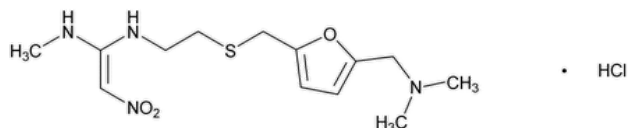


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Ranitidine Hydrochloride



$C_{13}H_{22}N_4O_3S \cdot HCl$ 350.86

1,1-Ethenediamine, *N*-[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-*N'*-methyl-2-nitro-, monohydrochloride.

N-[2-[[[5-[(Dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-*N'*-methyl-2-nitro-1,1-ethenediamine, hydrochloride CAS RN®: 66357-59-3; UNII: BK76465IHM.

» Ranitidine Hydrochloride contains not less than 97.5 percent and not more than 102.0 percent of $C_{13}H_{22}N_4O_3S \cdot HCl$, calculated on the dried basis.

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

USP REFERENCE STANDARDS (11).—

[USP Ranitidine Hydrochloride RS](#)

[USP Ranitidine Resolution Mixture RS](#)

It is a mixture of ranitidine hydrochloride and four related impurities: ranitidine-*N*-oxide, ranitidine complex nitroacetamide, ranitidine diamine hemifumarate, and ranitidine amino alcohol hemifumarate.

Ranitidine-N-oxide: *N,N*-dimethyl[5-[[[2-[[1-(methylamino)-2-nitroethenyl]amino]ethyl]sulphanyl]methyl]furan-2-yl]methanamine *N*-oxide.

Ranitidine complex nitroacetamide: *N*-[2-[[[5-[(dimethyl amino)methyl]furan-2-yl]methyl]sulphanyl]ethyl]-2-nitroacetamide.

Ranitidine diamine hemifumarate (related compound A): 5-[[[2-aminoethyl]thio]methyl]-*N,N*-dimethyl-2-furanmethanamine, hemifumarate salt.

Ranitidine amino alcohol hemifumarate: [5-[(dimethylamino)methyl]furan-2-yl]methanol.

Identification—

Change to read:

A: [▲Spectroscopic Identification Tests \(197\), Infrared Spectroscopy: 197M](#)▲ (CN 1-May-2020) .

Change to read:

B: [▲Spectroscopic Identification Tests \(197\), Ultraviolet-Visible Spectroscopy: 197U](#)▲ (CN 1-May-2020)

Solution: 10 µg per mL.

Medium: water.

Absorptivities at 229 nm and 315 nm, calculated on the dried basis, do not differ by more than 3.0%.

C: A solution of it meets the requirements of the tests for [Chloride \(191\)](#).

pH (791): between 4.5 and 6.0, in a solution (1 in 100).

Loss on Drying (731)—Dry it in vacuum at 60° for 3 hours: it loses not more than 0.75% of its weight.

Residue on Ignition (281): not more than 0.1%.

Chromatographic purity—

Diluent, Mobile phase, Resolution solution, and Chromatographic system—Proceed as directed in the Assay.

Standard solution—Prepare as directed for *Standard preparation* in the Assay.

Test solution—Prepare as directed for *Assay preparation* in the Assay.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and identify the ranitidine peak and the peaks due to impurities and degradation products listed in the table below.

Name	Relative Retention Time
Ranitidine simple nitroacetamide ¹	0.14
Ranitidine oxime ²	0.21
Ranitidine amino alcohol ³	0.45
Ranitidine diamine ⁴	0.57
Ranitidine S-oxide ⁵	0.64
Ranitidine N-oxide ⁶	0.72
Ranitidine complex nitroacetamide ⁷	0.84
Ranitidine formaldehyde adduct ⁸	1.36
Ranitidine bis-compound ⁹	1.75

¹ N-Methyl-2-nitroacetamide.

² 3-(Methylamino)-5,6-dihydro-2H-1,4-thiazin-2-one oxime.

³ {5-[(Dimethylamino)methyl]furan-2-yl}methanol.

⁴ 5-[(2-Aminoethyl)thio]methyl-N,N-dimethyl-2-furanmethanamine (ranitidine related compound A).

⁵ N-{2-[(5-[(Dimethylamino)methyl]-2-furanyl)methyl]sulfinyl}ethyl-N'-methyl-2-nitro-1,1-ethenediamine (ranitidine related compound C).

⁶ N,N-Dimethyl(5-[(2-[(1-(methylamino)-2-nitroethenyl]amino)ethyl)sulphonyl]methyl)furan-2-yl)methanamine N-oxide.

⁷ N-{2-[(5-[(Dimethylamino)methyl]furan-2-yl)methyl]sulphonyl}ethyl-2-nitroacetamide.

⁸ 2,2'-Methylenebis(N-{2-[(5-[(dimethylamino)methyl]furan-2-yl)methyl]sulphonyl}ethyl)-N'-methyl-2-nitroethene-1,1-diamine).

⁹ N,N'-bis{2-[(5-[(Dimethylamino)methyl]-2-furanyl)methyl]thio}ethyl-2-nitro-1,1-ethenediamine (ranitidine related compound B).

Measure the responses for the major peaks, and calculate the percentage of each impurity in the portion of Ranitidine Hydrochloride taken by the formula:

$$100CV/W(r_i/r_s)$$

in which C is the concentration, in mg per mL, of ranitidine hydrochloride in the *Standard solution*; V is the volume, in mL, of the *Test solution*; W is the weight, in mg, of Ranitidine Hydrochloride taken to prepare the *Test solution*; r_i is the peak response for each impurity obtained from the *Test solution*; and r_s is the ranitidine peak response obtained from the *Standard solution*: not more than 0.3% of ranitidine bis-compound is found, not more than 0.1% of any other single impurity is found, and not more than 0.5% of total impurities is found. The reporting level for impurities is 0.05%.

Assay—

Phosphate buffer—Place approximately 1900 mL of water in a 2.0-L volumetric flask, accurately add 6.8 mL of phosphoric acid, and mix. Accurately add 8.6 mL of 50% sodium hydroxide solution, and dilute with water to volume. If necessary, adjust with 50% sodium hydroxide solution or phosphoric acid to a pH of 7.1, and filter.

Solution A—Prepare a mixture of *Phosphate buffer* and acetonitrile (98:2).

Solution B—Prepare a mixture of *Phosphate buffer* and acetonitrile (78:22).

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 \(621\)](#)).

Diluent—Use *Solution A*.