Galantamine Tablets

Published on: 01.08.2024 **Last date for comments:** 14.09.2024

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

Description	Details
Document version	1.0
Monograph proposed for inclusion	IP 2026
Tentative effective date of monograph	July, 2026
First draft published on IPC website for public comments	01.08.2024
Draft revision published on IPC website for public comments	-
Further follow-up action as required.	

Galantamine Tablets

Galantamine Tablets contains Galantamine Hydrobromide equivalent to not less than 90.0 per cent and not more than 110.0 per cent of stated amount of galantamine, $C_{17}H_{21}NO_3$.

Usual strengths. 4 mg; 8 mg; 12 mg.

Identification

In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with reference solution (a).

Tests

Dissolution (2.5.2).

Apparatus No. 2 (Paddle),
Medium. 500 ml of *water,*
Speed and time. 50 rpm and 20 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Use the filtrate, dilute if necessary, with the dissolution medium.

Reference solution. A solution of *galantamine hydrobromide IPRS* containing 0.0008 per cent w/v of galantamine in the dissolution medium.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as ZORBAX Eclipse XDB-C18),
- column temperature: 30º,
- mobile phase: a mixture of 80 volumes of a buffer solution prepared by dissolving 3.45 g of *sodium dihydrogen orthophosphate* in *water,* add 1 ml of *triethylamine* and dilute to 1000 ml with *water,* adjusted to pH 4.5 with *orthophosphoric acid,* 10 volumes of *acetonitrile* and 10 volumes *methanol,*
- flow rate: 1 ml per minute,
- spectrophotometer set at 230 nm,
- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution

Calculate the content of $C_{17}H_{21}NO_3$ in the medium

Q. Not less than 80 per cent of the stated amount of $C_{17}H_{21}NO_3$.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. Dissolve 35.4 g of *disodium edetate* in 950 volumes of *water* and add 50 volumes of *methanol. [NOTE- First dissolve in water and then add methanol].*

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing 48 mg of Galantamine in the solvent mixture with the aid of ultrasound and dilute to 100.0 ml with the solvent mixture, filter.

Reference solution (a). A solution of *galantamine hydrobromide IPRS* containing 0.048 per cent w/v of galantamine in the solvent mixture.

Reference solution (b). A 0.06 per cent w/v solution of *galantamine hydrobromide related compound mixture IPRS* in the solvent mixture.

Reference solution (c). Dilute 1.0 ml of reference solution (a) to 100.0 ml with solvent mixture. Further dilute 1.0 ml of the solution to 10.0 ml with solvent mixture.

Chromatographic system

– a stainless steel column 10 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (3 µm) (Such as YMC-Pack Pro C18),
– column temperature: 35º,
– mobile phase: A. a mixture of 95 volumes of a buffer solution prepared by dissolving 5.34 g of *disodium hydrogen phosphate dihydrate* in 1000 ml of *water,* adjusted to pH 6.5 with *orthophosphoric acid* and 5 volumes of *methanol,*
B. a mixture of 95 volumes of *acetonitrile* and 5 volumes of *methanol,*
– a gradient programme using the conditions given below,
– flow rate: 1.5 ml per minute,
– spectrophotometer set at 230 nm,
– injection volume: 20 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	100	0
40	75	25
45	60	40
46	40	60
55	40	60
56	100	0
61	100	0

Name	Relative retention time	Correction factor
N-Desmethyl galantamine[1]	0.41	0.91
Galantamine *N*-oxide[2]	0.73	0.91
Dihydrogalantamine[3]*	0.86	---
Galantamine hydrobromide	1.0	---
6*S*-Galantamine[4]	1.15	0.91
Anhydrogalantamine[5]*	2.09	---

* Process related impurity, included for identification only. Not to be calculated and included in total degradation product.
[1](4a*S*,6*R*,8a*S*)-3-Methoxy-4a,5,9,10,11,12-hexahydro-6*H*-benzo[2,3]benzofuro[4,3-cd]azepin-6-ol.
[2](4a*S*,6*R*,8a*S*)-6-Hydroxy-3-methoxy-11-methyl-4a,5,9,10,11,12-hexahydro-6*H*-benzo[2,3]benzofuro[4,3-cd]azepine 11-oxide.
[3](4a*S*,6*R*,8a*S*)-3-Methoxy-11-methyl-4a,5,7,8,9,10,11,12-octahydro-6*H*-benzo[2,3]benzofuro[4,3-cd]azepin-6-ol.
[4](4a*S*,6*S*,8a*S*)-3-Methoxy-11-methyl-4a,5,9,10,11,12-hexahydro-6*H*-benzo[2,3]benzofuro[4,3-cd]azepin-6-ol.
[5](4a*S*,8a*S*)-3-Methoxy-11-methyl-9,10,11,12-tetrahydro-4a*H*-benzo[2,3]benzofuro[4,3-cd]azepine.

Inject reference solution (a), (b) and (c). The test is not valid unless the resolution between the peaks due to galantamine *N*-oxide and dihydrogalantamine is not less than 1.5 in the chromatogram obtained with reference solution (b), the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (a) and the signal-to-noise ratio of the principal peak is not less than 10 in the chromatogram obtained with reference solution (c).

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to *N*-Desmethyl galantamine and 6*S*-Galantamine, each of, is not more than 0.005 times the area of principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent), the area of any peak corresponding to galantamine *N*-oxide is not more than 0.0075 times the area of principal peak in the chromatogram obtained with reference solution (a) (0.75 per cent), the area of any other secondary peak is not more than 0.002 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent) and the sum of the areas of all the secondary peaks is not more than 0.015 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.5 per cent). Ignore any peak due to bromide and with an area less than 0.001 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent).

Uniformity of dosage unit (2.5.4). Complies with the test stated under Tablets.

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14) as described under Related substances.

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to galantamine *N*-oxide and dihydrogalantamine is not less than 1.5 in the chromatogram obtained with reference solution (b) and the relative standard deviation for replicate injections is not more than 1.0 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution.

Calculate the content of $C_{17}H_{21}NO_3$ in the tablets.

Storage. Store protected from moisture, at a temperature not exceeding 30°.
