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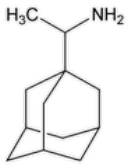
Rimantadine Hydrochloride



• HCl

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

Tricyclo[3.3.1.1^{3,7}]-decane-1-methanamine, α-methyl-, hydrochloride.

α-Methyl-1-adamantanemethylamine hydrochloride CAS RN®: 1501-84-4; UNII: JEI07OOS8Y.

» Rimantadine Hydrochloride contains not less than 98.0 percent and not more than 102.0 percent of $C_{12}H_{21}N \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers, and store between 15° to 30°.

USP Reference standards ⟨11⟩—
USP Rimantadine Hydrochloride RS

Identification—

A: *Spectroscopic Identification Tests* ⟨197⟩*, Infrared Spectroscopy: 197K*.

B: The retention time of the rimantadine peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Change to read:

▲**X-ray powder diffraction** ⟨941⟩▲ (CN 1-May-2022) —The X-ray diffraction pattern conforms to that of USP Rimantadine Hydrochloride RS, similarly determined.

Loss on drying ⟨731⟩—Dry it at 105° for 3 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.2%.

Ordinary impurities ⟨466⟩—

Test solution—Transfer 100 mg of Rimantadine Hydrochloride to a 10-mL centrifuge tube, add 2 mL of 1 N sodium hydroxide, and mix. Add 2 mL of chloroform, and mix on a vortex mixer for 1 minute. Allow the layers to separate, and apply 10 µL of the organic layer.

Standard solution—Proceed as directed for the *Test solution,* using USP Rimantadine Hydrochloride RS in place of the test specimen.

Eluant: a mixture of ethyl acetate, methanol, and ammonium hydroxide (80:10:4).

Procedure—Use a low-actinic glass tank. Dry the plate in a stream of hot air, then heat in an oven at 105° for 30 minutes. Allow the plate to cool to room temperature.

Visualization—Place the plate in an atmosphere of chlorine, prepared by mixing 1.5% potassium permanganate solution and diluted hydrochloric acid (1:1), for about 90 minutes. Allow to air-dry for 60 minutes, and follow with visualization technique 20.

Limit of toluene—

Standard solution—Transfer 10 µL of toluene to a 100-mL volumetric flask, dilute with chloroform to volume, and mix.

Test solution—Transfer about 750 mg of Rimantadine Hydrochloride, accurately weighed, to a 10-mL volumetric flask, dilute with chloroform to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The gas chromatograph is equipped with a flame-ionization detector and a 2-mm × 2-m column that contains 80- to 100-mesh support S1A. The column temperature is maintained at about 200°, and nitrogen is used as the carrier gas. The injection port and detector temperatures are maintained at about 250°. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the tailing factor is not more than 1.5 for toluene; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 5 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms for 9 minutes, and measure the responses for the toluene peaks. Calculate the percentage of toluene in the portion of

Rimantadine Hydrochloride taken by the formula:

$$0.867(100/W_U)(r_U/r_S)$$

in which 0.867 is the specific gravity of toluene; W_U is the weight, in mg, of Rimantadine Hydrochloride taken to prepare the *Test solution;* and r_U and r_S are the toluene peak responses obtained from the *Test solution* and the *Standard solution,* respectively: not more than 0.1% is found.

Assay—

Internal standard solution—Transfer about 400 mg of *n*-eicosane to a 250-mL volumetric flask, dilute with hexane to volume, and mix.

Standard preparation—Transfer about 40 mg of USP Rimantadine Hydrochloride RS, accurately weighed, to a 50-mL centrifuge tube, add 15 mL of 1 N sodium hydroxide, and mix. Add 25.0 mL of *Internal standard solution,* and shake by mechanical means for about 15 minutes. Allow the layers to separate, and filter a portion of the top hexane layer through anhydrous sodium sulfate. Use the clear filtrate.

Assay preparation—Using about 40 mg of Rimantadine Hydrochloride, accurately weighed, proceed as directed for *Standard preparation.*

Chromatographic system (see *Chromatography ⟨621⟩*)—The gas chromatograph is equipped with a flame-ionization detector and a 4-mm × 1.8-m glass column that is packed with 3% phase G19 on 100- to 200-mesh support S1A. The column temperature is maintained at about 160°, and the injection port and detector temperatures are maintained at about 250°. Nitrogen is used as the carrier gas. Adjust the carrier flow rate and temperature so that the *n*-eicosane elutes at about 8 minutes. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor is not more than 2.0 for rimantadine; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 2 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{12}H_{21}N \cdot HCl$ in the portion of Rimantadine Hydrochloride taken by the formula:

$$25C(R_U/R_S)$$

in which C is the concentration, in mg per mL, of USP Rimantadine Hydrochloride in the *Standard preparation;* and R_U and R_S are the ratios of the rimantadine peak response to the *n*-eicosane peak response obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

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

Chromatographic Database Information: Chromatographic Database

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