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

Ranitidine Tablets

General Notices

Action and use

Histamine H_2 receptor antagonist; treatment of peptic ulcer disease.

DEFINITION

Ranitidine Tablets contain Ranitidine Hydrochloride. They are coated.

The tablets comply with the requirements stated under Tablets and with the following requirements.

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

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing the equivalent of 25 mg of ranitidine with 5 mL of *methanol* for 5 minutes, filter and evaporate the filtrate to dryness. Add 1 mL of *petroleum spirit* (*boiling range, 60° to 80°*) to the residue, scratch the side of the vessel 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*).

TESTS

Dissolution

Comply with the requirements for Monographs of the British Pharmacopoeia in the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of *water*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a sample of the medium and filter. Dilute the filtrate, if necessary, with dissolution medium to produce a solution containing the equivalent of 0.0083% w/v of ranitidine. Measure the *absorbance*, Appendix II B, at the maximum at 314 nm using *water* in the reference cell.
(2) 0.0093% w/v of *ranitidine hydrochloride BPCRS*. Measure the *absorbance*, Appendix II B, at the maximum at 314 nm using *water* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of $C_{13}H_{22}N_4O_3S$ in the medium from the absorbances obtained and using the declared content of $C_{13}H_{22}N_4O_3S$ in *ranitidine hydrochloride BPCRS*.

Related substances

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

(1) Shake a quantity of powdered tablets containing the equivalent of 0.13 g of ranitidine with 100 mL *water* and filter (Whatman No. 42. paper is suitable).
(2) Dilute 1 volume of solution (1) to 50 volumes with *water*. Dilute 1 volume to 10 volumes with *water*.
(3) 0.0065% w/v of *ranitidine for impurity A identification EPCRS* in mobile phase A.
(4) Dissolve the contents of a vial of *ranitidine impurity J EPCRS* in 1 mL of solution (1).

CHROMATOGRAPHIC CONDITIONS

(a) Use 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) Use gradient elution using the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 35°.
(e) Use a detection wavelength of 230 nm.
(f) Inject 20 µL of 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 the buffer solution.

Mobile phase B

22 volumes of *acetonitrile* and 78 volumes of the 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

When the chromatograms are recorded under the prescribed conditions the retention times relative to ranitidine (retention time about 7 minutes) are; impurity H, about 0.1; impurity D, about 0.8; impurity J, about 0.9 and impurity A, about 1.7.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the impurity J and ranitidine is at least 1.5.

LIMITS

Identify any peak due to impurity A and impurity J in the chromatogram obtained with solution (1), using the chromatogram obtained with solutions (3) and (4) respectively. Multiply the area of the peak due to impurity J by a correction factor of 2.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any *secondary peaks* is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak with an area less than half the area of the principal peak in solution (2) (0.1%).

ASSAY

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

(1) Shake 10 tablets with 400 mL of the mobile phase until the tablets have completely disintegrated (about 15 minutes), dilute to 500 mL with the mobile phase, filter (Whatman GF/C paper is suitable) and dilute the filtrate with the mobile phase to produce a solution containing the equivalent of 0.01% w/v of ranitidine.
(2) 0.011% w/v of *ranitidine hydrochloride BPCRS* in the mobile phase.
(3) 0.011% w/v of *ranitidine hydrochloride BPCRS* and 0.0002% w/v of *dimethyl{5-[2-(1-methylamino-2-nitrovinylamino)ethylsulfinylmethyl]furfuryl}amine BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Partisil ODS 1 is suitable).
(b) Use isocratic elution using the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use ambient column temperature.
(e) Use a detection wavelength of 322 nm.
(f) Inject 20 µL of 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 tablets using the declared content of $C_{13}H_{22}N_4O_3S$ in *ranitidine hydrochloride BPCRS*.

STORAGE

Ranitidine Tablets should be protected from light.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of ranitidine.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Ranitidine Hydrochloride.