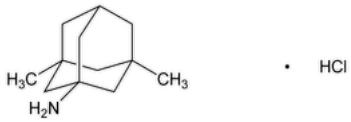
Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-63E790A9-F66D-445D-BB15-6D9483F04406_4_en-US
DOI: https://doi.org/10.31003/USPNF_M1040_04_01
DOI Ref: piy94

Memantine Hydrochloride



$C_{12}H_{21}N \cdot HCl$ 215.76

Tricyclo[3.3.1.1^{3,7}]decan-1-amine, 3,5-dimethyl-, hydrochloride;

1-Amino-3,5-dimethyladamantane hydrochloride CAS RN®: 41100-52-1; UNII: JY0WD0UA60.

DEFINITION

Memantine Hydrochloride contains NLT 98.0% and NMT 102.0% of memantine hydrochloride ($C_{12}H_{21}N \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

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

• **C.** **Identification Tests—General, *Chloride* ⟨191⟩:** Meets the requirements

ASSAY

• **Procedure**

Internal standard solution: 4.0 mg/mL of adamantane in *n*-hexane

Standard solution: 4.0 mg/mL of USP Memantine Hydrochloride RS in *Internal standard solution* prepared as follows. Transfer 100 mg of USP Memantine Hydrochloride RS to a 50-mL centrifuge tube. Add 15 mL of 1 N sodium hydroxide, and mix. Add 25 mL of *Internal standard solution*, and shake for 15 min. Allow the layers to separate, and filter a portion of the top hexane layer through anhydrous sodium sulfate. Use the clear filtrate.

Sample solution: 4.0 mg/mL of Memantine Hydrochloride in *Internal standard solution* prepared as follows. Transfer 100 mg of Memantine Hydrochloride to a 50-mL centrifuge tube. Add 15 mL of 1 N sodium hydroxide, and mix. Add 25 mL of *Internal standard solution*, and shake for 15 min. Allow the layers to separate, and filter a portion of the top hexane layer through anhydrous sodium sulfate. Use the clear filtrate.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 50-m × 0.32-mm; 0.52-µm packing G27

Temperatures

Injection port: 220°

Detector: 300°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	5	145	0
145	10	250	20

Carrier gas: Helium

Flow rate: 4.0 ± 0.4 mL/min

Injection volume: 1 µL

Injection type: Split ratio, 1:50

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 each for memantine and adamantane

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

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

R_U = peak response ratio of memantine to the internal standard from the *Sample solution*

R_S = peak response ratio of memantine to the internal standard from the *Standard solution*

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

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

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Standard stock solution A: 2.5 mg/mL each of USP Memantine Related Compound A RS, USP Memantine Related Compound B RS, USP Memantine Related Compound C RS, USP Memantine Related Compound D RS, and USP Memantine Related Compound E RS in *n*-hexane

Standard stock solution B: 2.5 mg/mL of USP Memantine Hydrochloride RS prepared as follows. To the flask containing a weighed amount of USP Memantine Hydrochloride RS, add 5.0 N sodium hydroxide to fill 20% of the final volume and *n*-hexane to fill 20% of the final volume. Shake for 10 min, and transfer the contents to a separator. Allow the layers to separate, filter a portion of the top hexane layer, dry the organic layer by swirling with anhydrous sodium sulfate, and allow to stand for a few min to ensure all the remaining water has been removed. Use the clear filtrate.

System suitability solution: 25 µg/mL each of USP Memantine Related Compound A RS, USP Memantine Related Compound B RS, USP Memantine Related Compound C RS, USP Memantine Related Compound D RS, and USP Memantine Related Compound E RS, from *Standard stock solution A* in *Standard stock solution B*. The concentration of USP Memantine Hydrochloride RS is 2.5 mg/mL.

Standard solution: 25 µg/mL each of USP Memantine Related Compound A RS, USP Memantine Related Compound B RS, USP Memantine Related Compound C RS, USP Memantine Related Compound D RS, USP Memantine Related Compound E RS, and USP Memantine Hydrochloride RS, from *Standard stock solution A* and *Standard stock solution B*, respectively, in *n*-hexane

Sample solution: 25 mg/mL of Memantine Hydrochloride prepared as follows. Transfer the weighed amount of Memantine Hydrochloride to a suitable volumetric flask. Add 5.0 N sodium hydroxide to fill 30% of the final volume and *n*-hexane to fill 40% of the final volume. Shake for 10 min, and transfer the contents to a separator. Allow the layers to separate, filter a portion of the top hexane layer, dry the organic layer by swirling with anhydrous sodium sulfate, and allow to stand for a few min to ensure all the remaining water has been removed. Use the clear filtrate.

Chromatographic system: Proceed as directed in the *Assay*.

System suitability

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

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 6.0 between memantine and memantine related compound B; NLT 2.0 between memantine related compound B and memantine related compound C, *System suitability solution*

Tailing factor: NMT 2.0 for memantine, *Standard solution*

Relative standard deviation: NMT 10.0% for memantine, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

[Note—Ignore the peaks at the relative retention times 0.11, 0.12, 0.13, 0.18, and 0.26 with respect to the memantine peak, as they correspond to residual solvents.]

Calculate the percentage of each of memantine related compounds A, B, C, D, and E in the portion of Memantine Hydrochloride taken:

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

r_U = peak response of memantine related compounds A, B, C, D, or E from the *Sample solution*

r_S = peak response of the corresponding USP Memantine Related Compound RS from the *Standard solution*

C_S = concentration of the corresponding USP Memantine Related Compound RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any other impurity in the portion of Memantine Hydrochloride taken:

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

r_U = peak response of any other impurity from the *Sample solution*

r_S = peak response of memantine hydrochloride from the *Standard solution*

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Memantine related compound A	0.77	0.15
Memantine	1.0	—
Memantine related compound B	1.03	0.15
Memantine related compound C	1.07	0.15
Memantine related compound D	1.19	0.15
Memantine related compound E	1.44	0.15
Any individual unspecified impurity	—	0.10
Total impurities	—	0.50

SPECIFIC TESTS

- **Water Determination, *Method I* ⟨921⟩:** NMT 1.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.
- **USP Reference Standards ⟨11⟩**

USP Memantine Hydrochloride RS

USP Memantine Related Compound A RS

1,3-Dimethyladamantane.

$C_{12}H_{20}$ 164.29

USP Memantine Related Compound B RS

3,5-Dimethyladamantane-1-ol.

$C_{12}H_{20}O$ 180.29

USP Memantine Related Compound C RS

1-Chloro-3,5-dimethyladamantane.

$C_{12}H_{19}Cl$ 198.73

USP Memantine Related Compound D RS

1-Bromo-3,5-dimethyladamantane.

$C_{12}H_{19}Br$ 243.18

USP Memantine Related Compound E RS

N-3,5-Dimethyladamantan-1-yl formamide.

$C_{13}H_{21}NO$ 207.31

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

Topic/Question	Contact	Expert Committee
MEMANTINE HYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 41(1)

Current DocID: GUID-63E790A9-F66D-445D-BB15-6D9483F04406_4_en-US

DOI: https://doi.org/10.31003/USPNF_M1040_04_01

DOI ref: piy94