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

Galantamine Tablets

General Notices

Action and use

Cholinesterase inhibitor; treatment of Alzheimer's disease.

DEFINITION

Galantamine Tablets contain Galantamine Hydrobromide.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of galantamine, $C_{17}H_{21}NO_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) To a quantity of powdered tablets containing the equivalent of 4 mg of galantamine, add 10 mL of *acetonitrile* and mix with the aid of ultrasound for 45 minutes. Centrifuge and use the supernatant liquid.
(2) 0.05% w/v of *galantamine hydrobromide BPCRS* in *acetonitrile*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel* (Merck silica gel 60 plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 8 cm.
(e) After removal of the plate, dry in air and spray with *potassium iodobismuthate solution*, then immediately with *hydrogen peroxide solution (3 per cent)*. Examine the plate in white light.

MOBILE PHASE

1 volume of *glacial acetic acid*, 4 volumes of *butan-1-ol* and 5 volumes of *water*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) is similar in position, colour and size to that in the chromatogram obtained with solution (2).

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

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

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 500 mL of *water*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a sample of the medium, filter and dilute with *water*, if necessary, to produce a solution containing the equivalent of 0.0008% w/v of galantamine. Measure the *absorbance* of this solution in a 5-cm cell, at 288 nm, Appendix II B, using *water* in the reference cell.
(2) 0.001% w/v of *galantamine hydrobromide BPCRS* in *water*. Measure the *absorbance* of this solution in a 5-cm cell, at 288 nm, Appendix II B, using *water* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of galantamine, $C_{17}H_{21}NO_3$, in the medium from the absorbances obtained and using the declared content of $C_{17}H_{21}NO_3$ in *galantamine hydrobromide BPCRS*.

LIMITS

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

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in *methanol* (50%).

(1) Mix with the aid of ultrasound a quantity of the powdered tablets containing the equivalent of 0.1 g of galantamine with 50 mL. Dilute to 100 mL, mix and filter through a 0.45-µm nylon filter.
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) 0.05% w/v of *galantamine natural for system suitability EPCRS*.
(4) 0.05% w/v of *galantamine synthetic for system suitability EPCRS*.
(5) 0.1% w/v of *galantamine hydrobromide impurity standard BPCRS*.
(6) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *end-capped octadecylsilyl amorphous organosilica polymer for chromatography* (3.5 µm) (Waters XTerra MS C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 55°.
(e) Use a detection wavelength of 230 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 5 volumes of *methanol* and 95 volumes of a solution containing 0.079% w/v of *disodium hydrogen orthophosphate dihydrate* and 0.246% w/v of *sodium dihydrogen orthophosphate*.

Mobile phase B *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-6	100	0	isocratic
6-20	100→95	0→5	linear gradient
20-35	95→85	5→15	linear gradient
35-50	85→80	15→20	linear gradient
50-51	80→100	20→0	linear gradient

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
51-60	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to galantamine (retention time about 18 minutes) are: impurity E, about 0.3; impurity 2, about 0.4; impurity 1, about 0.6; impurity C, about 0.8; impurity B, about 1.1; impurity A, about 1.5 and impurity D, about 1.9.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity C and galantamine is at least 4.5.

LIMITS

Identify any peaks in the chromatogram obtained with solution (1) corresponding to:

impurities A and E using the chromatogram obtained with solution (3) and the chromatogram supplied with *galantamine natural for system suitability EPCRS*;

impurities C and D using the chromatogram obtained with solution (4) and the chromatogram supplied with *galantamine synthetic for system suitability EPCRS*;

impurities B, 1, and 2 using the chromatogram obtained with solution (5) and the chromatogram supplied with *galantamine hydrobromide impurity standard BPCRS*.

Multiply the area of any peak corresponding to impurity A by a correction factor of 0.5.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity 1 is not greater than 1.8 times the area of the principal peak in the chromatogram obtained with solution (2) (0.9%);

the area of any peak corresponding to impurity E is not greater than 1.2 times the area of the principal peak in the chromatogram obtained with solution (2) (0.6%);

the area of any peak corresponding to impurity B is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any peak corresponding to impurity C or impurity D is not greater than 0.8 times the area of the principal peak in the chromatogram obtained with solution (2) (0.4% of each);

the area of any peak corresponding to impurity 2 is not greater than 0.6 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

the area of any other *secondary peak* is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of all *secondary peaks* is not greater than 4 times the area of the principal peak in the chromatogram obtained with solution (2) (2.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (6) (0.1%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

Solution A 0.4% w/v *potassium dihydrogen orthophosphate*, adjusted to pH 6.5 with 5M *sodium hydroxide*.

(1) To 10 whole tablets add 50 mL of *methanol*, and mix with the aid of ultrasound for 15 minutes. Add 75 mL of solution A, and mix with the aid of ultrasound for 30 minutes with intermittent shaking. Allow to cool and dilute to 250 mL with solution A. Filter the resulting solution through a 0.45-µm nylon filter and dilute with solution A to produce a solution containing the equivalent of 0.0032% w/v of galantamine.
(2) Dissolve 16 mg of *galantamine hydrobromide BPCRS* in 5 mL of *methanol* and dilute to 25 mL with solution A. Dilute 1 volume of the resulting solution to 10 volumes with solution A.
(3) 0.05% w/v of *galantamine synthetic for system suitability EPCRS* in *methanol (50%)*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *end-capped octadecylsilyl amorphous organosilica polymer for chromatography* (3.5 µm) (Waters XTerra MS C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 55°.
(e) Use a detection wavelength of 230 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

5 volumes of *methanol* and 95 volumes of a solution containing 0.079% w/v of *disodium hydrogen orthophosphate dihydrate* and 0.246% w/v of *sodium dihydrogen orthophosphate*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity C and galantamine is at least 4.5.

DETERMINATION OF CONTENT

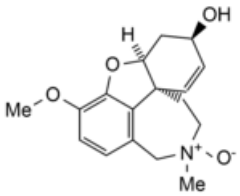
Calculate the content of $C_{17}H_{21}NO_3$ in the tablets using the declared content of $C_{17}H_{21}NO_3$ in *galantamine hydrobromide BPCRS*.

LABELLING

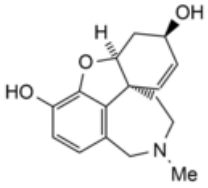
The quantity of active ingredient is stated in terms of the equivalent amount of galantamine.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A to E listed under *Galantamine Hydrobromide* and:



1. galantamine-*N*-oxide



2. *O*-demethylgalantamine