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Ranitidine in Sodium Chloride Injection

» Ranitidine in Sodium Chloride Injection is a sterile solution of Ranitidine Hydrochloride and Sodium Chloride in Water for Injection. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of both ranitidine ($C_{13}H_{22}N_4O_3S$) and sodium chloride.

Packaging and storage—Preserve in glass containers, preferably of Type I or Type II glass, or in containers of suitable plastic, protected from light. Store at a temperature between 2° and 25°. Do not freeze.

USP Reference standards ⟨11⟩—
USP Ranitidine Hydrochloride RS
USP Ranitidine Related Compound A RS
5-[[(2-Aminoethyl)thio]methyl]-*N*,*N*-dimethyl-2-furanmethanamine, hemifumarate salt.
USP Ranitidine Related Compound C RS
N-{2-[({5-[(Dimethylamino)methyl]-2-furanyl}methyl)sulfinyl]ethyl}-*N*′-methyl-2-nitro-1,1-ethenediamine.

Identification—

A: The R_F value of the principal spot observed in the chromatogram of the *Test preparation* obtained as directed in the *Chromatographic purity* test corresponds to that obtained from the *Standard preparation*.

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: Meets the requirements of the tests for *Sodium ⟨191⟩* and for *Chloride ⟨191⟩*.

Bacterial Endotoxins Test ⟨85⟩—It contains not more than 7.0 USP Endotoxin Units per mg of ranitidine.

pH ⟨791⟩: between 6.7 and 7.3.

Chromatographic purity—

Test preparation—[Note—Apply a quantity of extractives from Injection to the chromatographic plate to achieve a nominal loading of 200 µg of ranitidine.] Transfer an accurately measured volume of Injection, equivalent to 10 mg of ranitidine, to a suitable flask, add about 5 times this volume of alcohol, and evaporate to dryness at a temperature not exceeding 30°. Redissolve the residue in 1.0 mL of a mixture of methanol and water (50:50).

Standard preparation—Dissolve USP Ranitidine Hydrochloride RS in a mixture of methanol and water (50:50) to obtain a *Standard preparation* having a known concentration of 672 µg (equivalent to 600 µg of ranitidine base) per mL. Dilute portions of this *Standard preparation* quantitatively, and stepwise if necessary, with the mixture of methanol and water (50:50) to obtain solutions having concentrations of 448 µg per mL (*Diluted standard preparation A*), 224 µg per mL (*Diluted standard preparation B*), 112 µg per mL (*Diluted standard preparation C*), 56 µg per mL (*Diluted standard preparation D*), and 11 µg per mL (*Diluted standard preparation E*), respectively.

Resolution preparation—Dissolve USP Ranitidine Related Compound A RS in methanol to obtain a solution having a known concentration of 1.27 mg per mL.

Procedure—Apply separately 10 µL of the *Standard preparation*, the *Diluted standard preparations* (*A*, *B*, *C*, *D*, and *E*) and 20 µL (superposition of 2 × 10 µL) of the *Test preparation* to a suitable thin-layer chromatographic plate (see *Chromatography ⟨621⟩*) coated with a 0.25-mm layer of chromatographic silica gel mixture. In addition, apply separately a further loading of 10 µL of the *Test preparation* to the same plate, and on top of this application, apply 10 µL of the *Resolution preparation*. Allow the spots to dry, and develop the chromatograms in a solvent system consisting of a mixture of ethyl acetate, isopropyl alcohol, ammonium hydroxide, and water (25:15:5:1) until the solvent front has moved not less than 15 cm from the origin. Remove the plate from the developing chamber, mark the solvent front, and allow to air-dry. Expose the plate to iodine vapors in a closed chamber until the chromatogram is fully revealed. Examine the plate and compare the intensities of any secondary spots observed in the chromatogram of the *Test preparation* with those of the principal spots in the chromatograms of the *Standard preparation* and *Diluted standard preparations* (*A*, *B*, *C*, *D*, and *E*): the system suitability requirements are met when there is complete resolution between the primary spots of the *Test preparation* and the *Resolution preparation* and if a spot is observed in the chromatogram of *Diluted standard preparation E*. The major secondary spot is not greater in size or in intensity than the principal spot produced by the *Standard preparation* (3.0%), and no other secondary spot is greater in size or intensity than the principal spot produced by *Diluted standard preparation A* (2.0%). The sum of the intensities of all secondary spots obtained from the *Test preparation* corresponds to not more than 6.0%.

Other requirements—It meets the requirements under *Injections and Implanted Drug Products ⟨1⟩*.

Assay for ranitidine—

Mobile phase, Standard preparation, System suitability solution, and *Chromatographic system*—Prepare as directed in the *Assay* under *Ranitidine Injection.*

Assay preparation—Dilute an accurately measured volume of Injection, quantitatively and stepwise if necessary, with *Mobile phase* to obtain a solution having a concentration of 0.1 mg of ranitidine per mL.

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 area responses for the major peaks. Calculate the quantity, in mg, of $C_{13}H_{22}N_4O_3S$ in the portion of Injection taken by the formula:

$$(314.40/350.87)(L/D)(C)(r_U/r_S)$$

in which 314.40 and 350.87 are the molecular weights of ranitidine and ranitidine hydrochloride, respectively; *L* is the labeled quantity of ranitidine in the Injection taken; *D* is the concentration, in mg per mL, of ranitidine in the *Assay preparation*, on the basis of the labeled quantity and the extent of dilution; *C* is the concentration, in mg per mL, of USP Ranitidine Hydrochloride RS in the *Standard preparation* and r_U and r_S are the peak area responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Assay for sodium chloride—Dilute an accurately measured volume of Injection, quantitatively and stepwise if necessary, with water to obtain a suitable volume of a solution having a concentration of about 0.5 mg of sodium chloride per mL. Titrate with 0.1 N silver nitrate VS using a silver-silver chloride electrode. Each mL of 0.1 N silver nitrate is equivalent to 3.545 mg of chloride. From the determined concentration per mL, subtract the quantity (35.453/314.40)*W* so as to correct for the chloride present as ranitidine hydrochloride where *W* is the quantity, in mg per mL, of ranitidine as determined in the *Assay for ranitidine*. Multiplication of the answer by 1.648 gives the amount of sodium chloride per mL.

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

Topic/Question	Contact	Expert Committee
RANITIDINE IN SODIUM CHLORIDE INJECTION	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

Most Recently Appeared In:
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