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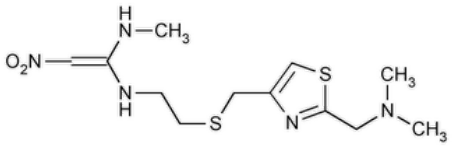
Nizatidine



$C_{12}H_{21}N_5O_2S_2$ 331.46

1,1-Ethenediamine, *N*-[2-[[[2-[(dimethylamino)methyl]-4-thiazolyl]methyl]thio]ethyl]-*N*'-methyl-2-nitro-.

N-[2-[[[2-[(Dimethylamino)methyl]-4-thiazolyl]methyl]thio]ethyl]- *N*'-methyl-2-nitro-1,1-ethenediamine CAS RN®: 76963-41-2; UNII: P41PML4GHR.

» Nizatidine contains not less than 98.0 percent and not more than 101.0 percent of $C_{12}H_{21}N_5O_2S_2$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩—
USP Nizatidine RS

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 of the *Standard preparation* as obtained in the *Assay*.

Loss on drying ⟨731⟩—Dry about 2 g, accurately weighed, at 100° for 1 hour: it loses not more than 1.0% of its weight.

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

Chromatographic purity—

Solution A—Use *Buffer solution* prepared as directed in the *Assay*.

Solution B—Use methanol.

Diluent—Prepare a mixture of *Solution A* and *Solution B* (76:24).

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

Standard solutions—Dissolve an accurately weighed quantity of USP Nizatidine RS quantitatively, and stepwise if necessary, in *Diluent*, sonicating if necessary, to obtain a solution having a known concentration of 50 µg per mL (*Standard solution 1*). Quantitatively dilute portions of *Standard solution 1* with *Diluent* to obtain *Standard solution 2* and *Standard solution 3* having known concentrations of 25 µg per mL and 15 µg per mL, respectively.

Test solution—Prepare a solution of Nizatidine in *Diluent* having a concentration of about 5 mg per mL.

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 5-µm packing L1. The flow rate is about 1 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0–3	76	24	isocratic
3–20	76→50	24→50	linear gradient
20–45	50	50	isocratic

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
45–50	50→76	50→24	linear gradient
50–70	76	24	isocratic

Make adjustments to the composition of the *Mobile phase*, if necessary, to obtain a retention time of about 12 minutes for the main nizatidine peak (see *System Suitability* under *Chromatography* ⟨621⟩). Chromatograph *Standard solution 1*, and record the peak areas as directed for *Procedure:* the tailing factor is not more than 2.0.

Procedure—Separately inject equal volumes (about 50 µL) of *Standard solution 1*, *Standard solution 2*, *Standard solution 3*, and the *Test solution* into the chromatograph, and allow the *Test solution* to elute for not less than three times the retention time of nizatidine. Record the chromatograms, and measure the areas for all the peaks. The sum of the peak areas, excluding the nizatidine peak area, obtained from the *Test solution* is not more than three times the main peak area obtained from *Standard solution 2;* and no single peak area obtained from the *Test solution* is greater than the main peak area obtained from *Standard solution 3:* not more than 0.3% of any individual impurity is found; and not more than 1.5% of total impurities is found.

Assay—

Buffer solution—Prepare a 0.1 M solution by dissolving 5.9 g of ammonium acetate in 760 mL of water. Add 1 mL of diethylamine, and adjust with acetic acid to a pH of 7.5.

Mobile phase—Prepare a filtered and degassed mixture of *Buffer solution* and methanol (76:24). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Nizatidine RS in *Mobile phase*, sonicating if necessary, to obtain a solution having a known concentration of about 0.3 mg per mL.

Assay preparation—Transfer an accurately weighed quantity of 15 mg of Nizatidine to a 50-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 4.6-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation*, and record the peak areas as directed for *Procedure:* the column efficiency is not less than 1500 theoretical plates; the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 1.5%.

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 areas for the major peaks. Calculate the quantity, in mg, of $C_{12}H_{21}N_5O_2S_2$ in the portion of Nizatidine taken by the formula:

$$50C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Nizatidine RS in the *Standard preparation;* and r_U and r_S are the peak areas 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
NIZATIDINE	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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