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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-µm 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 × 15.0-cm; 5-µm packing L1

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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*):

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

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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*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

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

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

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

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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*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

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

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

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

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Buffer: To each liter of 6.8 g/L of monobasic potassium phosphate in water add 3.0 mL of triethylamine, and adjust the resulting solution with phosphoric acid to a pH of 2.5. Pass through a suitable membrane filter of 0.45-µm pore size, and use the filtrate.

Mobile phase: Acetonitrile and *Buffer* (8:92)

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. Replace the portion of solution withdrawn with an equal volume of *Medium*.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 15.0-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 50 µL

Run time: NLT 2 times the retention time of galantamine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2

Relative standard deviation: NMT 3.0%

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*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

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

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

$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

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 and replaced with *Medium* (mL)

Tolerances: See *Table 4*.

Table 4

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Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	18–43
2	2	30–50
3	4	40–65
4	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 4: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.

Medium: pH 6.5 phosphate buffer (6.8 g/L of monobasic potassium phosphate in water adjusted, if necessary, with 5 N sodium hydroxide TS to a pH of 6.5); 900 mL

Apparatus 2: 50 rpm, with sinkers

Times: 1, 4, and 12 h

Buffer: 6.8 g/L of monobasic potassium phosphate adjusted, if necessary, with 5 N sodium hydroxide TS to a pH of 7.5

Mobile phase: Acetonitrile and *Buffer* (15:85)

Standard stock solution: 0.11 mg/mL of USP Galantamine Hydrobromide RS (equivalent to 0.09 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: 4.6-mm × 15.0-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1.4 mL/min

Injection volume: 100 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*):

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$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

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

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

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 5*.

Table 5

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	NMT 40
2	4	45–70
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 5: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 5*.

Medium: pH 6.5 phosphate buffer (6.8 g/L of monobasic potassium phosphate adjusted, if necessary, with 0.2 N sodium hydroxide TS to a pH of 6.5); 900 mL

Apparatus 2: 50 rpm with sinkers

Times: 1, 4, and 12 h

Buffer: To each liter of water add 7 mL of triethylamine.

Mobile phase: Methanol and *Buffer* (25:75); adjusted with phosphoric acid or a solution of triethylamine and water (5:95) to a pH of 6.5

Standard solution: 0.025 mg/mL of USP Galantamine Hydrobromide RS (equivalent to 0.02 mg/mL of galantamine) in *Medium*

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 280 nm

Column: 4.6-mm × 15.0-cm; 5-µm packing L7

Flow rate: 1 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 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*

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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*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

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

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

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 6*.

Table 6

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	10–30
2	4	45–65
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 6: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 6*.

Medium: pH 6.5 phosphate buffer [6.8 g/L of monobasic potassium phosphate and 0.46 g/L of sodium hydroxide in water adjusted, if necessary, with 0.2 N sodium hydroxide TS or hydrochloric acid and water (1.6:98.4) to a pH of 6.5]; 900 mL

Apparatus 2: 50 rpm

Times: 1, 4, 10, and 12 h

Buffer: 2.7 g/L of monobasic potassium phosphate in water. To each liter, add 5 mL of triethylamine and adjust with phosphoric acid, if necessary, to a pH of 4.8.

Mobile phase: Methanol and *Buffer* (10:90)

Standard stock solution: 0.11 mg/mL of USP Galantamine Hydrobromide RS (equivalent to 0.09 mg/mL of galantamine) in *Medium*. Sonication may be used to promote dissolution.

Standard solution: (*L*/900) mg/mL of USP Galantamine Hydrobromide RS 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. Replace the portion of solution withdrawn with an equal volume of *Medium*.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 235 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Column temperature: 40°

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Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 2 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*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

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

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

$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

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 and replaced with *Medium* (mL)

Tolerances: See *Table 7*.

Table 7

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	15–35
2	4	45–65
3	10	NLT 70
4	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*.

- **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

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IMPURITIES

• **Organic Impurities**

Solution A: 1.7 g/L of dibasic potassium phosphate and 3.0 g/L of monobasic potassium phosphate in water

Solution B: Acetonitrile

Mobile phase: See *Table 8*.

Table 8

Time (min)	Solution A (%)	Solution B (%)	Flow Rate (mL/min)
0	97	3	0.7
22	69	31	0.7
24	25	75	1.2
27	25	75	1.2
29	97	3	0.7
35	97	3	0.7

Diluent: Methanol and *Solution A* (60:40)

System suitability solution: 0.31 mg/mL of USP Galantamine Hydrobromide Related Compounds Mixture RS in *Diluent*

Standard solution: 1.5 µg/mL of USP Galantamine Hydrobromide RS (equivalent to 1.2 µg/mL of galantamine) in *Diluent*

Sensitivity solution: 0.15 µg/mL of USP Galantamine Hydrobromide RS (equivalent to 0.12 µg/mL of galantamine) from the *Standard solution* in *Diluent*

Sample solution: Nominally 240 µg/mL of galantamine from NLT 20 Capsules prepared as follows. Transfer a suitable portion of the contents of NLT 20 Capsules to a suitable volumetric flask, and dilute with *Diluent* to volume. Sonication and shaking may be used to promote dissolution. Allow the solution to sit for NLT 24 h, and then clarify the solution using a suitable filter of 0.45-µm pore size.

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: See *Table 8*.

Injection volume: 10 µL

System suitability

Samples: *System suitability solution, Standard solution,* and *Sensitivity solution*

[Note—See *Table 9* for relative retention times.]

Suitability requirements

Resolution: NLT 3.4 between galantamine and 6*S*-galantamine, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each degradation product 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 of each degradation product from the *Sample solution*

r_S = peak response of galantamine from the *Standard solution*

C_S = concentration of USP Galantamine Hydrobromide RS in the *Standard solution* (µg/mL)

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

M_{r1} = molecular weight of galantamine, 287.35

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

Acceptance criteria: See *Table 9*. The reporting threshold is 0.05%.

Table 9

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
N-Desmethyl galantamine[a,b]	0.57	0.5
Galantamine *N*-oxide[c]	0.75	0.5
Dihydrogalantamine[d,e]	0.87	—
Galantamine	1.0	—
6*S*-Galantamine[f]	1.1	0.2
Anhydrogalantamine[e,g]	1.9	—
Any unspecified degradation product	—	0.2
Total degradation products	—	1.2

[a] (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.

[b] This degradation product may be found if the drug substance is isolated from a natural source.

[c] (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.

[d] (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.

[e] This is a process impurity and is listed for information only. It is controlled in the drug substance. It is not to be reported and is not to be included in the total degradation products.

[f] (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.

[g] (4a*S*,8a*S*)-3-Methoxy-11-methyl-9,10,11,12-tetrahydro-4a*H*-benzo[2,3]benzofuro[4,3-*cd*]azepine.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at controlled room temperature.

• **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Galantamine Hydrobromide RS

USP Galantamine Hydrobromide Related Compounds Mixture RS

Contains a mixture of the following five compounds:

Galantamine hydrobromide.

Galantamine *N*-oxide;

(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. $C_{17}H_{21}NO_4$ 303.35

Dihydrogalantamine;

(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. $C_{17}H_{23}NO_3$ 289.37

6*S*-Galantamine;

(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. $C_{17}H_{21}NO_3$ 287.35

Anhydrogalantamine;

(4a*S*,8a*S*)-3-Methoxy-11-methyl-9,10,11,12-tetrahydro-4a*H*-benzo[2,3]benzofuro[4,3-*cd*]azepine. $C_{17}H_{19}NO_2$ ▲269.34▲ (ERR 1-Nov-2020)

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[NOTE—The contents have previously been referred to as galantamine hydrobromide, 6β-hexahydrogalantamine, 6β-octahydrogalantamine, 6α-hexahydrogalantamine, and tetrahydrogalantamine, respectively.]

[1] A suitable sinker is catalog number CAPWHT-2S from www.gla-llc.com.

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

Topic/Question	Contact	Expert Committee
GALANTAMINE EXTENDED-RELEASE CAPSULES	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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