Status: Currently Official on 13-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-5C18BF39-709E-43C6-8BB3-0AB712ACA46F_3_en-US
DOI: https://doi.org/10.31003/USPNF_M1418_03_01
DOI Ref: f7wjf

Atomoxetine Capsules

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click 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 × 7.5-cm; 3.5-µm packing L7

  Column temperature: 35°

  Flow rate: 1.5 mL/min

  Injection volume: 10 µL

  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

Column: 4.6-mm × 15-cm; 3.5-µm packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: 2.3 times the retention time of atomoxetine

System suitability

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

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

Suitability requirements

Resolution: NLT 2.6 between atomoxetine and atomoxetine *N*-amide, *System suitability solution*

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

Analysis

Sample: *Sample solution*

Calculate the percentage of each individual impurity in the portion of Capsules 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 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Desmethyl atomoxetine[a]	0.76	0.3
Atomoxetine	1.0	—
Atomoxetine *N*-amide[b]	1.2	0.2
Any individual unspecified degradation product	—	0.2
Total impurities	—	1.0

[a] (*R*)-*N*-Methyl-3-phenoxy-3-phenylpropan-1-amine.

[b] (*R*)-1-Methyl-1-[3-phenyl-3-(*o*-tolyloxy)propyl]urea.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at controlled room temperature.
- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Atomoxetine Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
ATOMOXETINE CAPSULES	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 44(1)

Current DocID: GUID-5C18BF39-709E-43C6-8BB3-0AB712ACA46F_3_en-US

DOI: https://doi.org/10.31003/USPNF_M1418_03_01

DOI ref: f7wjf