

Ranitidine Injection

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

Packaging and storage—Preserve in single-dose or in multiple-dose containers of Type I glass, protected from light. Store below 30°. Do not freeze.

Labeling—Label Injection to state both the content of the active moiety and the content of the salt used in formulating the article.

USP Reference standards (11)—*USP Ranitidine Hydrochloride RS*. *USP Ranitidine Related Compound A RS*. *USP Ranitidine Related Compound C RS*.

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*.

Bacterial endotoxins (85)—It contains not more than 7.00 USP Endotoxin Units per mg of ranitidine.

pH (791): between 6.7 and 7.3.

Particulate matter (788): meets the requirements under small-volume injections.

Chromatographic purity—

Test preparation—Dilute Injection quantitatively with water, if necessary, to obtain a solution containing 25 mg of ranitidine per mL. [NOTE—Use Injection of lower concentration without dilution as directed under *Procedure*.]

Standard preparation—Dissolve USP Ranitidine Hydrochloride RS in water to obtain a solution having a known concentration of 560 µg per mL. Dilute portions of this *Standard preparation* quantitatively with water to obtain solutions having concentrations of 280 µg per mL (*Diluted standard preparation A*), 140 µg per mL (*Diluted standard preparation B*), 84 µg per mL (*Diluted standard preparation C*), 28 µg per mL (*Diluted standard preparation D*), and 14 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*, *Diluted standard preparations A, B, C, D* and *E*, and the required volume of the *Test preparation*, equivalent to 250 µg of ranitidine, 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 the same volume 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 intensity than the principal spot produced by the *Standard preparation* (2.0%), and no other secondary spot is greater in size or intensity than the principal

spot produced by *Diluted standard preparation A* (1.0%). The sum of the intensities of all secondary spots obtained from the *Test preparation*, corresponds to not more than 5.0%.

Other requirements—It meets the requirements under *Injections* (1).

Assay—

Mobile phase—Prepare a filtered and degassed mixture of methanol and 0.1M aqueous ammonium acetate (85:15). Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

Standard preparation—Dissolve an accurately weighed quantity of USP Ranitidine Hydrochloride RS in *Mobile phase* to obtain a solution having a known concentration of about 0.112 mg (equivalent to 0.100 mg of ranitidine base) per mL.

System suitability solution—Dissolve accurately weighed quantities of USP Ranitidine Hydrochloride RS and USP Ranitidine Related Compound C RS in *Mobile phase* to obtain a solution having known concentrations of about 0.112 mg per mL and 0.01 mg per mL, respectively.

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.

Chromatographic system (see *Chromatography* (621))—The liquid chromatograph is equipped with a 322-nm detector and a 4.6-mm × 20- to 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure*: the resolution, R , between ranitidine hydrochloride and *N*-[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]sulfinyl]ethyl]-*N*-methyl-2-nitro-1,1-ethenediamine (ranitidine related compound C) is not less than 1.5. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the tailing factor for the ranitidine hydrochloride peak is not more than 2.0; the column efficiency determined from the ranitidine hydrochloride peak is not less than 700 theoretical plates; and the relative standard deviation for replicate injections is not more than 2%.

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.