4-(2,3-Dichlorophenyl)-*N*-methyl-1,2,3,4-tetrahydronaphthalen-1-amine.

[b] (1*RS*,4*RS*)-4-(3-Chlorophenyl)-*N*-methyl-1,2,3,4-tetrahydronaphthalen-1-amine.

[c] (1*RS*,4*RS*)-4-(4-Chlorophenyl)-*N*-methyl-1,2,3,4-tetrahydronaphthalen-1-amine. ▲▲ (USP 1-May-2021)

Change to read:

• **Organic Impurities, Procedure 2**

▲**Solution A:** 250 g/L of anhydrous potassium carbonate in water▲ (USP 1-May-2021)

System suitability solution: Dissolve 50 mg of USP Sertraline Hydrochloride RS and 0.5 mg of USP Sertraline Hydrochloride Related Compound A RS in 2 mL of methanol in a stoppered centrifuge tube. Add 0.2 mL of ▲*Solution A*,▲ (USP 1-May-2021) and mix in a vortex mixer for 30 s. Add 8 mL of methylene chloride. Stopper the tube, and mix in a vortex mixer for 60 s. Add 1 g of anhydrous sodium sulfate. Mix well, and centrifuge for 5 min.

Sample solution: Dissolve 250 mg of Sertraline Hydrochloride in 2 mL of methanol in a stoppered centrifuge tube. Add 0.2 mL of ▲*Solution A*,▲ (USP 1-May-2021) and mix in a vortex mixer for 30 s. Add 8 mL of methylene chloride. Stopper the tube, and mix in a vortex mixer for 60 s. Add 1 g of anhydrous sodium sulfate. Mix well, and centrifuge for 5 min.

Chromatographic system

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

Mode: GC

Detector: Flame-ionization

Column: 30-m × 0.53-mm fused silica column coated with a 1.0-µm film of phase G3

Temperatures

Injection port: 250°

Detector: 280°

Column: See *Table 2*.

Table 2

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
200	0	200	1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
200	2	260	8

Carrier gas: Helium

Flow rate: 9 mL/min

Injection volume: 1 µL

Injection type: Split; split ratio 1:10

System suitability

Sample: *System suitability solution*

[NOTE—See *Table 3* for the relative retention times.]

Suitability requirements

Peak-to-valley ratio: ▲▲ (USP 1-May-2021) NLT 15 ▲between sertraline related compound A and sertraline▲ (USP 1-May-2021)

Analysis

Sample: *Sample solution*

Calculate the percentage of each individual impurity in the portion of Sertraline Hydrochloride taken:

$$\text{Result} = (r_U/r_T) \times 100$$

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

r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria: See *Table 3*. ▲The reporting threshold is 0.05%.▲ (USP 1-May-2021)

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
3,4-Deschlorosertraline[a]	0.5	0.2
3-Deschlorosertraline[b] and 4-deschlorosertraline[c]	0.7	0.8
Sertraline	1.0	—
Sertraline related compound A	1.05	0.2
Sertralone[d]	1.1	0.2
Any individual unspecified impurity	—	0.10
Total impurities[e]	—	1.5

[a] (1*RS*,4*RS*)-4-Phenyl-*N*-methyl-1,2,3,4-tetrahydronaphthalen-1-amine.

[b] (1*RS*,4*RS*)-4-(4-Chlorophenyl)-*N*-methyl-1,2,3,4-tetrahydronaphthalen-1-amine.

[c] (1*RS*,4*RS*)-4-(3-Chlorophenyl)-*N*-methyl-1,2,3,4-tetrahydronaphthalen-1-amine.

[d] 4-(3,4-Dichlorophenyl)-3,4-dihydronaphthalen-1(2*H*)-one.

[e] Does not include mandelic acid and 1*R*,4*R*-sertraline hydrochloride. ▲▲ (USP 1-May-2021)

Change to read:

• **LIMIT OF MANDELIC ACID**

Perform this test only if *Organic Impurities, Procedure 2*, is used.

Solution A: Dissolve 1 g of ▲sodium dodecyl sulfate▲ (USP 1-May-2021) in 800 mL of water. Add 200 mL of acetonitrile and 1 mL of phosphoric acid.

Solution B: Dissolve 1 g of ▲sodium dodecyl sulfate▲ (USP 1-May-2021) in 100 mL of water. Add 900 mL of acetonitrile and 1 mL of phosphoric acid.

Diluent: *Solution A* and *Solution B* (50:50)

Mobile phase: See *Table 4*.

Table 4

Time (min)	Solution A (%)	Solution B (%)
0	60	40
8	60	40
9	10	90
16	10	90
16.1	60	40
20	60	40

System suitability solution: 0.005 mg/mL each of USP Benzoic Acid RS and USP Mandelic Acid RS in *Diluent*

Standard solution: 0.002 mg/mL of USP Mandelic Acid RS in *Diluent*

Sample solution: 1 mg/mL of Sertraline Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; 3-µm packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—The relative retention times for mandelic acid, benzoic acid, and sertraline are 0.2, 0.3, and 1.0 respectively.]

Suitability requirements

Resolution: NLT 5 between benzoic acid and mandelic acid, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of mandelic acid 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 mandelic acid from the *Sample solution*

r_S = peak response of mandelic acid from the *Standard solution*

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

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

Acceptance criteria: NMT 0.2%

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I, Method Ia*: NMT 0.50%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers at a temperature NMT 40°.

• **Labeling:** Label to indicate the *Organic Impurities* procedure with which the article complies, if *Organic Impurities, Procedure 1*, is not used.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Benzoic Acid RS

USP Mandelic Acid RS

USP Sertraline Hydrochloride RS

USP Sertraline Hydrochloride Racemic Mixture RS

(1*RS*,4*RS*)-4-(3,4-Dichlorophenyl)-*N*-methyl-1,2,3,4-tetrahydro-1-naphthylamine hydrochloride.

$C_{17}H_{17}Cl_2$▲N▲ (ERR 1-May-2021) · HCl 342.69

USP Sertraline Hydrochloride Related Compound A RS

(1*RS*,4*SR*)-4-(3,4-Dichlorophenyl)-*N*-methyl-1,2,3,4-tetrahydro-1-naphthylamine hydrochloride.

$C_{17}H_{17}Cl_2N$ · HCl 342.69

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

Topic/Question	Contact	Expert Committee
SERTRALINE HYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

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