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Vigabatrin Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-vigabatrin-tabs-20230428.

DEFINITION
Vigabatrin Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of vigabatrin ($C_6H_{11}NO_2$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

Sample: Grind an appropriate number of Tablets to prepare a 50-mg/mL solution of vigabatrin in water. Pass a portion of the solution through a suitable filter, and prepare a 2-mg/mL solution by mixing a suitable portion of the filtrate with acetone. Evaporate the solution to dryness in a stream of nitrogen. Prepare a potassium bromide pellet using a suitable amount of the residue. Alternatively, the *Sample* may be prepared by directly mixing an amount of finely ground Tablets (NLT 2) equivalent to about of 3 mg of vigabatrin with about 200 mg of potassium bromide.

Acceptance criteria: The IR spectrum of the *Sample* is consistent with a similarly prepared pellet of USP Vigabatrin RS.

• **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 potassium phosphate, monobasic in water

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

System suitability solution: 1.0 mg/mL of USP Vigabatrin RS and 12 µg/mL of USP Vigabatrin Related Compound A RS in *Mobile phase*

Standard solution: 1.0 mg/mL of USP Vigabatrin RS in *Mobile phase*

Sample stock solution: Nominally 5.0 mg/mL of vigabatrin from Tablets (NLT 10) prepared as follows. Transfer a suitable number of Tablets to a suitable volumetric flask. Add *Mobile phase* to about 80% of the flask volume, and stir for 1 h to give a uniform dispersion of fine particulate. Dilute with *Mobile phase* to volume, and pass a portion of the solution through a suitable filter of 0.45-µm pore size.

Sample solution: Nominally 1.0 mg/mL of vigabatrin from the *Sample stock solution* and *Mobile phase*. Pass a portion of the solution through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 10-µm packing L9

Flow rate: 1.5 mL/min

Injection volume: 50 µL

System suitability

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

[Note—The relative retention times for vigabatrin related compound A and vigabatrin are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between vigabatrin related compound A and vigabatrin, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of vigabatrin ($C_6H_{11}NO_2$) in the portion of Tablets taken:

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

r_U = peak response of vigabatrin from the *Sample solution*

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Mobile phase: Dissolve 6 g of sodium phosphate, monobasic in 800 mL of water. Add 100 mL of acetonitrile, and dilute with water to 1 L. Adjust with phosphoric acid to a pH of 2.3.

System suitability solution: 0.6 mg/mL of USP Vigabatrin RS and 6 µg/mL of USP Vigabatrin Related Compound A RS in *Mobile phase*

Standard solution: (*L*/900) mg/mL of USP Vigabatrin RS in water

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 210 nm

Column: 4.6-mm × 25-cm; 10-µm packing L9

Flow rate: 1.0 mL/min

Injection volume: 50 µL

System suitability

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

[Note—The relative retention times for vigabatrin related compound A and vigabatrin are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between vigabatrin related compound A and vigabatrin, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage (*Q*) of the labeled amount of vigabatrin ($C_6H_{11}NO_2$) dissolved:

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

r_U = peak response of vigabatrin from the *Sample solution*

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

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

L = label claim (mg/Tablet)

V = volume of *Medium*

Tolerances: NLT 75% (*Q*) of the labeled amount of vigabatrin ($C_6H_{11}NO_2$) is dissolved in 30 min.

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

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 75 rpm

Time: 30 min

Mobile phase: Dissolve 6.9 g of sodium phosphate, monobasic in 800 mL of water. Add 100 mL of acetonitrile, and dilute with water to 1 L. Adjust with diluted phosphoric acid to a pH of 2.3.

System suitability solution: 0.6 mg/mL of USP Vigabatrin RS and 6 µg/mL of USP Vigabatrin Related Compound A RS in *Mobile phase*. Sonicate to dissolve if necessary.

Standard solution: (*L*/900) mg/mL of USP Vigabatrin RS in *Medium*, where *L* is the label claim, in mg/Tablet. Sonicate to dissolve.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 4 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 10-µm packing L9

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: NLT 1.7 times the retention time of vigabatrin

System suitability

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

[NOTE—The relative retention times for vigabatrin related compound A and vigabatrin are about 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between vigabatrin related compound A and vigabatrin, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of vigabatrin ($C_6H_{11}NO_2$) dissolved:

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

r_U = peak response of vigabatrin from the *Sample solution*

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

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of vigabatrin ($C_6H_{11}NO_2$) is dissolved.

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

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Buffer: Dissolve 6.0 g of sodium phosphate, monobasic, anhydrous in 800 mL of water.

Mobile phase: Acetonitrile, *Buffer*, and water (10:80:10). Adjust with phosphoric acid to a pH of 2.3.

System suitability solution: 0.6 mg/mL of USP Vigabatrin RS and 6 µg/mL of USP Vigabatrin Related Compound A RS in *Mobile phase*

Standard solution: (*L*/900) mg/mL of USP Vigabatrin RS in *Medium*, where *L* is the label claim, in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first NLT 2 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Columns

Guard: 1.0-mm × 1-cm; 5-µm packing L3

Analytical: 4.6-mm × 25-cm; 10-µm packing L9

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: NLT 1.6 times the retention time of vigabatrin

System suitability

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

[NOTE—The relative retention times for vigabatrin related compound A and vigabatrin are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between vigabatrin related compound A and vigabatrin, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of vigabatrin ($C_6H_{11}NO_2$) dissolved:

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

r_U = peak response of vigabatrin from the *Sample solution*

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

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of vigabatrin ($C_6H_{11}NO_2$) is dissolved.▲ (RB 1-May-2023)

• **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

• **ORGANIC IMPURITIES**

Buffer: 1.5 g/L of ammonium acetate in water

Mobile phase: Acetonitrile and *Buffer* (5:95)

System suitability solution: 0.1 mg/mL each of USP Vigabatrin RS, USP Vigabatrin Related Compound A RS, USP Vigabatrin Related Compound B RS, and USP Povidone RS in *Mobile phase*

Sensitivity solution: 0.01 mg/mL of USP Vigabatrin Related Compound A RS in *Mobile phase*

Standard solution: 0.07 mg/mL of USP Vigabatrin Related Compound A RS in *Mobile phase*

Sample solution: Nominally 22 mg/mL of vigabatrin prepared as follows. Transfer a suitable amount of finely powdered Tablets (NLT 10) to a suitable volumetric flask. Add *Mobile phase* to 80% of the flask volume. Sonication may be used to aid in dissolution. Allow the resulting solution to cool to room temperature, and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Flow rate: 1.0 mL/min

Injection volume: 10 µL

Run time: 12 times the retention time of the vigabatrin peak

System suitability

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

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

Suitability requirements

Resolution: NLT 2.0 between vigabatrin related compound B and povidone, *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 impurity in the portion of Tablets taken:

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

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

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

C_S = concentration of ▲USP Vigabatrin Related Compound A RS▲ (ERR 1-May-2023) in the *Standard solution*

C_U = nominal concentration of vigabatrin in the *Sample solution*

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor[a]	Acceptance Criteria, NMT (%)
Vigabatrin	0.12	—	—
Vigabatrin related compound B[b]	0.13	—	—
Povidone[c]	0.25	—	—
N-Carboxymethyl vinylpyrrolidinone[d]	0.38	2.1	0.15
Vigabatrin related compound A	1.0	1.0	0.3
N-3-Oxocarboxypentyl vinylpyrrolidinone[e]	1.28	1.0	0.15
Any individual unspecified degradation product	—	0.026	0.15
Total impurities	—	—	1.0

[a] RRF relative to vigabatrin related compound A.

[b] Included for peak identification only. Not to be included in *Total impurities* as it is controlled in the drug substance.

[c] Povidone is due to excipient. Included for identification only. Not to be included in *Total impurities*.

[d] 2-(2-Oxo-5-vinylpyrrolidin-1-yl)acetic acid.

[e] 4-Oxo-6-(2-oxo-5-vinylpyrrolidin-1-yl) hexanoic acid.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Povidone RS

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

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

Topic/Question	Contact	Expert Committee
VIGABATRIN TABLETS	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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