

Galantamine Extended-Release Capsules

DEFINITION

Galantamine Extended-Release Capsules contain galantamine hydrobromide ($C_{17}H_{21}NO_3 \cdot HBr$) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of galantamine ($C_{17}H_{21}NO_3$).

[NOTE—Throughout the following procedures, protect samples, the Reference Standard, and solutions containing them from light.]

IDENTIFICATION

- A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 197K](#)**

Sample: Prepare a potassium bromide dispersion as follows. Remove 4 beads from within 1 Capsule. Grind the beads into a fine powder, and combine with [potassium bromide](#).

Standard: Prepare a potassium bromide dispersion using [USP Galantamine Hydrobromide RS](#).

Acceptance criteria: The IR spectra of the *Sample* and the *Standard* exhibit similar absorption bands at 2800–2400 cm^{-1} , 1700–1500 cm^{-1} , and 850–750 cm^{-1} .
- 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**

Buffer: 4.0 g/L of [monobasic potassium phosphate](#) in [water](#); adjusted with [5 N sodium hydroxide TS](#) to a pH of 6.5

Mobile phase: [Acetonitrile](#) and *Buffer* (10:90)

Standard stock solution: 0.62 mg/mL of [USP Galantamine Hydrobromide RS](#) (equivalent to 0.48 mg/mL of galantamine) prepared as follows. Transfer a suitable quantity of [USP Galantamine Hydrobromide RS](#) to a suitable flask, and dissolve in 20% of the flask volume of [methanol](#). Dilute with *Buffer* to volume.

Standard solution: 0.048 mg/mL of galantamine from the *Standard stock solution* in *Buffer*

Sample stock solution: Prepare the solution using the appropriate nominal concentration of galantamine stated in [Table 1](#). Transfer the contents of 10 Capsules to a suitable volumetric flask. Add 20% of the flask volume of [methanol](#), sonicate for 15 min, and stir for 20 min. Add a suitable volume of *Buffer* such that 80% of the flask volume is filled, and stir for 90 min. Dilute with *Buffer* to volume.

Table 1

Capsule Strength (mg/Capsule)	Nominal Concentration of Galantamine (mg/mL)
8	0.32
16	0.32
24	0.48

Sample solution: Nominally 0.048 mg/mL of galantamine prepared as follows from the *Sample stock solution*. Transfer a suitable volume of the *Sample stock solution* to an appropriate volumetric flask, and dilute with *Buffer* to volume. Pass through a suitable filter of 0.45- μ m pore size. Discard the first 5 mL, and use the filtrate.

Chromatographic system
(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 288 nm

Column: 4.6-mm $\times$ 15.0-cm; 5- μ m packing [L1](#)

Flow rate: 1.2 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of galantamine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.7

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of galantamine ($C_{17}H_{21}NO_3$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Galantamine Hydrobromide RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of galantamine in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of galantamine, 287.35

M_{r2} = molecular weight of galantamine hydrobromide, 368.27

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1

Medium: [0.05 M monobasic potassium phosphate, pH 6.5](#); 900 mL

Apparatus 2: 50 rpm with sinkers ¹

Times: 1, 4, and 12 h

Buffer: 1 g/L of [sodium 1-hexanesulfonate](#) in [water](#). Add 0.5 mL of [phosphoric acid](#) per liter.

Mobile phase: [Acetonitrile](#) and *Buffer* (20:80)

Standard stock solution: 0.57 mg/mL of [USP Galantamine Hydrobromide RS](#) (equivalent to 0.44 mg/mL of galantamine) in *Medium*

Standard solution: (L/900) mg/mL of galantamine from the *Standard stock solution* in *Medium*, where L is the label claim of galantamine in mg/Capsule

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 15.0-cm; 5-µm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: NLT 1.5 times the retention time of galantamine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of galantamine ($C_{17}H_{21}NO_3$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Galantamine Hydrobromide RS](#) in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of galantamine, 287.35

M_{r2} = molecular weight of galantamine hydrobromide, 368.27

Calculate the percentage of the labeled amount of galantamine ($C_{17}H_{21}NO_3$) dissolved at each time point (i):

$$\text{Result}_1 = C_i \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_s)] + (C_1 \times V_s)\} \times (1/L) \times 100$$

$$\text{Result}_3 = \{[C_3 \times [V - (2 \times V_s)]] + [(C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

C_i = concentration of galantamine in the portion of sample withdrawn at time point i (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

V_s = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See [Table 2](#).

Table 2

Time Point (i)	Time (h)	Amount Dissolved (%)
1	1	20–40
2	4	40–65
3	12	NLT 75

The percentage of the labeled amount of galantamine ($C_{17}H_{21}NO_3$) dissolved at the times specified conforms to [Dissolution \(711\)](#).

[Acceptance Table 2](#).

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: [0.05 M monobasic potassium phosphate, pH 6.5](#); 900 mL

Apparatus 2: 50 rpm

Times: 1, 4, and 12 h

Solution A: Transfer 0.5 mL of [phosphoric acid](#) to a 100-mL volumetric flask containing 50% of the flask volume of [water](#). Dilute with [water](#) to volume.

Mobile phase: [Acetonitrile](#) and *Solution A* (7:93)

Standard stock solution: 0.23 mg/mL of [USP Galantamine Hydrobromide RS](#) (equivalent to 0.18 mg/mL of galantamine) in *Medium*

Standard solution: ($L/900$) mg/mL of galantamine from the *Standard stock solution* in *Medium*, where L is the label claim of galantamine, in mg/Capsule

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 230 nm

Column: 3.0-mm × 15.0-cm; 5-μm packing [L1](#)

Column temperature: 35°

Flow rate: 0.7 mL/min

Injection volume: 10 µL

Run time: NLT 1.6 times the retention time of galantamine

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of galantamine ($C_{17}H_{21}NO_3$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Galantamine Hydrobromide RS](#) in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of galantamine, 287.35

M_{r2} = molecular weight of galantamine hydrobromide, 368.27

Calculate the percentage of the labeled amount of galantamine ($C_{17}H_{21}NO_3$) dissolved at each time point (i):

$$\text{Result}_1 = C_i \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = \{[C_3 \times [V - (2 \times V_S)]] + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of galantamine in the portion of sample withdrawn at time point i (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

V_S = volume of the *Sample solution* withdrawn from the *Medium* (mL)

Tolerances: See [Table 3](#).

Table 3

Time Point (i)	Time (h)	Amount Dissolved (%)
1	1	22–38
2	4	50–70
3	12	NLT 80

The percentage of the labeled amount of galantamine ($C_{17}H_{21}NO_3$) dissolved at the times specified conforms to [Dissolution <711>](#).

[Acceptance Table 2](#).

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: [pH 6.5 phosphate buffer](#) (6.8 g/L of [monobasic potassium phosphate](#) and 0.56 g/L of [sodium hydroxide](#) adjusted, if necessary, with [phosphoric acid](#) or [10 N sodium hydroxide TS](#) to a pH of 6.5); 900 mL

Apparatus 2: 50 rpm, with stainless steel wire helix sinkers

Times: 1, 2, 4, and 12 h