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Torsemide Tablets

DEFINITION

Torsemide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of torsemide ($C_{16}H_{20}N_4O_3S$).

IDENTIFICATION

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲2S *(USP41)*

ASSAY

Change to read:

• **Procedure**

Buffer: 2.72 g/L of monobasic potassium phosphate▲▲2S *(USP41)*

Solution A: Acetonitrile and methanol (10:90)

Mobile phase: *Buffer* and *Solution A* (50:50). Adjust with diluted phosphoric acid (1 in 10 v/v) to a pH of 4.0.

Standard solution: 0.4 mg/mL of USP Torsemide RS prepared as follows. To a quantity of USP Torsemide RS in a suitable flask, add methanol to 30% of the flask volume and sonicate for NLT 8 min. Add *Buffer* to fill 75% of the flask volume, cool, and dilute with *Mobile phase*. Pass through a membrane filter of 0.45-µm pore size.

Sample solution: Nominally 0.4 mg/mL of torsemide prepared as follows. Place ▲▲2S *(USP41)* 40 mg ▲of torsemide▲2S *(USP41)* from NLT 20 powdered Tablets in a 100-mL volumetric flask. Add methanol to 30% of the flask volume and sonicate for NLT 8 min. Add *Buffer* to fill 75% of the flask volume, cool, and dilute with *Mobile phase*. Pass through a membrane filter of 0.45-µm pore size. ▲The *Sample solution* is not stable at room temperature but is stable for 12 h at 6°.▲2S *(USP41)*

Chromatographic system

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

Mode: LC

Detector: UV 288 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲2S *(USP41)*

Column: 4.6-mm × 15-cm; 5-µm packing L1

Temperatures

▲**Autosampler:** 6°▲2S *(USP41)*

Column: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 2 times the retention time of torsemide▲2S *(USP41)*

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of torsemide ($C_{16}H_{20}N_4O_3S$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 15 min

Buffer, Mobile phase, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Standard stock solution: 0.55 mg/mL ▲of USP Torsemide RS▲2S *(USP41)* prepared as follows. Transfer a quantity of USP Torsemide RS to a suitable volumetric flask. Add methanol to 30% of the flask volume and sonicate until dissolved. Add *Buffer* to fill 75% of the flask volume, cool to room temperature, and dilute with *Mobile phase* to volume.

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of (*L*/900) mg/mL, 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.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of torsemide ($C_{16}H_{20}N_4O_3S$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \text{ ▲▲2S } \textit{(USP41)} \times V \times 100$$

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

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

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

L = label claim (mg/Tablet)

▲▲2S *(USP41)*

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (*Q*) of the labeled amount of torsemide ($C_{16}H_{20}N_4O_3S$) is dissolved.

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: 50 rpm

Time: 30 min

Standard stock solution: 0.11 mg/mL of USP Torsemide RS in *Medium*

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of (*L*/900) mg/mL, where *L* is the label claim in mg/Tablet.

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 285 nm

Cell: 1.0 cm for 5-, 10-, and 20-mg Tablets and 0.1 cm for 100-mg Tablets

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of torsemide ($C_{16}H_{20}N_4O_3S$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of torsemide ($C_{16}H_{20}N_4O_3S$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

• **Organic Impurities**

Buffer and **Solution A:** Prepare as directed in the *Assay*.

Mobile phase: *Buffer* and *Solution A* (55:45). Adjust with diluted phosphoric acid (1 in 10 v/v) to a pH of 4.0.

▲**Standard stock solution A:**▲2S *(USP41)* 0.1 mg/mL of USP Torsemide Related Compound A RS and 0.02 mg/mL of USP Torsemide Related Compound E RS prepared as follows. Dissolve a suitable quantity each of USP Torsemide Related Compound A RS and USP Torsemide Related Compound E RS in methanol to 32% of the flask volume and sonicate to dissolve. Dilute with *Mobile phase* to volume.

System suitability solution: ▲ 0.4 mg/mL of USP Torsemide RS, 4 µg/mL of USP Torsemide Related Compound A RS, and 0.8 µg/mL of USP Torsemide Related Compound E RS prepared as follows. To a quantity of USP Torsemide RS in a suitable flask add methanol to 30% of the flask volume and sonicate to dissolve. Add *Buffer* to fill 75% of the flask volume, and cool. Add a suitable volume of *Standard stock solution A* and dilute with *Mobile phase* to volume.

Standard stock solution B: 0.4 mg/mL each of USP Torsemide RS prepared as follows. To a suitable amount of USP Torsemide RS in a suitable flask, add methanol to 30% of the flask volume and sonicate for NLT 8 min. Add *Buffer* to fill 75% of the flask volume, cool, and dilute with *Mobile phase* to volume.

Sensitivity solution: 0.4 µg/mL of USP Torsemide RS in *Mobile phase* from *Standard stock solution B*▲2S *(USP41)*

Standard solution: 4 µg/mL each of USP Torsemide RS and USP Torsemide Related Compound A RS and 0.8 µg/mL of USP Torsemide Related Compound E RS in *Mobile phase* from ▲*Standard stock solution A* and *Standard stock solution B*▲2S *(USP41)*

Sample solution: Nominally 0.4 mg/mL of torsemide prepared as follows. Weigh 40 mg of torsemide from NLT 20 powdered Tablets into a 100-mL volumetric flask. Add methanol to 30% of the flask volume, mix, and sonicate for NLT 8 min. Add *Buffer* to fill 75% of the flask volume, cool to room temperature, dilute with *Mobile phase* to volume, and mix. ▲The *Sample solution* is not stable at room temperature, but is stable for 15 h at 6°.▲2S *(USP41)*

Chromatographic system

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

Mode: LC

Detector: UV 288 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

▲**Autosampler temperature:** 6°▲2S *(USP41)*

Flow rate: 0.8 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution*, ▲*Sensitivity solution*,▲2S *(USP41)* and *Standard solution*

▲[Note—See *Table 1* for relative retention times.]▲2S *(USP41)*

Suitability requirements

Resolution: NLT 2.5 between torsemide related compound A and torsemide related compound E, *System suitability solution*

Tailing factor: NMT 2.0 ▲for the torsemide peak, *System suitability solution*▲2S *(USP41)*

Relative standard deviation: NMT 5.0% ▲for the torsemide peak,▲2S *(USP41)* *Standard solution*

▲**Signal-to-noise ratio:** NLT 10.0, *Sensitivity solution*▲2S *(USP41)*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of torsemide related compound A or torsemide related compound E in the portion of Tablets taken:

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

r_U = peak response of torsemide related compound A or torsemide related compound E from the *Sample solution*

r_S = peak response of torsemide related compound A or torsemide related compound E from the *Standard solution*

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

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

Calculate the percentage of any ▲unspecified degradation product▲2S *(USP41)* in the portion of Tablets taken:

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

r_U = peak response of any ▲unspecified degradation product▲2S *(USP41)* from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Torsemide related compound A▲▲2S *(USP41)*	0.39	0.6
Torsemide related compound E▲▲2S *(USP41)*	0.50	0.3
Torsemide related compound C▲[a,b]▲2S *(USP41)*	0.62	—
Torsemide ▲related compound▲2S *(USP41)* D▲[b,c]▲2S *(USP41)*	0.75	—
Torsemide	1.00	—
Torsemide related compound B▲[b,d]▲2S *(USP41)*	1.96	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Any ▲unspecified degradation product▲2S *(USP41)*	—	0.2
Total impurities	—	1.1

▲a *N*-(Ethylcarbamoyl)-4-(3-tolylamino)pyridine-3-sulfonamide. ▲2S *(USP41)*

▲b Process-related impurity controlled in the drug substance. ▲2S *(USP41)*

▲c Ethyl {[4-(3-tolylamino)pyridin-3-yl]sulfonyl}carbamate. ▲2S *(USP41)*

▲d *N*-(Butylcarbamoyl)-4-(3-tolylamino)pyridine-3-sulfonamide.▲2S *(USP41)*

ADDITIONAL REQUIREMENTS

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

• **Labeling:** The labeling indicates the *Dissolution* test with which the product complies, if *Test 1* is not used.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Torsemide RS

USP Torsemide Related Compound A RS

4-[(3-Methylphenyl)amino]-3-pyridinesulfonamide.

$C_{12}H_{13}N_3O_2S$ 263.32

USP Torsemide Related Compound E RS

▲4-(3-Tolyl)-2*H*-pyrido[4,3-e][1,2,4]thiadiazin-3(4*H*)-one 1,1-dioxide.▲2S *(USP41)*

$C_{13}H_{11}N_3O_3S$ 289.31

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

Topic/Question	Contact	Expert Committee
TORSEMIDE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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