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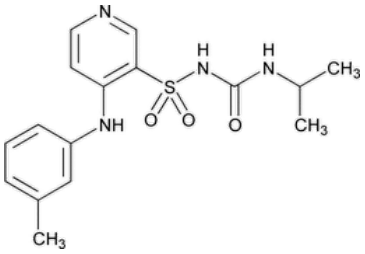
# Torsemide



$C_{16}H_{20}N_4O_3S$ 348.42

3-Pyridinesulfonamide, *N*-[[(1-methylethyl)amino]carbonyl]-4-[(3-methylphenyl)amino]-.

1-Isopropyl-3-[(4-*m*-toluidino-3-pyridyl)sulfonyl]urea CAS RN®: 56211-40-6; UNII: W31X2H97FB.

» Torsemide contains not less than 98.0 percent and not more than 102.0 percent of $C_{16}H_{20}N_4O_3S$, calculated on the anhydrous basis.

**Packaging and storage**—Preserve in well-closed containers.

**USP Reference standards** ⟨11⟩—

USP Torsemide RS

(Form 1)

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 B RS

*N*-[(*n*-Butylamino)carbonyl]-4-[(3-methylphenyl)amino]-3-pyridinesulfonamide].

$C_{17}H_{22}N_4O_3S$ 362.45

USP Torsemide Related Compound C RS

*N*-[(Ethylamino)carbonyl]-4-[(3-methylphenyl)amino]-3-pyridinesulfonamide.

$C_{15}H_{18}N_4O_3S$ 334.39

**Identification**—

***Change to read:***

**A:** ▲*Spectroscopic Identification Tests* ⟨197⟩, *Infrared Spectroscopy: 197K*▲ (CN 1-May-2020) ·

**B:** The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

**Water Determination,** *Method I* ⟨921⟩**:** not more than 1.0%.

**Residue on ignition** ⟨281⟩**:** not more than 0.1%.

**Related compounds**—

*0.02 M Potassium phosphate buffer* and *Mobile phase*—Prepare as directed in the *Assay*.

*Resolution solution*—Transfer about 3 mg each of USP Torsemide RS and USP Torsemide Related Compound A RS to a 10-mL volumetric flask, add 3 mL of methanol, mix, and sonicate for not less than 8 minutes. Add 4.5 mL of *0.02 M Potassium phosphate buffer*, cool to room temperature, dilute with *Mobile phase* to volume, and mix.

*Standard solution*—Transfer about 8 mg each of USP Torsemide Related Compound A RS, USP Torsemide Related Compound B RS, and USP Torsemide Related Compound C RS, accurately weighed, to a 100-mL volumetric flask, add 30 mL of methanol, mix, and sonicate for not less than 8 minutes. Add 45 mL of *0.02 M Potassium phosphate buffer*, cool to room temperature, dilute with *Mobile phase* to volume, and mix. Quantitatively dilute a portion of this solution with *Mobile phase* to obtain a solution having a known concentration of about 0.0019 mg per mL.

*Test solution*—Use the *Assay preparation.*

*Chromatographic system*—Prepare as directed in the *Assay.* Chromatograph the *Resolution solution* and the *Standard solution*, and record the peak responses over a period three times the retention time of torsemide as directed for *Procedure:* the resolution, *R,* between torsemide and torsemide related compound A is not less than 1.0; the tailing factors are not more than 2.0; and the relative standard deviation for replicate injections is not more than 10.0%.

*Procedure*—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak areas for torsemide related compound A, torsemide related compound B, and torsemide related compound C. Calculate the percentage of each related compound, if present, in the portion of Torsemide taken by the formula:

$$100(C_S/C_U)(r_U/r_S)$$

in which $C_S$ is the concentration, in mg per mL, of the relevant USP Reference Standard in the *Standard solution;* $C_U$ is the concentration of Torsemide, in mg per mL, in the *Test solution;* and $r_U$ and $r_S$ are the peak areas for the relevant torsemide related compound obtained from the *Test solution* and the *Standard solution*, respectively: not more than 0.2% of torsemide related compound C, not more than 0.3% of torsemide related compound B, and not more than 0.5% of torsemide related compound A are found. Calculate the percentage of any other impurity in the portion of Torsemide taken by the formula:

$$100(r_i/r_s)$$

in which $r_i$ is the peak response for each other impurity obtained from the *Test solution;* and $r_s$ is the sum of the responses of all the peaks obtained from the *Test solution:* not more than 0.1% of any other impurity is found, not more than 0.2% of total other impurities is found, and not more than 1.0% of total impurities (including torsemide related compounds A, B, and C) is found.

**Assay**—

*0.02 M Potassium phosphate buffer*—Dissolve 2.7 g of monobasic potassium phosphate in about 900 mL of water. Adjust with phosphoric acid to a pH of 3.5, dilute with water to 1000 mL, and mix.

*Mobile phase*—Prepare a filtered and degassed mixture of *0.02 M Potassium phosphate buffer* and methanol (3:2). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

*Standard preparation*—Transfer about 19 mg of USP Torsemide RS, accurately weighed, to a 50-mL volumetric flask, add 15 mL of methanol, mix, and sonicate for not less than 8 minutes. Add 22.5 mL of *0.02 M Potassium phosphate buffer*, cool to room temperature, dilute with *Mobile phase* to volume, and mix.

*Assay preparation*—Transfer about 38 mg of Torsemide, accurately weighed, to a 100-mL volumetric flask, add 30 mL of methanol, mix, and sonicate for not less than 8 minutes. Add 45 mL of *0.02 M Potassium phosphate buffer*, cool to room temperature, dilute with *Mobile phase* to volume, and mix.

*Chromatographic system* (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 288-nm detector and a 4.6-mm × 15-cm column that contains 7-µm packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

*Procedure*—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the amount, in mg, of $C_{16}H_{20}N_4O_3S$ in the portion of Torsemide taken by the formula:

$$100C(r_U/r_S)$$

in which *C* is the concentration, in mg per mL, of USP Torsemide RS in the *Standard preparation;* and $r_U$ and $r_S$ are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.



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

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

**Chromatographic Database Information:** Chromatographic Database

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