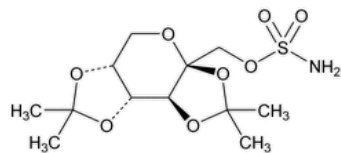


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## Topiramate



$C_{12}H_{21}NO_8S$  339.36

$\beta$ -D-Fructopyranose, 2,3:4,5-bis-O-(1-methylethylidene)-, sulfamate;

2,3:4,5-Di-O-isopropylidene- $\beta$ -D-fructopyranose sulfamate CAS RN<sup>®</sup>: 97240-79-4; UNII: 0H73WJJ391.

### DEFINITION

Topiramate contains NLT 98.0% and NMT 102.0% of topiramate ( $C_{12}H_{21}NO_8S$ ), calculated on the anhydrous basis.

[CAUTION—Great care must be exercised in handling topiramate because it is a suspected teratogen.]

### IDENTIFICATION

**Change to read:**

- **A.** <sup>▲</sup>[SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), *Infrared Spectroscopy: 197K* <sup>▲</sup> (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

**Mobile phase:** Acetonitrile and [water](#) (50:50)

**Standard solution:** 2 mg/mL of [USP Topiramate RS](#) in *Mobile phase*

**Sample solution:** 2 mg/mL of Topiramate in *Mobile phase*

**System suitability solution:** 0.02 mg/mL each of [USP Fructose RS](#) and [USP Topiramate Related Compound A RS](#) in the *Sample solution*

#### Chromatographic system

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

**Mode:** LC

**Detector:** Refractive index

**Column:** 4.6-mm × 25-cm; 5- $\mu$ m packing [L1](#)

#### Temperatures

**Column:** 50°

**Detector:** 55°

**Flow rate:** 0.6 mL/min

**Injection volume:** 20  $\mu$ L

**Run time:** NLT 3 times the retention time of topiramate

#### System suitability

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

[NOTE—See [Table 1](#) for the relative retention times for fructose, topiramate related compound A, and topiramate.]

#### Suitability requirements

**Resolution:** NLT 1.5 between topiramate related compound A and topiramate, *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 topiramate ( $C_{12}H_{21}NO_8S$ ) in the portion of Topiramate 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 Topiramate RS](#) in the *Standard solution* (mg/mL)

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

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

## IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.2%

• **LIMIT OF SULFAMATE AND SULFATE**

[NOTE—Use water with resistivity of NLT 18 megohm-cm for preparation of the *Mobile phase*, *Standard solution*, and *Sample solution*.]

**Buffer:** 0.8 g/L of [p-hydroxybenzoic acid](#) in [water](#)

**Mobile phase:** Methanol and *Buffer* (2.5:97.5). Adjust with [sodium hydroxide](#) solution to a pH of  $9.4 \pm 0.5$ .

**Standard solution:** 0.0045 mg/mL of [sodium sulfate](#) and 0.0030 mg/mL of [sulfamic acid](#) in *Mobile phase*

**Sample solution:** 6.0 mg/mL of Topiramate in *Mobile phase*

## Chromatographic system

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

**Mode:** LC

**Detector:** Conductivity

**Column:** 4.6-mm  $\times$  15-cm; 5- $\mu$ m packing [L47](#)

**Detector temperature:** 30°

**Flow rate:** 1.5 mL/min

[NOTE—A suitable background suppression unit may be used.]

**Injection volume:** 70  $\mu$ L

## System suitability

**Sample:** *Standard solution*

[NOTE—The relative retention time of sulfamate is 0.44 relative to sulfate.]

## Suitability requirements

**Relative standard deviation:** NMT 15.0% for sulfamate and sulfate

## Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of sulfate ions in the portion of Topiramate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

$r_U$  = peak response of the sulfate ion from the *Sample solution*

$r_S$  = peak response of the sulfate ion from the *Standard solution*

$C_S$  = concentration of sodium sulfate in the *Standard solution* (mg/mL)

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

$M_{r1}$  = molecular weight of the sulfate anion, 96.04

$M_{r2}$  = molecular weight of anhydrous sodium sulfate, 142.04

Calculate the percentage of sulfamate ions in the portion of Topiramate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

$r_U$  = peak response of the sulfamate ion from the *Sample solution*

$r_S$  = peak response of the sulfamate ion from the *Standard solution*

$C_S$  = concentration of sulfamic acid in the *Standard solution* (mg/mL)