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Amantadine Hydrochloride Oral Solution

DEFINITION

Amantadine Hydrochloride Oral Solution contains NLT 95.0% and NMT 105.0% of the labeled amount of amantadine hydrochloride ($C_{10}H_{17}N \cdot HCl$).

IDENTIFICATION

Change to read:

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

Cell: 1 mm

Sample solution: Place a volume of Oral Solution, equivalent to 200 mg of amantadine hydrochloride, in a vessel, dissolve in 0.1 N hydrochloric acid, and filter. Transfer the filtrate to a separator, add 10 mL of 0.5 N sodium hydroxide, and extract with 5 mL of methylene chloride. Filter the extract through anhydrous sodium sulfate, and rinse the anhydrous sodium sulfate with 2 mL of methylene chloride.

Acceptance criteria: Meets the requirements

• **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**

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* to a separatory funnel and add 10 mL of 5 N sodium hydroxide solution. Add 25 mL of *Internal standard solution* and shake for 10 min. Collect the *n*-heptane upper layer and swirl with anhydrous sodium sulfate to remove traces of water.

Sample stock solution: Nominally 1 mg/mL of amantadine hydrochloride from a portion of Oral Solution in water

Sample solution: Transfer 10 mL of *Sample stock solution* to a separatory funnel and add 10 mL of 5 N sodium hydroxide solution. Add 25 mL of *Internal standard solution* and shake for 10 min. Collect the *n*-heptane upper layer 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 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

Tailing factor: NMT 2.0 for the amantadine peak

Relative standard deviation: NMT 2.0% for the peak response ratio of amantadine to adamantane

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amantadine hydrochloride ($C_{10}H_{17}N \cdot HCl$) in the portion of Oral Solution 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 = nominal concentration of amantadine hydrochloride in the *Sample stock solution* (mg/mL)

Acceptance criteria: 95.0%–105.0%

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*, 10 mL of 5 N sodium hydroxide solution, and 25 mL of *Internal standard solution* to a separatory funnel 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: Nominally 10.0 mg/mL of amantadine hydrochloride from Oral Solution in water

Sample solution: Transfer 25 mL of *Sample stock solution*, equivalent to 250 mg of amantadine hydrochloride, 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 and adamantane

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual unspecified impurity in the portion of Oral Solution taken:

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

R_U = peak response ratio of any individual unspecified impurity 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 = nominal concentration of amantadine hydrochloride in the *Sample stock solution* (mg/mL)

Acceptance criteria: see *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Amantadine	1.0	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Amantadine related compound A[a]	1.2	—
Amantadine related compound B[a]	1.9	—
Any individual unspecified impurity	—	0.2
Total impurities	—	2.0

[a] Process impurity included in the table for identification only. Process impurities are controlled in the drug substance, and are not to be reported or included in the total impurities for the drug product.

ADDITIONAL REQUIREMENTS

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

USP Amantadine Hydrochloride RS

USP Amantadine Related Compound A RS

1-Chloroadamantane.

$C_{10}H_{15}Cl$ 170.68

USP Amantadine Related Compound B RS

N-(Adamantan-1-yl)acetamide.

$C_{12}H_{19}NO$ 193.29

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

Topic/Question	Contact	Expert Committee
AMANTADINE HYDROCHLORIDE ORAL SOLUTION	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

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