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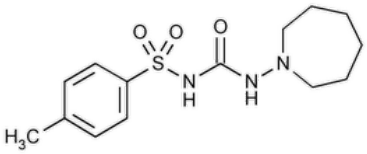
Tolazamide



$C_{14}H_{21}N_3O_3S$ 311.40

Benzenesulfonamide, *N*-[[(hexahydro-1*H*-azepin-1-yl)amino]carbonyl]-4-methyl-.

1-(Hexahydro-1*H*-azepin-1-yl)-3-(*p*-tolylsulfonyl)urea CAS RN®: 1156-19-0; UNII: 9LT1BRO48Q.

» Tolazamide contains not less than 97.5 percent and not more than 102.5 percent of $C_{14}H_{21}N_3O_3S$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—

USP Tolazamide RS

Identification—

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

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

Loss on drying ⟨731⟩—Dry it at a pressure not exceeding 5 mm of mercury at 60° for 3 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.2%.

Change to read:

▲**Selenium** ⟨291⟩*, Procedures, Procedure 1*▲ (CN 1-Jun-2023): 0.003%, a 200-mg specimen being used.

Limit of N-aminohexamethyleneimine—

Trisodium pentacyanoaminoferroate solution—Mix 1.0 g of sodium nitroferricyanide and 3.2 mL of ammonium hydroxide in a glass-stoppered flask, insert the stopper in the flask, and refrigerate the mixture overnight. Pour the solution into 10 mL of dehydrated alcohol, and collect the yellow precipitate that is formed on coarse filter paper in a Buchner-type funnel by filtration under reduced pressure. Wash the residue on the filter with anhydrous ether, and store the dry solid in a desiccator. Dissolve a portion of the dry solid in water to obtain a solution containing 1.0 mg per mL, store in a refrigerator, and use within 7 days.

Buffer solution—Dissolve 0.96 g of anhydrous citric acid and 2.92 g of dibasic sodium phosphate in 200 mL of water. Adjust by adding phosphoric acid or 1 N sodium hydroxide, if necessary, to a pH of 5.4 ± 0.1.

Standard solution—Transfer, with the aid of a syringe, 100 mg of N-aminohexamethyleneimine to a 200-mL volumetric flask, dilute with acetone to volume, and mix. Dilute the resulting solution quantitatively with acetone to obtain a solution containing 12.5 µg per mL. Pipet 2 mL of this solution into a 25-mL glass-stoppered flask, add 8.0 mL of *Buffer solution*, shake the mixture, allow to stand for 15 minutes, and filter. Collect the filtrate in a suitable glass-stoppered tube, and use the filtrate as the *Standard solution*.

Test solution—Transfer 0.50 g of Tolazamide to a glass-stoppered, 25-mL flask, add 2.0 mL of acetone, insert the stopper in the flask, and shake the mixture vigorously for 15 minutes. Add 8.0 mL of *Buffer solution*, shake the mixture, allow to stand for 15 minutes, and filter. Collect the filtrate in a suitable glass-stoppered tube, and use the filtrate as the *Test solution*.

Procedure—Add 1.0 mL of *Trisodium pentacyanoaminoferroate solution* to the *Standard solution* and to the *Test solution*, and mix both solutions: the intensity of any pink color that may develop in the *Test solution* within 30 minutes does not exceed that produced in the *Standard solution* within 30 minutes (0.005%).

Chromatographic purity—

Mobile phase—Prepare a filtered and degassed mixture of water, acetonitrile, and glacial acetic acid (100:100:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

System suitability solution—Dissolve an accurately weighed quantity of USP Tolazamide RS in *Mobile phase,* and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 0.014 mg per mL.

Test solution—[NOTE—Make solution fresh before each injection.]

Transfer about 140 mg of Tolazamide, accurately weighed, to a 100-mL volumetric flask, dissolve in *Mobile phase*, sonicating if necessary, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *CHROMATOGRAPHY ⟨621⟩*)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1.0 mL per minute. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 4000 theoretical plates; the tailing factor is not more than 3.0; and the relative standard deviation for replicate injections is not more than 5.0%.

Procedure—Inject a volume (about 50 µL) of the *Test solution* into the chromatograph, record the chromatogram, and measure all of the peak responses. Calculate the percentage of each impurity in the portion of Tolazamide taken by the formula:

$$100(1/F)(r_i/r_s)$$

in which F is the relative response factor, which is equal to 0.52 for the *p*-toluenesulfonic acid peak eluting at a relative retention time of 0.23 and equal to 1.0 for all other peaks; r_i is the peak response for each impurity; and r_s is the sum of the responses of all the peaks: not more than 0.5% of any individual impurity is found; and not more than 1.5% of total impurities is found.

Assay—

Mobile phase—Prepare a filtered and degassed mixture of hexane, water-saturated hexane, tetrahydrofuran, alcohol, and glacial acetic acid (475:475:20:15:9). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Internal standard solution—Dissolve a suitable quantity of Tolbutamide in alcohol-free chloroform to obtain a solution having a known concentration of about 1.5 mg per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP Tolazamide RS in *Internal standard solution* to obtain a solution having a known concentration of about 3 mg per mL.

Assay preparation—Transfer about 30 mg of Tolazamide, accurately weighed, to a 10-mL volumetric flask, dissolve in and dilute with *Internal standard solution* to volume, and mix.

Chromatographic system (see *CHROMATOGRAPHY ⟨621⟩*)—The liquid chromatograph is equipped with a 254-nm detector and a 4-mm × 30-cm column that contains 10-µm packing L3. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the resolution, *R*, between the analyte and internal standard peaks is not less than 2.0; and the relative standard deviation for four replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 0.6 for the internal standard and 1.0 for tolazamide. Calculate the quantity, in mg, of $C_{14}H_{21}N_3O_3S$ in the portion of Tolazamide taken by the formula:

$$10C(R_U/R_S)$$

in which C is the concentration, in mg per mL, of USP Tolazamide RS in the *Standard preparation*; and R_U and R_S are the ratios of the analyte peak response to the internal standard peak response 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
TOLAZAMIDE	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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