Edition: BP 2025 (Ph. Eur. 11.6 update)

Ranitidine Injection

General Notices

Action and use

Histamine H_2 receptor antagonist; treatment of peptic ulcer disease.

DEFINITION

Ranitidine Injection is a sterile solution of Ranitidine Hydrochloride in Water for Injections.

The injection complies with the requirements stated under Parenteral Preparations and with the following requirements.

Content of ranitidine, $C_{13}H_{22}N_4O_3S$

92.5 to 105.0% of the stated amount.

IDENTIFICATION

A. To a volume of the injection containing the equivalent of 25 mg of ranitidine add 20 mL of *methanol*, mix and evaporate to dryness. Add 1 mL of *petroleum spirit* (*boiling range, 60° to 80°*) to the resulting residue, scratch the side of the vessel with a glass rod to induce crystallisation, evaporate to dryness and dry the residue at 60° for 10 minutes. The *infrared absorption spectrum* of the dried residue, Appendix II A, is concordant with the *reference spectrum* of ranitidine hydrochloride (*RS 311*).
B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is the same as that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Acidity or alkalinity

Buffered formulations, pH 6.7 to 7.3; unbuffered formulations, pH 4.5 to 7.0, Appendix V L.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dilute, if necessary, a volume of the injection with *water* to contain the equivalent of 0.1% w/v of ranitidine.
(2) Dilute 1 volume of solution (1) to 50 volumes with *water*.
(3) Dilute 1 volume of solution (1) to 100 volumes with *water*.
(4) Dilute 1 volume of solution (1) to 200 volumes with *water*.
(5) Dilute 1 volume of solution (3) to 5 volumes with *water*.
(6) Dissolve the contents of a vial of *ranitidine impurity J EPCRS* in 1 mL of solution (1).

CHROMATOGRAPHIC CONDITIONS

(a) A stainless steel column (10 cm × 4.6 mm) packed with *octadecylsilyl amorphous organosilica polymer* (3.5 µm) (Waters XTerra MS C18 is suitable).
(b) Gradient elution using the mobile phase described below.
(c) Flow rate of 1.5 mL per minute.
(d) Column temperature of 35°.
(e) Detection wavelength of 230 nm.
(f) Injection volume of 20 µL for each solution.

MOBILE PHASE

Buffer solution Adjust the pH of 950 mL of 0.05M potassium dihydrogen orthophosphate to 7.1 by adding strong sodium hydroxide solution and dilute to 1 litre.

Mobile phase A 2 volumes of *acetonitrile* and 98 volumes of buffer solution.

Mobile phase B 22 volumes of *acetonitrile* and 78 volumes of buffer solution.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-10	100 → 0	0 → 100	linear gradient
10-15	0	100	isocratic
15-16	0 → 100	100 → 0	linear gradient
16-20	100	0	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (6), the *resolution* between the two principal peaks is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (2%);

the area of not more than one *secondary peak* is greater than the area of the principal peak in the chromatogram obtained with solution (3) (1%);

the area of not more than two other *secondary peaks* is greater than the area of the principal peak in the chromatogram obtained with solution (4) (0.5%);

the area of not more than two further *secondary peaks* is greater than the principal peak in solution (5) (0.2%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dilute a volume of the injection with sufficient of the mobile phase to contain the equivalent of 0.01% w/v of ranitidine.
(2) 0.0112% w/v of *ranitidine hydrochloride BPCRS* in mobile phase.
(3) 0.0112% w/v of *ranitidine hydrochloride BPCRS* and 0.0002% w/v of *dimethyl{5-[2-(1-methylamino-2-nitrovinylamino)ethylsulfinylmethyl]furfuryl}amine BPCRS* in mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) A stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Partisil ODS 1 is suitable).
(b) Isocratic elution using the mobile phase described below.
(c) Flow rate of 2 mL per minute.
(d) Ambient column temperature.

(e) Detection wavelength of 322 nm.

(f) Injection volume of 20 µL for each solution.

MOBILE PHASE

15 volumes of 0.1M *ammonium acetate* and 85 volumes of *methanol*.

SYSTEM SUITABILITY

The assay is not valid unless the peak due to ranitidine in the chromatogram obtained with solution (3) shows baseline separation from the peak due to dimethyl{5-[2-(1-methylamino-2-nitrovinylamino)ethylsulfinylmethyl] furfuryl}amine.

DETERMINATION OF CONTENT

Calculate the content of $C_{13}H_{22}N_4O_3S$ in the injection using the declared content of $C_{13}H_{22}N_4O_3S$ in *ranitidine hydrochloride BPCRS*.

STORAGE

Ranitidine Injection should be protected from light.

LABELLING

The label states (1) the quantity of active ingredient in terms of the equivalent amount of ranitidine; (2) where appropriate, that the injection is buffered.