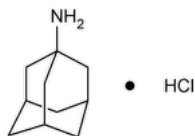


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Amantadine Hydrochloride



$C_{10}H_{17}N \cdot HCl$ 187.71

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

1-Adamantanamine hydrochloride CAS RN[®]: 665-66-7; UNII: M6Q1EO9TD0.

DEFINITION

Amantadine Hydrochloride contains NLT 98.0% and NMT 102.0% of amantadine hydrochloride ($C_{10}H_{17}N \cdot HCl$).

IDENTIFICATION

Change to read:

- **A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#):** 197A, 197K, [▲]or[▲] (ERR 1-Sep-2023) 197S

▲Procedure for 197S▲ (ERR 1-Sep-2023)

Cell: 1 mm

Sample solution: 50 mg in 10 mL of 0.1 N [hydrochloric acid](#). Filter, transfer the filtrate to a suitable separator, add 1 mL of 5 N [sodium hydroxide](#), and extract with 5 mL of methylene chloride.

Acceptance criteria: Meets the requirements

- **B.** The retention time of the amantadine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **C. [IDENTIFICATION TESTS—GENERAL \(191\)](#), [Chemical Identification Tests, Chloride](#)**

ASSAY

• PROCEDURE

Internal standard solution: 0.3 mg/mL of adamantane in [n-heptane](#)

Standard stock solution: 1 mg/mL of [USP Amantadine Hydrochloride RS](#) in [water](#)

Standard solution: Transfer 10 mL of *Standard stock solution* and 10 mL of 5 N [sodium hydroxide](#) solution to a separatory funnel. Add 25 mL of *Internal standard solution* and shake for 10 min. Collect the upper layer of [n-heptane](#) and swirl with [anhydrous sodium sulfate](#) to remove traces of water.

Sample stock solution: 1 mg/mL of Amantadine Hydrochloride in [water](#)

Sample solution: Transfer 10 mL of *Sample stock solution* and 10 mL of 5 N [sodium hydroxide](#) solution to a separatory funnel. Add 25 mL of *Internal standard solution* and shake for 10 min. Collect the upper layer of [n-heptane](#) and swirl with [anhydrous sodium sulfate](#) to remove traces of water.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 30-m base deactivated fused-silica; coated with 1.0-μm film of stationary phase [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)
120	0	120	3
120	8	250	10

Carrier gas: Helium

Flow rate: 4 mL/min

Injection volume: 2 µL

Injection type: Split, split ratio 5:1 (deactivated split liner with glass wool)

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for adamantane and amantadine are about 0.7 and 1.0, respectively.]

Suitability requirements

Relative standard deviation: NMT 1.0% for the peak response ratio of amantadine to adamantane

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amantadine hydrochloride ($C_{10}H_{17}N \cdot HCl$) in the portion of Amantadine Hydrochloride taken:

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

R_U = peak response ratio of amantadine to adamantane from the *Sample solution*

R_S = peak response ratio of amantadine to adamantane from the *Standard solution*

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

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

Acceptance criteria: 98.0%–102.0%

IMPURITIES

• ORGANIC IMPURITIES

Internal standard solution: 0.1 mg/mL of adamantane in [n-heptane](#)

Peak identification solution: 0.03 mg/mL each of [USP Amantadine Related Compound A RS](#) and [USP Amantadine Related Compound B RS](#) in *Internal standard solution* prepared as follows. Transfer suitable amounts of [USP Amantadine Related Compound A RS](#) and [USP Amantadine Related Compound B RS](#) to a suitable volumetric flask. Add [methylene chloride](#) to about 5% of the flask volume to dissolve, and dilute with *Internal standard solution* to volume.

Standard stock solution: 0.03 mg/mL of [USP Amantadine Hydrochloride RS](#) in [water](#)

Standard solution: Transfer 25 mL of *Standard stock solution* and 10 mL of 5 N [sodium hydroxide](#) solution to a separatory funnel. Add 25 mL of *Internal standard solution* and shake for 10 min. Collect the upper layer of [n-heptane](#) and swirl with [anhydrous sodium sulfate](#) to remove traces of water.

Sample stock solution: 10 mg/mL of Amantadine Hydrochloride in [water](#)

Sample solution: Transfer 25 mL of *Sample stock solution* and 10 mL of 5 N [sodium hydroxide](#) solution to a separatory funnel. Add 25 mL of *Internal standard solution* and shake for 10 min. Collect the upper layer of [n-heptane](#) and swirl with [anhydrous sodium sulfate](#) to remove traces of [water](#).

Chromatographic system: Proceed as directed in the Assay.

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for adamantane and amantadine are 0.7 and 1.0, respectively.]

Suitability requirements

Relative standard deviation: NMT 3.0% for the peak response ratio of amantadine to adamantane

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Amantadine Hydrochloride taken:

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

R_U = peak response ratio of any individual impurity to adamantane from the *Sample solution*

R_S = peak response ratio of amantadine to adamantane from the *Standard solution*