Edition: BP 2025 (Ph. Eur. 11.6 update)

Amantadine Capsules

General Notices

Action and use

Viral replication inhibitor (influenza A); dopamine receptor agonist; treatment of influenza and Parkinson's disease.

DEFINITION

Amantadine Capsules contain Amantadine Hydrochloride.

The capsules comply with the requirements stated under Capsules and with the following requirements.

Content of amantadine hydrochloride, $C_{10}H_{17}N,HCl$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the contents of the capsules containing 0.2 g of Amantadine Hydrochloride in 10 mL of 0.1M *hydrochloric acid* on a water bath and filter. Add 1 mL of 5M *sodium hydroxide* to the filtrate and extract with 5 mL of *dichloromethane*. Filter the lower layer through *anhydrous sodium sulfate*, wash the sodium sulfate with 2 mL of *dichloromethane* and evaporate the solution to dryness. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of amantadine *(RS 006)*.

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 75 revolutions per minute.
(b) Use 900 mL of *water*, at a temperature of 37°, as the medium.

PROCEDURE

Carry out the method for *gas chromatography*, Appendix III B, using the following solutions. Prepare a 0.6% w/v solution of *naphthalene* (internal standard) in *toluene* (solution A).

(1) After 45 minutes withdraw a sample of the medium and filter. Transfer 3 mL to a centrifuge tube. Add 1 mL of 5M *sodium hydroxide* and 2 mL of solution A. Shake the tube for approximately 10 minutes and allow the layers to separate. Use the top layer for injection.
(2) To 3 mL of a 0.011% w/v solution of *amantadine hydrochloride BPCRS* in the medium, add 1 mL of 5M *sodium hydroxide* and 2 mL of solution A. Shake the flask for approximately 10 minutes and allow the layers to separate. Use the

top layer for injection.

CHROMATOGRAPHIC CONDITIONS

(a) Use a fused silica capillary column (30 m × 0.25 mm) bonded with a 0.25-µm layer of *methylpolysiloxane* (Agilent DB-1 is suitable).
(b) Use *helium* as the carrier gas at 1 mL per minute.
(c) Use the gradient conditions described below.
(d) Use an inlet temperature of 180°.
(e) Use a flame ionisation detector at a temperature of 250°.
(f) Inject 1 µL of each solution
(g) Use a split ratio of 1:10.

Time (Minutes)	Temperature	Comment
0-16	100°→200°	linear gradient
16-20	200°	isothermal

DETERMINATION OF CONTENT

Calculate the total content of amantadine hydrochloride, $C_{10}H_{17}N,HCl$, in the medium using the ratios of the area of the peak corresponding to amantadine to the area of the peak due to the internal standard in the chromatograms obtained with solutions (1) and (2), and using the declared content of $C_{10}H_{17}N,HCl$ in *amantadine hydrochloride BPCRS*.

LIMITS

The amount of amantadine hydrochloride released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *gas chromatography*, Appendix III B using the following solutions.

(1) Dissolve a quantity of the contents of the capsules containing 0.1 g of Amantadine Hydrochloride in 2 mL of *water*, add 2 mL of a 20% w/v solution of *sodium hydroxide* and 10 mL of *toluene* and shake for 10 minutes. Separate the upper layer, dry over *anhydrous sodium sulfate* and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes with *toluene*. Further dilute 1 volume to 10 volumes with *toluene*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

When the chromatograms are recorded under the prescribed conditions, the retention time of amantadine is about 7 minutes.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than 0.2% by *normalisation*;

the sum of the areas of any *secondary peaks* is not greater than 1.0% by *normalisation*.

Disregard any peak with an area less than 0.1% by *normalisation*.

ASSAY

Weigh the contents of 20 capsules. Mix, and powder if necessary. Carry out the method for *gas chromatography*, Appendix III B. Prepare a 0.6% w/v solution of *naphthalene* (internal standard) in *toluene* (solution A).

(1) Dissolve a quantity of the contents of the capsules containing 0.1 g of Amantadine Hydrochloride in 2 mL of *water*, add 2 mL of a 20% w/v solution of *sodium hydroxide* and 10 mL of solution A and shake for 10 minutes. Separate the upper layer, dry over *anhydrous sodium sulfate* and filter.

(2) Prepare the solution in the same manner as for solution (1) but using 0.1 g of *amantadine hydrochloride BPCRS* in 10 mL of *water* in place of the preparation being examined.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_{10}H_{17}N,HCl$ in the capsules using the ratios of the area of the peak corresponding to amantadine to the area of the peak due to the internal standard in the chromatograms obtained with solutions (1) and (2), and using the declared content of $C_{10}H_{17}N,HCl$ in *amantadine hydrochloride BPCRS*.