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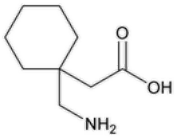
Gabapentin



$C_9H_{17}NO_2$ 171.24

Cyclohexaneacetic acid, 1-(aminomethyl)-;

1-(Aminomethyl)cyclohexaneacetic acid CAS RN®: 60142-96-3; UNII: 6CW7F3G59X.

DEFINITION

Gabapentin contains NLT 98.0% and NMT 102.0% of gabapentin ($C_9H_{17}NO_2$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K▲ (CN 1-May-2020)

• **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**

Diluent: 2.32 g/L of monobasic ammonium phosphate in water. Adjust with phosphoric acid to a pH of 2.0.

Buffer: 0.58 g/L of monobasic ammonium phosphate and 1.83 g/L of sodium perchlorate in water. Adjust with perchloric acid to a pH of 1.8.

Mobile phase: Acetonitrile and *Buffer* (24:76)

Standard solution: 14.0 mg/mL of USP Gabapentin RS in *Diluent*

System suitability solution: 2.3 mg/mL of USP Gabapentin RS from the *Standard solution* in *Diluent*

Sample solution: 14 mg/mL of Gabapentin in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 5 times the retention time of gabapentin

System suitability

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

Suitability requirements

Column efficiency: NLT 1900 theoretical plates for the gabapentin peak, *System suitability solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of gabapentin ($C_9H_{17}NO_2$) in the portion of Gabapentin taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Gabapentin RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Early-Eluting Organic Impurities**

Diluent, Buffer, and **Mobile phase:** Prepare as directed in the *Assay*.

System suitability stock solution: 1.4 mg/mL of USP Gabapentin Related Compound A RS and 0.84 mg/mL of USP Gabapentin Related Compound B RS in methanol

System suitability solution: Dissolve a suitable quantity of USP Gabapentin RS in *Diluent* in a suitable volumetric flask, and add an appropriate volume of *System suitability stock solution* to obtain a solution containing 14.0 mg/mL of USP Gabapentin RS, 14 µg/mL of USP Gabapentin Related Compound A RS, and 8.4 µg/mL of USP Gabapentin Related Compound B RS in *Diluent*. Inject within 24 h.

Standard solution: 0.0084 mg/mL of USP Gabapentin Related Compound E RS in *Diluent*

Sample solution: 14 mg/mL of Gabapentin in *Diluent*. Inject within 24 h.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Temperatures

Autosampler: 5 ± 2°

Column: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 5 times the retention time of gabapentin

System suitability

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

Suitability requirements

Resolution: NLT 2.3 between gabapentin related compound A and gabapentin related compound B, *System suitability solution*

Relative standard deviation: NMT 5.0% for gabapentin related compound E, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any impurity in the portion of Gabapentin taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of any impurity from the *Sample solution*

r_S = peak response of gabapentin related compound E from the *Standard solution*

C_S = concentration of USP Gabapentin Related Compound E RS in the *Standard solution* (mg/mL)

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time[a]	Relative Response Factor[b]	Acceptance Criteria, NMT (%)
Gabapentin	1.0	—	—
Gabapentin related compound E	2.9	1.0	0.10
Gabapentin related compound A	3.5	5.3	0.1
Gabapentin related compound B	3.8	0.35	0.06

Name	Relative Retention Time[a]	Relative Response Factor[b]	Acceptance Criteria, NMT (%)
Any other individual impurity	—	0.41	0.10

[a] The relative retention times are calculated based on the retention time of gabapentin.

[b] The relative response factors are calculated based on the response of gabapentin related compound E due to the low absorptivity of gabapentin at the monitoring wavelength (215 nm).

• **Late-Eluting Organic Impurities**

Diluent, Buffer, and **Sample solution:** Prepare as directed in the *Assay*.

Mobile phase: Acetonitrile, methanol, and *Buffer* (35:30:35)

Standard solution: 0.0028 mg/mL of USP Gabapentin Related Compound D RS in *Diluent*. Initially dissolve USP Gabapentin Related Compound D RS in a small amount of methanol, then dilute with *Diluent*.

Sample solution: 14 mg/mL of Gabapentin in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of gabapentin related compound D

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 13,600 theoretical plates

Relative standard deviation: NMT 7.0%

Analysis

Samples: *Sample solution* and *Standard solution*

[Note—Disregard peaks with a relative retention time of NMT 0.35, relative to gabapentin related compound D.]

Calculate the percentage of any impurity in the portion of Gabapentin taken:

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

r_U = peak response of any impurity from the *Sample solution*

r_S = peak response of gabapentin related compound D from the *Standard solution*

C_S = concentration of USP Gabapentin Related Compound D RS in the *Standard solution* (mg/mL)

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

Acceptance criteria

Individual impurities: NMT 0.10%

Total impurities: NMT 0.5% (including impurities found in the test for *Early-Eluting Organic Impurities*)

SPECIFIC TESTS

• **pH ⟨791⟩**

Sample solution: 20 mg/mL in water

Acceptance criteria: 6.5–8.0

• **Water Determination ⟨921⟩, *Method I*:** NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature.

• **USP Reference Standards ⟨11⟩**

USP Gabapentin RS

USP Gabapentin Related Compound A RS

2-Azaspiro[4.5]decan-3-one.

$C_9H_{15}NO$ 153.22

USP Gabapentin Related Compound B RS

(1-Cyanocyclohexyl)acetic acid.

$C_9H_{13}NO_2$ 167.21

USP Gabapentin Related Compound D RS

[1-(3-Oxo-2-aza-spiro[4.5]dec-2-ylmethyl)cyclohexyl]acetic acid.

$C_{18}H_{29}NO_3$ 307.43

USP Gabapentin Related Compound E RS

Carboxymethylcyclohexanecarboxylic acid.

$C_9H_{14}O_4$ 186.21

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

Topic/Question	Contact	Expert Committee
GABAPENTIN	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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