

Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Feb-2025
Document Type: USP Monographs
DocId: GUID-78AE918E-308D-42F7-A437-9837C4D7B2BA_4_en-US
DOI: https://doi.org/10.31003/USPNF_M7709_04_01
DOI Ref: lqo1m

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Topiramate Extended-Release Capsules

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DEFINITION

Topiramate Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of topiramate ($C_{12}H_{21}NO_8S$).

IDENTIFICATION

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

Sample for [Infrared Spectroscopy 197K](#): Grind the contents of Capsules (NLT 20). Transfer an amount of powder equivalent to 250 mg of topiramate to a 250-mL separating funnel. Add 50 mL of 10% [alcohol](#) and shake for 5 min. Add 50 mL of [chloroform](#) and extract for 10 min, and allow the layers to separate. Filter the chloroform layer through [anhydrous sodium sulfate](#). Evaporate the [chloroform](#) to dryness. Use the dry residue.

Acceptance criteria: The spectrum obtained from the *Sample* shows bands at approximately 3383 cm^{-1} , 3111 cm^{-1} , 2941 cm^{-1} , 2908 cm^{-1} , 1377 cm^{-1} , 1186 cm^{-1} , and 1072 cm^{-1} , similar to the spectrum from the *Standard* similarly obtained. Peak positions may vary slightly (within $\pm 10\text{ cm}^{-1}$). [NOTE—Other peaks may be present in the spectra that do not appear in this list.]

- **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: 1.54 g/L of [ammonium acetate](#) in [water](#). Adjust with [glacial acetic acid](#) to a pH of 4.0.

Mobile phase: [Methanol](#) and *Buffer* (40:60)

Diluent: [Acetonitrile](#) and [water](#) (30:70)

Standard solution: 2 mg/mL of [USP Topiramate RS](#) in *Diluent*. Sonicate to dissolve.

Sample solution: Nominally 2 mg/mL of topiramate in *Diluent* prepared as follows. Transfer a suitable quantity of topiramate from the contents of Capsules (NLT 20) to a suitable volumetric flask. Add 60% of the final volume of *Diluent* and sonicate with occasional shaking for NLT 10 min. Allow the solution to cool at room temperature and dilute with *Diluent* to volume. Pass a portion of this solution through a suitable filter of 0.45- μm or finer pore size, discarding NLT the first 1 mL of filtrate.

Chromatographic system

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

Mode: LC

Detector: Refractive index

Column: 4.6-mm $\times$ 10-cm; 5- μm packing [L1](#)

Temperatures

Column: 35°

Detector: 35°

Flow rate: 1 mL/min

Injection volume: 40 μL

Run time: NLT 1.5 times the retention time of topiramate

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of topiramate ($C_{12}H_{21}NO_8S$) in the portion of Capsules taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#)

Test 1

Medium: 0.05 M phosphate buffer, pH 7.5 (dissolve 6.8 g of [monobasic potassium phosphate](#) in 1 L of [water](#); adjust with 10% [sodium hydroxide](#) to a pH of 7.5); 750 mL

Apparatus 2: 50 rpm. Use a suitable sinker, if necessary.

Times: 2, 4, 8, and 12 h

Buffer: 1.54 g/L of [ammonium acetate](#) in [water](#). Adjust with [glacial acetic acid](#) to a pH of 4.0.

Mobile phase: [Methanol](#) and *Buffer* (40:60)

Standard stock solution: 1.7 mg/mL of [USP Topiramate RS](#) prepared as follows. Transfer a suitable amount of [USP Topiramate RS](#) to a suitable volumetric flask. Add 10% of the flask volume of [acetonitrile](#) and sonicate to dissolve. Dilute with *Medium* to volume.

Standard solution: ($L/750$) mg/mL of [USP Topiramate RS](#) in *Medium*, from the *Standard stock solution*, where L is the label claim in mg/Capsule

Sample solution: At the times specified, withdraw a known volume of the solution under test and pass it through a suitable filter of 0.45- μ m or finer pore size, discarding NLT the first 5 mL of filtrate. Replace the volume withdrawn with an equal volume of fresh *Medium*.

Chromatographic system

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

Mode: LC

Detector: Refractive index

Column: 4.6-mm $\times$ 10-cm; 5- μ m packing [L1](#)

Temperatures

Column: 35°

Detector: 35°

Flow rate: 1 mL/min

Injection volume: 100 μ L

Run time: NLT 1.5 times the retention time of topiramate

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 topiramate ($C_{12}H_{21}NO_8S$) in the sample withdrawn from the vessel at each time point (i):

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

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

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

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

Calculate the percentage of the labeled amount of topiramate ($C_{12}H_{21}NO_8S$) dissolved at each time point (i).



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

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

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

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

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

V = volume of *Medium*, 750 mL

L = label claim (mg/Capsule)

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

Tolerances: See [Table 1](#).

Table 1

Time Point (<i>i</i>)	Time (h)	Amount Dissolved (%)
1	2	22–47
2	4	48–73
3	8	70–90
4	12	NLT 80

The percentages of the labeled amount of topiramate ($C_{12}H_{21}NO_8S$) dissolved at the times specified conform 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: Tris buffer, pH 7.2 (1.18 g/L of [tris\(hydroxymethyl\)aminomethane](#) and 6.35 g/L of [tris\(hydroxymethyl\)aminomethane hydrochloride](#) in [water](#)); 900 mL

Apparatus 1: 100 rpm

Times: 1, 2, and 6 h

Mobile phase: [Methanol](#) and [water](#) (45:55)

Standard solution: 0.22 mg/mL of [USP Topiramate RS](#) in *Medium*. Sonicate to dissolve, if necessary.

Sample solution: At the times specified, pass a portion of the solution under test through a suitable filter of 10-μm pore size.

Chromatographic system

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

Mode: LC

Detector: Refractive index

Columns

Guard: 3.0-mm × 4-mm; packing [L87](#)

Analytical: 4.6-mm × 15-cm; 4-μm packing [L87](#)

Temperatures

Column: 35°

Detector: 35°

Flow rate: 1.5 mL/min

Injection volume: 75 μL

Run time: NLT 2 times the retention time of topiramate

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%