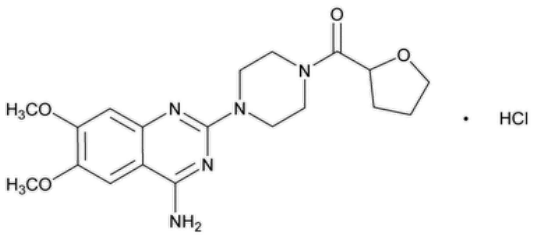
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Dec-2024
Document Type: USP Monographs
DocId: GUID-57BE356B-7C6C-4C18-868A-9D9D50A1B65B_5_en-US
DOI: https://doi.org/10.31003/USPNF_M80835_05_01
DOI Ref: dq3g2

Terazosin Hydrochloride

Change to read:



$C_{19}H_{25}N_5O_4 \cdot HCl \cdot 2H_2O$ ▲459.93▲ (CN 1-Dec-2024)

Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-[(tetrahydro-2-furanyl)carbonyl]-, monohydrochloride, dihydrate.

1-(4-Amino-6,7-dimethoxy-2-quinazolinyl)-4-(tetrahydro-2-furoyl)piperazine monohydrochloride dihydrate CAS RN®: 70024-40-7; UNII: D32S14F082.

Anhydrous ▲423.90▲ (CN 1-Dec-2024) CAS RN®: 63074-08-8; UNII: 8QOP8Z9955.

» Terazosin Hydrochloride contains not less than 98.0 percent and not more than 102.0 percent of $C_{19}H_{25}N_5O_4 \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers, and store at a temperature between 20° and 25°.

Change to read:

USP Reference standards ⟨11⟩—

USP Terazosin Hydrochloride RS

USP Terazosin Related Compound A RS

▲6,7-Dimethoxy-2-(piperazin-1-yl)quinazolin-4-amine dihydrochloride.▲ (CN 1-Dec-2024)

$C_{14}H_{19}N_5O_2 \cdot 2HCl$ ▲362.26▲ (CN 1-Dec-2024)

USP Terazosin Related Compound B RS

▲[4-(4-Hydroxy-6,7-dimethoxyquinazolin-2-yl)piperazin-1-yl](tetrahydrofuran-2-yl)methanone.▲ (CN 1-Dec-2024)

$C_{19}H_{24}N_4O_5$ 388.42

USP Terazosin Related Compound C RS

▲2,2'-(Piperazine-1,4-diyl)bis(6,7-dimethoxyquinazolin-4-amine) dihydrochloride.▲ (CN 1-Dec-2024)

$C_{24}H_{28}N_8O_4 \cdot 2HCl$ ▲565.46▲ (CN 1-Dec-2024)

Color and clarity of solution—Dissolve a quantity of Terazosin Hydrochloride in methanol solution (90 in 100) to obtain a 1 in 100 solution: this solution is clear and colorless to pale yellow, when compared to methanol solution (90 in 100).

Identification—

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

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.*

C: It meets the requirements of the tests for *Chloride* ⟨191⟩, a solution prepared by dissolving 100 mg in 10 mL of methanol solution (90 in 100) being examined.

Loss on drying ⟨731⟩—Dry it in vacuum at 105° for 3 hours: it loses not more than 9.0% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.2%, determined on a 1.0-g specimen.

Limit of tetrahydro-2-furancarboxylic acid—

Blank solution—Transfer 2.0 mL of glacial acetic acid to a 100-mL volumetric flask, dilute with acetone to volume, and mix. Mix 5.0 mL of this solution and 5.0 mL of acetone; pass through a nylon membrane filter having a 0.45-µm or finer porosity, previously washed with acetone; and discard the first 1 mL of the filtrate.

Internal standard solution—Transfer about 100 mg of capric acid, accurately weighed, to a 100-mL volumetric flask; dissolve in and dilute with acetone to volume; and mix. Transfer 10.0 mL of this solution and 2.0 mL of glacial acetic acid to a 100-mL volumetric flask, dilute with acetone to volume, and mix.

Standard stock solution—Dissolve an accurately weighed amount of tetrahydro-2-furancarboxylic acid in acetone to obtain a solution having a known concentration of about 1.0 mg per mL. Dilute with acetone quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 100 µg per mL.

Standard solution—Transfer 5.0 mL of the *Standard stock solution* and 5.0 mL of *Internal standard solution* to a 50-mL centrifuge tube, and mix. Pass through a nylon membrane filter having a 0.45-µm or finer porosity, previously washed with acetone; and discard the first 1 mL of the filtrate.

Test solution—Transfer about 100 mg of Terazosin Hydrochloride, accurately weighed, to a 50-mL centrifuge tube; add 5.0 mL of acetone and 5.0 mL of *Internal standard solution;* and shake for about 30 minutes. Centrifuge for about 10 minutes; pass through a nylon membrane filter having a 0.45-µm or finer porosity, previously washed with acetone; and discard the first 1 mL of the filtrate.

Chromatographic system (see Chromatography ⟨621⟩)—The gas chromatograph is equipped with a flame-ionization detector and a 0.53-mm × 10-m fused-silica capillary column coated with a 1.2-µm film of liquid phase G25. The column temperature is maintained at about 170°. The injection port is configured for splitless injection, and its temperature is maintained at about 230°. The detector temperature is maintained at about 240°. The carrier gas is helium, flowing at a rate of about 9 mL per minute. Chromatograph the *Blank solution,* and measure the peak responses as directed for *Procedure:* ensure that there are no extraneous peaks. Chromatograph the *Standard solution,* and measure the peak responses as directed for *Procedure:* the relative retention times are 1.0 for tetrahydro-2-furancarboxylic acid and 1.2 for capric acid; the resolution, *R,* between tetrahydro-2-furancarboxylic acid and capric acid is not less than 2.3; and the relative standard deviation, determined from the peak response ratios of tetrahydro-2-furancarboxylic acid to capric acid for replicate injections is not more than 6.5%.

Procedure—Separately inject equal volumes (about 0.2 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of tetrahydro-2-furancarboxylic acid in the portion of Terazosin Hydrochloride taken by the formula:

$$(C/W)(R_U/R_S)$$

in which C is the concentration, in µg per mL, of tetrahydro-2-furancarboxylic acid in the *Standard solution; W* is the weight, in mg, of Terazosin Hydrochloride taken to prepare the *Test solution;* and R_U and R_S are the peak response ratios obtained from the *Test solution* and the *Standard solution,* respectively: not more than 0.1% is found.

Limit of 1-[(tetrahydro-2-furanyl)carbonyl]piperazine—

Derivatization solution—Dissolve about 2.0 g of 3,5-dinitrobenzoyl chloride in 250 mL of acetonitrile.

Phosphate buffer solution—Transfer about 96.3 g of dibasic potassium phosphate and 3.85 g of monobasic potassium phosphate, each accurately weighed, to a 500-mL volumetric flask. Dissolve in and dilute with water to volume. Adjust with phosphoric acid solution (10 in 100) or sodium hydroxide solution (10 in 100) to a pH of 8.0 ± 0.1. Transfer 25.0 mL of this solution to a 100-mL volumetric flask, and dilute with water to volume. Adjust with phosphoric acid solution (10 in 100) or sodium hydroxide solution (10 in 100) to a pH of 8.0 ± 0.1.

Solution A—Use filtered and degassed water.

Solution B—Use filtered and degassed acetonitrile.

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system.* Make adjustments if necessary (see *System Suitability* under Chromatography ⟨621⟩).

Blank solution—Use acetonitrile.

Standard solution—Dissolve an accurately weighed quantity of 1-[(tetrahydro-2-furanyl)carbonyl]piperazine in acetonitrile to obtain a solution having a known concentration of about 1.0 mg per mL. Dilute quantitatively, and stepwise if necessary, with acetonitrile, to obtain a solution having a known concentration of about 5 µg per mL.

Test solution—Transfer about 125 mg of Terazosin Hydrochloride, accurately weighed, to a 25-mL volumetric flask; dissolve in and dilute with a mixture of acetonitrile and water (1:1) to volume; and mix.

Derivatization procedure—Transfer 5-mL portions of the *Blank solution,* the *Standard solution,* and the *Test solution,* each to a separate 100-mL volumetric flask, and proceed with each as follows. Add 5.0 mL of *Phosphate buffer solution,* and mix. Add 10.0 mL of *Derivatization solution* while swirling, allow to stand at room temperature for about 20 minutes, and mix. Dilute with a mixture of acetonitrile and water (1:1) to volume, and mix.

Chromatographic system (see Chromatography ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm analytical column that contains packing L7. The flow rate is 1.5 mL per minute, except it is changed to 2.0 mL per minute during the period

between 40 and 80 minutes. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0–35	82	18	isocratic
35–40	82→10	18→90	linear gradient
40–75	10	90	isocratic
75–80	10→82	90→18	linear gradient
80–100	82	18	isocratic

Separately inject equal volumes (about 50 µL) of the derivatized *Blank solution* and the derivatized *Standard solution,* and measure the peak responses as directed for *Procedure,* ensuring that the peaks in the chromatogram of the derivatized *Standard solution* that correspond to those obtained from the derivatized *Blank solution* do not interfere with the determination: the retention time for 1-[(tetrahydro-2-furanyl)carbonyl]piperazine is more than 22 minutes; the column efficiency is not less than 3500 theoretical plates; and the relative standard deviation for replicate injections is not more than 3.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the derivatized *Standard solution* and the derivatized *Test solution* into the chromatograph, record the chromatograms, and measure the peak areas. Calculate the percentage of 1-[(tetrahydro-2-furanyl)carbonyl]piperazine in the portion of Terazosin Hydrochloride taken by the formula:

$$2500(C/W)(r_U/r_S)$$

in which C is the concentration, in mg per mL, of 1-[(tetrahydro-2-furanyl)carbonyl]piperazine in the *Standard solution; W* is the weight, in mg, of Terazosin Hydrochloride taken to prepare the *Test solution;* and r_U and r_S are the peak areas for 1-[(tetrahydro-2-furanyl)carbonyl]piperazine derivative obtained from the derivatized *Test solution* and the derivatized *Standard solution,* respectively: not more than 0.1% is found.

Related compounds—

pH 3.2 Citrate buffer, Standard stock preparation, and *Mobile phase*—Proceed as directed in the *Assay.*

Diluent 1—Dissolve 6.0 g of sodium citrate and 4.0 g of anhydrous citric acid in water, dilute with water to 1.0 L, and mix.

Diluent 2—Prepare a mixture of water, acetonitrile, and methanol (60:30:10).

Standard stock solution 1—Dissolve an accurately weighed quantity of USP Terazosin Related Compound A RS in *Diluent 1,* and dilute with *Diluent 1* to obtain a solution having a known concentration of about 0.5 mg per mL.

Standard stock solution 2—Dissolve an accurately weighed quantity of USP Terazosin Related Compound B RS in methanol, and dilute with methanol to obtain a solution having a known concentration of about 0.5 mg per mL.

Standard stock solution 3—Dissolve an accurately weighed quantity of USP Terazosin Related Compound C RS in *Diluent 2,* and dilute with *Diluent 2* to obtain a solution having a known concentration of about 0.1 mg per mL.

Standard solution—Transfer 5.0 mL of *Standard stock preparation,* 4.0 mL of *Standard stock solution 1,* 4.0 mL of *Standard stock solution 2,* and 20 mL of *Standard stock solution 3* to a 100-mL volumetric flask containing about 60 mL of *Diluent 2.* Dilute with *Diluent 2* to volume, and mix. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Test solution—Use the *Assay stock preparation* prepared as directed in the *Assay.*

Chromatographic system—Prepare as directed in the *Assay.* Chromatograph the *Mobile phase,* and record the peak responses as directed for *Procedure:* ensure that there are no significant interfering peaks. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.2 for terazosin related compound A, 1.0 for terazosin, 1.48 for terazosin related compound B, and 2.57 for terazosin related compound C; the resolution, *R,* between terazosin and terazosin related compound B is not less than 9.0; the column efficiency determined from the terazosin peak is not less than 12,000 theoretical plates; the tailing factor for the terazosin related compound C peak is not more than 3.0; and the relative standard deviation for replicate injections determined from the terazosin peak is not more than 2.0%, and not more than 5.0% determined from the terazosin related compound C peak.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms for about 60 minutes, and measure the peak responses. Separately calculate the quantities, in mg, of terazosin related compound A and terazosin related compound C in the portion of Terazosin Hydrochloride taken by the formula:

$$200C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of the appropriate USP Reference Standard in the *Standard solution;* and r_U and r_S are the peak responses for the corresponding related compound obtained from the *Test solution* and the *Standard solution,* respectively: not more than

0.3% of terazosin related compound A is found; and not more than 0.4% of terazosin related compound C is found. Calculate the quantity, in mg, of each impurity in the portion of Terazosin Hydrochloride taken by the formula:

$$200C(r_i/r_T)$$

in which C is the concentration, in mg per mL, of USP Terazosin Hydrochloride RS in the *Standard solution;* r_i is the peak response for each impurity, other than terazosin related compound A and terazosin related compound C, obtained from the *Test solution;* and r_T is the terazosin peak response obtained from the *Standard solution:* not more than 0.3% of any impurity eluting prior to the terazosin peak is found; not more than 0.1% of any other impurity is found; and not more than 0.6% of total impurities is found.

Assay—

pH 3.2 Citrate buffer—Dissolve 12.0 g of sodium citrate dihydrate and 28.5 g of anhydrous citric acid in 1.95 L of water. Adjust with anhydrous citric acid or sodium citrate to a pH of 3.2 ± 0.1. Dilute with water to 2.0 L, and mix.

Mobile phase—Prepare a filtered and degassed mixture of *pH 3.2 Citrate buffer* and acetonitrile (1685:315). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard stock preparation—Dissolve an accurately weighed quantity of USP Terazosin Hydrochloride RS in *Mobile phase,* and dilute with *Mobile phase* to obtain a solution having a known concentration of about 0.5 mg per mL.

Standard preparation—Transfer 10.0 mL of *Standard stock preparation* to a 50-mL volumetric flask, and dilute with *Mobile phase* to volume. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume; and mix.

Assay stock preparation—Transfer about 100 mg of Terazosin Hydrochloride, accurately weighed, to a 200-mL volumetric flask; dissolve in and dilute with *Mobile phase* to volume; and mix.

Assay preparation—Transfer 10.0 mL of *Assay stock preparation* to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Transfer l0.0 mL of this solution to a l00-mL volumetric flask, 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 4.6-mm × 25-cm column that contains packing L7. The column temperature is maintained at about 30°. The flow rate is about 1.0 mL per minute. Chromatograph the *Mobile phase,* and record the peak responses as directed for *Procedure:* ensure that there are no significant interfering peaks. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 12,000 theoretical plates; the tailing factor is not less than 0.9 and not more than 1.3; and the relative standard deviation for replicate injections is not more than 0.9%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms for about 45 minutes, and measure the peak responses. Calculate the quantity, in mg, of $C_{19}H_{25}N_5O_4 \cdot HCl$ in the portion of Terazosin Hydrochloride taken by the formula:

$$10{,}000C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Terazosin Hydrochloride 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
TERAZOSIN HYDROCHLORIDE	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No.

Current DocID: GUID-57BE356B-7C6C-4C18-868A-9D9D50A1B65B_5_en-US
DOI: https://doi.org/10.31003/USPNF_M80835_05_01
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