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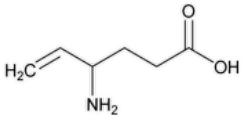
Vigabatrin



$C_6H_{11}NO_2$ 129.16

5-Hexenoic acid, 4-amino-;

4-Amino-5-hexenoic acid CAS RN®: 68506-86-5; UNII: GR120KRT6K.

DEFINITION

Vigabatrin contains NLT 98.0% and NMT 102.0% of vigabatrin ($C_6H_{11}NO_2$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197M ▲ (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**

Buffer: 3.4 g/L of monobasic potassium phosphate

Mobile phase: Acetonitrile, methanol, and *Buffer* (4:40:1000). Adjust with phosphoric acid to a pH of 2.8.

Standard solution: 2.0 mg/mL of USP Vigabatrin RS in *Mobile phase*

System suitability solution: 12 µg/mL of USP Vigabatrin Related Compound A RS in the *Standard solution*

Sample solution: 2.0 mg/mL of Vigabatrin in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25.0-cm; 10-µm packing L9

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 1.8 times the retention time of vigabatrin

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for vigabatrin related compound A and vigabatrin are about 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between vigabatrin related compound A and vigabatrin

Relative standard deviation: NMT 1.0% for the vigabatrin peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of vigabatrin ($C_6H_{11}NO_2$) in the portion of Vigabatrin 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 Vigabatrin RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

- **Limit of γ-Aminobutyric Acid**

Solution A: 1.6 g/L of 9-fluorenylmethyl chloroformate (FMOC) in acetone

Buffer A: 4.1 g/L of anhydrous sodium acetate. Adjust with glacial acetic acid to a pH of 4.2.

Buffer B: 31 g/L of boric acid. Adjust with 0.5 g/mL of sodium hydroxide to a pH of 7.7.

Mobile phase: Acetonitrile and *Buffer A* (32:68)

System suitability stock solution: 2.0 mg/mL of USP Vigabatrin RS and 4 µg/mL of USP γ-Aminobutyric Acid RS in water

System suitability solution: Transfer 1.0 mL of *System suitability stock solution* to a suitable container. Pipet 2 mL of *Buffer B* into the container, and mix. Pipet 3 mL of *Solution A* into the container, mix, and allow to stand for 5 min. Pipet 3 mL of ethyl acetate into the container, shake for a few seconds, and allow the layers to separate. Use the lower layer within 8 h of preparation.

Standard stock solution: 4 µg/mL of USP γ-Aminobutyric Acid RS in water

Standard solution: Transfer 1.0 mL of *Standard stock solution* to a suitable container. Pipet 2 mL of *Buffer B* into the container, and mix. Pipet 3 mL of *Solution A* into the container, mix, and allow to stand for 5 min. Pipet 3 mL of ethyl acetate into the container, shake for a few seconds, and allow the layers to separate. Use the lower layer within 8 h of preparation.

Sample stock solution: 2.0 mg/mL of Vigabatrin in water

Sample solution: Transfer 1.0 mL of *Sample stock solution* to a suitable container. Pipet 2 mL of *Buffer B* into the container, and mix. Pipet 3 mL of *Solution A* into the container, mix, and allow to stand for 5 min. Pipet 3 mL of ethyl acetate into the container, shake for a few seconds, and allow the layers to separate. Use the lower layer within 8 h of preparation.

Chromatographic system

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

Mode: LC

Detector: UV 263 nm

Column: 4.6-mm × 15.0-cm; 5-µm packing L11

Flow rate: 1 mL/min

Injection volume: 25 µL

Run time: NLT 1.5 times the retention time of FMOC-vigabatrin

System suitability

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

[Note—The relative retention times for (9-fluorenyl)methanol (FMOC-OH), FMOC-γ-aminobutyric acid, and FMOC-vigabatrin are about 0.5, 0.6, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between FMOC-OH and FMOC-γ-aminobutyric acid, *System suitability solution*

Relative standard deviation: NMT 2.0% for the FMOC-γ-aminobutyric acid peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of γ-aminobutyric acid in the portion of Vigabatrin taken:

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

r_U = peak response of FMOC-γ-aminobutyric acid from the *Sample solution*

r_S = peak response of FMOC-γ-aminobutyric acid from the *Standard solution*

C_S = concentration of USP γ-Aminobutyric Acid RS in the *Standard stock solution* (mg/mL)

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

Acceptance criteria: NMT 0.2% of γ-aminobutyric acid

- **Organic Impurities**

Buffer: 58.5 g/L of monobasic sodium phosphate in dilute phosphoric acid (23 in 1000)

Mobile phase: Acetonitrile, *Buffer*, and water (25:25:950)

System suitability solution: 6 µg/mL of USP Vigabatrin Related Compound A RS, 8 µg/mL of USP Vigabatrin Related Compound B RS, 8 µg/mL of USP Vigabatrin Related Compound E RS, and 4.0 mg/mL of USP Vigabatrin RS in *Mobile phase*

Standard solution: 6 µg/mL of USP Vigabatrin Related Compound A RS, 8 µg/mL of USP Vigabatrin Related Compound B RS, and 8 µg/mL of USP Vigabatrin Related Compound E RS in *Mobile phase*

Sample solution: 4.0 mg/mL of Vigabatrin in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Columns: *Column A* and *Column B* are coupled in series before the *Detector*.

Column A: 4.6-mm × 25.0-cm; 5-µm packing L15

Column B: 4.6-mm × 25.0-cm; 10-µm packing L9

Flow rate: 1.0 mL/min

Injection volume: 20 µL

Run time: NLT 2.2 times the retention time of vigabatrin

System suitability

Sample: *System suitability solution*

[NOTE—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between vigabatrin related compound A and vigabatrin

Tailing factor: NMT 2.0 each for vigabatrin related compound A and vigabatrin related compound E

Relative standard deviation: NMT 5.0% for vigabatrin related compound E

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of vigabatrin related compound A, vigabatrin related compound B, or vigabatrin related compound E in the portion of Vigabatrin taken:

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

r_U = peak response of vigabatrin related compound A, vigabatrin related compound B, or vigabatrin related compound E from the *Sample solution*

r_S = peak response of vigabatrin related compound A, vigabatrin related compound B, or vigabatrin related compound E from the *Standard solution*

C_S = concentration of USP Vigabatrin Related Compound A RS, USP Vigabatrin Related Compound B RS, or USP Vigabatrin Related Compound E RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any other individual impurity in the portion of Vigabatrin taken:

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

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

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

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Vigabatrin related compound E	0.5	0.1
Vigabatrin related compound A	0.9	0.1
Vigabatrin	1.0	—
Vigabatrin related compound B	1.4	0.1
Any other individual impurity	—	0.1
Total impurities[a]	—	0.5

[a] Sum of all impurities found in the tests for *Organic Impurities* and *Limit of γ-Aminobutyric Acid*.

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

SPECIFIC TESTS

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

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP γ-Aminobutyric Acid RS
4-Aminobutyric acid.
$C_4H_9NO_2$ 103.12

USP Vigabatrin RS

USP Vigabatrin Related Compound A RS
5-Vinylpyrrolidin-2-one.
C_6H_9NO 111.14

USP Vigabatrin Related Compound B RS
(*E*)-2-(2-Aminoethyl)but-2-enoic acid hydrochloride.
$C_6H_{11}NO_2 \cdot HCl$ 165.62

USP Vigabatrin Related Compound E RS
2-(2-Aminobut-3-enyl)malonic acid.
$C_7H_{11}NO_4$ 173.17

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

Topic/Question	Contact	Expert Committee
VIGABATRIN	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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