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Ranitidine Injection

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-ranitidine-inj-20230331.

DEFINITION

Ranitidine Injection is a sterile solution of Ranitidine Hydrochloride in Water for Injection. It contains the equivalent of NLT 90.0% and NMT 110.0% of the labeled amount of ranitidine ($C_{13}H_{22}N_4O_3S$).

IDENTIFICATION

- **A.** The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in *Organic Impurities*.
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Buffer: 0.1 M ammonium acetate in water

Mobile phase: Methanol and *Buffer* (85:15)

System suitability solution: 0.112 mg/mL of USP Ranitidine Hydrochloride RS and 0.01 mg/mL of USP Ranitidine Related Compound C RS in *Mobile phase*

Standard solution: 0.112 mg/mL of USP Ranitidine Hydrochloride RS in *Mobile phase* (equivalent to 0.100 mg/mL of ranitidine)

Sample solution: Nominally 0.1 mg/mL of ranitidine from Injection in *Mobile phase*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 322 nm

Column: 4.6-mm × 20- to 30-cm; packing L1

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 1.5 between ranitidine and ranitidine related compound C, *System suitability solution*

Column efficiency: NLT 700 theoretical plates, *Standard solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 2%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ranitidine ($C_{13}H_{22}N_4O_3S$) in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of ranitidine from the *Sample solution*

r_S = peak response of ranitidine from the *Standard solution*

C_S = concentration of USP Ranitidine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of ranitidine in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of ranitidine, 314.40

M_{r2} = molecular weight of ranitidine hydrochloride, 350.87

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Organic Impurities**

System suitability solution: 1.27 mg/mL of USP Ranitidine Related Compound A RS in methanol

Standard solution A: 560 µg/mL of USP Ranitidine Hydrochloride RS in water

Standard solution B: 280 µg/mL of USP Ranitidine Hydrochloride RS from *Standard solution A* in water

Standard solution C: 140 µg/mL of USP Ranitidine Hydrochloride RS from *Standard solution A* in water

Standard solution D: 84 µg/mL of USP Ranitidine Hydrochloride RS from *Standard solution A* in water

Standard solution E: 28 µg/mL of USP Ranitidine Hydrochloride RS from *Standard solution A* in water

Standard solution F: 14 µg/mL of USP Ranitidine Hydrochloride RS from *Standard solution A* in water

Sample solution: Nominally 25 mg/mL of ranitidine from Injection in water

[Note—Use Injection of lower concentration without dilution as directed for *Application volume*.]

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

For the *Sample solution*, use a volume equivalent to 250 µg of ranitidine.

Developing solvent system: Ethyl acetate, isopropyl alcohol, ammonium hydroxide, and water (25:15:5:1)

Visualization: Iodine vapors

System suitability

Samples: Apply a volume of *Sample solution* equivalent to 250 µg of ranitidine. On top of this application, apply 10 µL of the *System suitability solution*.

Suitability requirements: Complete resolution between the primary spots of the combined *Sample solution* and *System suitability solution*; a spot is observed for *Standard solution F* in the *Analysis*.

Analysis

Samples: *Standard solutions A*, *B*, *C*, *D*, *E*, and *F*, and *Sample solution*

[Note—*System suitability sample* should also appear on this plate.]

Allow the spots to dry, and develop the chromatograms until the solvent front has moved NLT 15 cm from the origin. Remove the plate from the chamber, mark the solvent front, and air-dry. Expose the plate to iodine vapor in a closed chamber until the chromatogram is fully revealed. Examine the plate, and compare the intensities of any secondary spots from the *Sample solution* with those of the principal spots from *Standard solutions A, B, C, D, E,* and *F*.

Acceptance criteria: No secondary spot of the *Sample solution* is larger or more intense than the principal spot of *Standard solution A* (2.0%), and no other secondary spot is larger or more intense than the principal spot of *Standard solution B* (1.0%). The sum of the intensities of all secondary spots from the *Sample solution* corresponds to NMT 5.0%.

SPECIFIC TESTS

• **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections

• **Bacterial Endotoxins Test ⟨85⟩:** Contains NMT 7.00 USP Endotoxin Units/mg of ranitidine.

• **pH ⟨791⟩:** 6.7–7.3

• **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers▲, preferably▲ (RB 1-Apr-2023) of Type I glass. Store below 30°, protected from light. 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

5-{[(2-Aminoethyl)thio]methyl}-*N*,*N*-dimethyl-2-furanmethanamine, hemifumarate salt.

$C_{10}H_{18}N_2OS \cdot ½\ C_4H_4O_4$ 272.36

USP Ranitidine Related Compound C RS

N-{2-[({5-[(Dimethylamino)methyl]-2-furanyl}methyl)sulfinyl]ethyl}-*N*′-methyl-2-nitro-1,1-ethenediamine.

$C_{13}H_{22}N_4O_4S$ 330.40

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

Topic/Question	Contact	Expert Committee
RANITIDINE 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

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