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

Nizatidine Infusion

General Notices

Nizatidine Intravenous Infusion

Action and use

Histamine H_2 receptor antagonist; treatment of peptic ulcer.

DEFINITION

Nizatidine Infusion is a sterile solution containing Nizatidine. It is prepared by diluting Nizatidine Sterile Concentrate with a suitable diluent in accordance with the manufacturer's instructions.

The infusion complies with the requirements stated under Parenteral Preparations.

NIZATIDINE STERILE CONCENTRATE

DEFINITION

Nizatidine Sterile Concentrate is a sterile solution of Nizatidine in Water for Injections.

The concentrate complies with the requirements for Concentrates for Injections or Infusions stated under Parenteral Preparations and with the following requirements.

Content of nizatidine, $C_{12}H_{21}N_5O_2S_2$

95.0 to 105.0% of the stated amount.

CHARACTERISTICS

A clear, colourless to yellow solution that darkens on storage.

IDENTIFICATION

Shake a volume of the concentrate containing 50 mg of Nizatidine with 10 mL of *dichloromethane* for 5 minutes. Filter the *dichloromethane* layer through *anhydrous sodium sulfate* and evaporate the filtrate to dryness on a rotary evaporator at 40°. Cool the residue in a refrigerator for 15 hours and, if necessary, induce crystallisation by scratching the wall of the container with a glass rod. The *infrared absorption spectrum* of the dried residue, Appendix II A, is concordant with the *reference spectrum* of nizatidine (*RS 410*).

TESTS

Acidity or alkalinity

pH of the concentrate diluted with *water* to contain 1.0% w/v of Nizatidine, 6.0 to 8.0, Appendix V L.

Colour of solution

Dilute the concentrate with *water* to produce a solution containing 1.0% w/v of Nizatidine. The *absorbance* of the solution at 410 nm, Appendix II B, is not more than 0.40 determined using water in the reference cell.

Related substances

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

(1) Dilute the concentrate with mobile phase A to produce a solution containing 0.5% w/v of Nizatidine.
(2) Dilute 1 volume of solution (1) to 100 volumes with mobile phase A.
(3) 0.005% w/v of *nizatidine EPCRS* and 0.005% w/v of *nizatidine impurity F EPCRS* in mobile phase A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Supelco LC-18-DB and Kromasil C18 are suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.

Mobile phase A Dissolve 5.9 g of *ammonium acetate* in 760 mL of *water*, add 1 mL of *diethylamine* and adjust the pH to 7.5 with 6M *acetic acid* (solution A). Prepare a mixture of 24 volumes of *methanol* and 76 volumes of solution A.

Mobile phase B 50 volumes of *methanol* and 50 volumes of solution A.

Time (minutes)	Mobile phase A % v/v	Mobile phase B % v/v
0 – 3	100	0
3 – 20	100 → 0	0 → 100
20 – 45	0	100

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the retention time of Nizatidine is between 10 and 20 minutes and the *symmetry factor* of the peak due to Nizatidine is not greater than 2.0.

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the peak due to Nizatidine (first peak) and Nizatidine impurity F (second peak) is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak with a relative retention time of about 0.7 (impurity E) is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (2%);

the area of any peak corresponding to impurity F is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (1%);

the area of any other *secondary peak* is not greater than 0.3 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

the sum of the areas of all the *secondary peaks* is not greater than 3.5 times the area of the principal peak in the chromatogram obtained with solution (2) (3.5%).

Disregard any peak with an area less than 0.05 times the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY

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

(1) Dilute the concentrate with mobile phase A to produce a solution containing 0.03% w/v of Nizatidine.
(2) 0.03% w/v solution of *nizatidine EPCRS* in mobile phase A.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *symmetry factor* of the peak due to Nizatidine is not greater than 2.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{12}H_{21}N_5O_2S_2$ in the concentrate using the declared content of $C_{12}H_{21}N_5O_2S_2$ in *nizatidine EPCRS*.

STORAGE

Nizatidine Sterile Concentrate should be protected from light.