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Atomoxetine Capsules

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<https://www.uspnf.com/rb-atomoxetine-caps-20200131>.

DEFINITION

Atomoxetine Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of atomoxetine ($C_{17}H_{21}NO$).

IDENTIFICATION

Change to read:

- **A.** ▲ **SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K or 197A▲ (CN 1-May-2020)

Standard: 6 mg/mL of [USP Atomoxetine Hydrochloride RS](#) in [methanol](#). Dry the solution to a dry powder under an air or nitrogen purge for a minimum of 3 h.

Sample: Shake the contents of a sufficient number of Capsules, equivalent to about 60 mg of atomoxetine, with 10 mL of [methanol](#). Centrifuge at 4000 rpm for 5 min. Evaporate the solution to a dry powder with the aid of a current of air or stream of nitrogen.

Acceptance criteria: The IR spectrum exhibits main bands at (± 2) wavenumbers (cm^{-1}) 2955, 2855, 1599–1604, 1492, 1048, 1023, and 1010.

- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

• PROCEDURE

Buffer: 5.8 g/L of [monobasic potassium phosphate](#) in [water](#). To each liter of this solution add 3.0 mL of [triethylamine](#), and adjust with [phosphoric acid](#) to a pH of 2.5.

Mobile phase: [Acetonitrile](#) and *Buffer* (38:62)

System suitability solution: 0.1 mg/mL of atomoxetine (free base) from [USP Atomoxetine Hydrochloride RS](#) and 0.02 mg/mL of o-cresol in *Mobile phase*. Sonicate to aid in dissolution.

Standard solution: 0.1 mg/mL of atomoxetine (free base) from [USP Atomoxetine Hydrochloride RS](#) in *Mobile phase*. Sonicate to aid in dissolution.

Sample stock solution: From NLT 10 Capsules (including shells) prepared as follows. Add the intact Capsules to a suitable volumetric flask. Add *Mobile phase* to fill 65% of the final volume. Allow to stand for at least 10 min, then shake for 20 min. Dilute with *Mobile phase* to volume.

Sample solution: Nominally 0.1 mg/mL of atomoxetine, prepared by diluting a suitable volume of *Sample stock solution* with *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm $\times$ 7.5-cm; 3.5- μ m packing [L7](#)

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection volume: 10 μ L

Run time: 1.7 times the retention time of atomoxetine

System suitability

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

[NOTE—The relative retention times for atomoxetine and o-cresol are 1.0 and 1.3, respectively.]

Suitability requirements

Resolution: NLT 3.5 between atomoxetine and o-cresol, *System suitability solution*

Tailing factor: NMT 2.0 for atomoxetine, *System suitability solution*

Relative standard deviation: NMT 1.0% for atomoxetine, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of atomoxetine ($C_{17}H_{21}NO$) in the portion of Capsules 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 atomoxetine in the *Standard solution* (mg/mL)

C_U = nominal concentration of atomoxetine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#)

Medium: 0.1 N hydrochloric acid; 1000 mL, deaerated, ▲if needed▲ (RB 1-May-2020)

Apparatus 2: 50 rpm, with ▲suitable▲ (RB 1-May-2020) sinker

Time: 30 min

Buffer and Mobile phase: Prepare as directed in the Assay.

Standard stock solution: 0.1 mg/mL of atomoxetine (free base) from [USP Atomoxetine Hydrochloride RS](#) in *Medium*. Sonicate to aid in dissolution.

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of $(L/1000)$ mg/mL, where L is the Capsule label claim in mg.

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system: Proceed as directed in the Assay.

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.4%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of atomoxetine ($C_{17}H_{21}NO$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of atomoxetine in the *Standard solution* (mg/mL)

L = label claim (mg/Capsule)

V = volume of *Medium* (mL)

Tolerances: NLT 80% (Q) of the labeled amount of atomoxetine ($C_{17}H_{21}NO$) is dissolved.

• [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meet the requirements

IMPURITIES

• ORGANIC IMPURITIES

Buffer: Dissolve 4.9 g of [sodium 1-decanesulfonate](#) and 6.9 g of [monobasic potassium phosphate](#) in 1 L of [water](#). Adjust with [phosphoric acid](#) to a pH of 3.1.

Mobile phase: [Acetonitrile](#) and *Buffer* (41:59)

Sensitivity solution: 0.1 µg/mL of atomoxetine in *Mobile phase*

System suitability solution: 1 mg/mL of atomoxetine containing atomoxetine *N*-amide prepared as follows. Weigh equal amounts of [USP Atomoxetine Hydrochloride RS](#) and [urea](#), and place in a volumetric flask. Add [water](#) to fill 10% of the final volume. Sonicate for 3 min. Place the flask in an 85° oven for 40 min. Allow the solution to cool to room temperature. Dilute with *Mobile phase* to volume. [NOTE—The oven temperature and time in the oven can be adjusted to give a suitable level of atomoxetine *N*-amide peak.]

Sample solution: 1 mg/mL of atomoxetine in *Mobile phase*, from the contents of NLT 5 Capsules prepared as follows. Transfer the Capsule contents to a suitable volumetric flask. Fill 50% of the final volume with *Mobile phase*. Swirl, and let stand for 15 min. Dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm