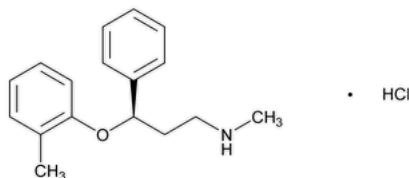


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Atomoxetine Hydrochloride

Change to read:



$C_{17}H_{21}NO \cdot HCl$ 291.82

Benzenepropanamine, *N*-methyl-γ-(2-methylphenoxy)-, hydrochloride, (-);

(-)-*N*-Methyl-3-phenyl-3-(*o*-tolylloxy)propylamine hydrochloride;

▲(*R*)-▲ (USP 1-May-2023) *N*-Methyl-3-phenyl-3-(2-tolylloxy)propylamine hydrochloride CAS RN®: 82248-59-7; UNII: 57WVB6I2W0.

DEFINITION

Atomoxetine Hydrochloride contains NLT 98.0% and NMT 102.0% of atomoxetine hydrochloride ($C_{17}H_{21}NO \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the atomoxetine *R*-isomer from the *System suitability solution*, as obtained in the test for *Organic Impurities, Procedure 2*.
- **C. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Chloride:** Meets the requirements

ASSAY

PROCEDURE

Solution A: 280 g/L of [potassium hydroxide](#) in [water](#)

Buffer: 2.9 g/L of [phosphoric acid](#) in [water](#). Adjust with *Solution A* to a pH of 2.5. To 1 L of this solution add 5.9 g of [octanesulfonic acid sodium salt monohydrate](#).

Mobile phase: [*n*-Propyl alcohol](#) and *Buffer* (27:73). [NOTE—The ratio of [n-propyl alcohol](#) in *Buffer* can be varied between 26:74 and 29:71 to meet system suitability requirements.]

System suitability solution: 0.1 mg/mL of [USP Mandelic Acid RS](#), 0.15 mg/mL of [USP Atomoxetine Related Compound A RS](#), and 0.25 mg/mL of [USP Atomoxetine Hydrochloride RS](#) in *Mobile phase*

Standard solution: 0.25 mg/mL of [USP Atomoxetine Hydrochloride RS](#) in *Mobile phase*. Sonication may be used to aid in dissolution.

Sample solution: 0.25 mg/mL of Atomoxetine Hydrochloride in *Mobile phase*. Sonication may be used to aid in dissolution.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 15-cm; 3.5-μm packing [L7](#)

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 10 μL

Run time: NLT 1.3 times the retention time of atomoxetine

System suitability

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

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

Suitability requirements

Resolution: NLT 5.0 between mandelic acid and atomoxetine related compound A, *System suitability solution*

Tailing factor: NMT 1.5 for atomoxetine, *System suitability solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of atomoxetine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) in the portion of Atomoxetine Hydrochloride taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **RESIDUE ON IGNITION (281):** NMT 0.1%

• **ORGANIC IMPURITIES, PROCEDURE 1**

[NOTE—It is required to perform *Organic Impurities, Procedure 1* and *Organic Impurities, Procedure 2*.]

Buffer, Mobile phase, and System suitability solution: Prepare as directed in the Assay.

Sensitivity solution: 0.0013 mg/mL of [USP Atomoxetine Hydrochloride RS](#) in *Mobile phase*

Standard solution: 0.0025 mg/mL of [USP Atomoxetine Hydrochloride RS](#) in *Mobile phase*

Sample solution: 2.5 mg/mL of Atomoxetine Hydrochloride in *Mobile phase*

Chromatographic system: Proceed as directed in the Assay, except for *Run time*.

Run time: NLT 2.6 times the retention time of atomoxetine

System suitability

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

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

Suitability requirements

Resolution: NLT 5.0 between mandelic acid and atomoxetine related compound A, *System suitability solution*

Tailing factor: NMT 1.5 for atomoxetine, *System suitability solution*

Relative standard deviation: NMT 5%, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Atomoxetine 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 atomoxetine from the *Standard solution*

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

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

Acceptance criteria: See [Table 1](#). The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Mandelic acid	0.20	0.10
Atomoxetine related compound A	0.27	0.10
Desmethyl atomoxetine ^a	0.73	0.3
Atomoxetine	1.0	—
Any individual unspecified impurity	—	0.10
Total impurities	—	0.5

^a (R)-N-Methyl-3-phenoxy-3-phenylpropan-1-amine.