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Memantine Hydrochloride Tablets

DEFINITION

Memantine Hydrochloride Tablets contain an amount of memantine hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of memantine hydrochloride ($C_{12}H_{21}N \cdot HCl$).

IDENTIFICATION

Change to read:

- **A.** ▲ [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 197K](#) ▲ (CN 1-MAY-2020)

Analytical range: 4000–400 cm^{-1}

Standard: 6.7 mg/mL of [USP Memantine Hydrochloride RS](#) in dichloromethane. Shake for 10 min, and pass through a suitable filter.

Evaporate the solvent at room temperature. Collect the residue powder, and dry at 60° for 15 min. Prepare an approximate 1% (w/w) dispersion of the sample in [potassium bromide](#).

Sample: 6.7 mg/mL of memantine hydrochloride in dichloromethane from NLT 20 crushed Tablets. Shake for 10 min, and centrifuge for 10 min. Pass the supernatant through a suitable filter. Evaporate the solvent at room temperature. Collect the residue powder, and dry at 60° for 15 min. Prepare an approximate 1% (w/w) dispersion of the sample in [potassium bromide](#).

Acceptance criteria: Fingerprint region of the *Standard* and *Sample* spectrum exhibit maxima at the same wave numbers.

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

ASSAY

PROCEDURE

Solution A: 200 mg/mL of [sodium hydroxide](#) in [water](#)

Internal standard solution: 25 µg/mL of [USP Amantadine Hydrochloride RS](#) in [water](#)

Standard stock solution: 25 µg/mL of [USP Memantine Hydrochloride RS](#) prepared as follows. Weigh a suitable quantity of the Standard into a volumetric flask. Add methanol to fill 40% of the final flask volume, and sonicate. Dilute with [water](#) to volume.

Standard solution: Pipet 4.0 mL each of the *Internal standard solution* and the *Standard stock solution* into a test tube. Add 2 mL of *Solution A*, and mix on a vortex mixer for 1 min. Add 4.0 mL of [toluene](#), and mix on a vortex mixer for 3 min. Allow the two layers to separate. Inject the toluene layer.

Sample stock solution: Nominally 20 µg/mL of memantine hydrochloride prepared as follows. Transfer a suitable number of Tablets to a volumetric flask to obtain a 0.1 mg/mL memantine hydrochloride solution. Add methanol to fill 40% of the final flask volume, and sonicate for 30 min with intermittent shaking. Add [water](#) to fill 40% of the final flask volume, and sonicate for 30 min with intermittent shaking. Dilute with [water](#) to volume, and centrifuge a portion for 10 min. Pipet a suitable volume of the clear centrifugate into a volumetric flask, and dilute with [water](#) to volume.

Sample solution: Pipet 5.0 mL of the *Sample stock solution*, 4.0 mL of the *Internal standard solution*, and 2 mL of *Solution A* into a test tube, and mix on a vortex mixer for 1 min. Add 4.0 mL of [toluene](#), and mix on a vortex mixer for 5 min. Allow the two layers to separate. Inject the toluene layer.

Blank: To 5.0 mL of 80 µL/mL of methanol in [water](#) add 2 mL of *Solution A*, and mix on a vortex mixer for 1 min. Add 4.0 mL of [toluene](#), and mix on a vortex mixer for 5 min. Allow the two layers to separate. Inject the toluene layer.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 30-m × 0.32-mm; 0.25-µm packing [G27](#)

Temperatures

Injection port: 210°

Detector: 300°

Oven: See [Table 1](#).

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	0	50	2
50	20	140	0
140	30	200	5

Carrier gas: Helium

Flow rate: 34.8 psi

Injection volume: 4 µL

Injection type: Split ratio, 1:10

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for amantadine and memantine are 0.97 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between amantadine and memantine

Tailing factor: NMT 2.5 for amantadine; NMT 2.0 for memantine

Relative standard deviation: NMT 2.0% for the ratio of the peak areas of amantadine and memantine

Analysis

Samples: *Standard solution, Sample solution, and Blank*

Calculate the percentage of the labeled amount of memantine hydrochloride ($C_{12}H_{21}N \cdot HCl$) in the portion of Tablets taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak area ratio of memantine to amantadine from the *Sample solution*

R_S = peak area ratio of memantine to amantadine from the *Standard solution*

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

C_U = nominal concentration of memantine hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Medium: [0.1 N hydrochloric acid](#) with [sodium chloride](#) (2 g/L of [sodium chloride](#) in [water](#)), adjusted with [hydrochloric acid](#) to a pH of 1.2; 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard stock solution: (L/900) mg/mL of [USP Memantine Hydrochloride RS](#) in *Medium*, where L is the label claim in mg/Tablet

Internal standard solution: 28 µg/mL of [USP Amantadine Hydrochloride RS](#) in *Medium*

Standard solution

For Tablets labeled to contain 5 mg: Transfer 5 mL of the *Standard stock solution* to a test tube, add 1 mL of the *Internal standard solution* and 2 mL of [5 N sodium hydroxide](#), and mix for 1 min. Add 3 mL of [toluene](#), and mix for 2 min. Use the toluene layer.

For Tablets labeled to contain 10 mg: Transfer 5 mL of the *Standard stock solution* to a test tube, add 2 mL of the *Internal standard solution* and 2 mL of [5 N sodium hydroxide](#), and mix for 1 min. Add 3 mL of [toluene](#), and mix for 2 min. Use the toluene layer.

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

For Tablets labeled to contain 5 mg: Transfer 5 mL of the filtrate to a test tube, add 1 mL of the *Internal standard solution* and 2 mL of [5 N sodium hydroxide](#), and mix for 1 min. Add 3 mL of [toluene](#), and mix for 2 min. Use the toluene layer.

For Tablets labeled to contain 10 mg: Transfer 5 mL of the filtrate to a test tube, add 2 mL of the *Internal standard solution* and 2 mL of [5 N sodium hydroxide](#), and mix for 1 min. Add 3 mL of [toluene](#), and mix for 2 min. Use the toluene layer.

Chromatographic system

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

Mode: GC, splitless

Detector: Flame ionization

Column: 30-m × 0.32-mm; 0.25-µm packing [G27](#)

Flow rate: 34.8 psi

Temperatures

Injection port: 210°