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

Norfloxacin Tablets

General Notices

Action and use

Fluoroquinolone antibacterial.

DEFINITION

Norfloxacin Tablets contain Norfloxacin.

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

Content of norfloxacin, $C_{16}H_{18}FN_3O_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions, protected from light.
(1) Add 2 mL of *water* to a quantity of whole tablets containing 0.4 g of Norfloxacin and disperse with the aid of ultrasound. Add 100 mL of a solution containing 50 volumes of *dichloromethane* and 50 volumes of a solution prepared by adding 9 mL of *hydrochloric acid* to 1000 mL of *methanol*. Mix with the aid of ultrasound until a uniform suspension is produced, add sufficient of the same solvent mixture to produce 200 mL and centrifuge 25 mL of the final solution.
(2) Dissolve, with the aid of ultrasound, 50 mg of *norfloxacin BPCRS* in 15 mL of a solution containing 50 volumes of *dichloromethane* and 50 volumes of a solution prepared by adding 9 mL of *hydrochloric acid* to 1000 mL of *methanol*; add sufficient of the same solvent mixture to produce 25 mL.

CHROMATOGRAPHIC CONDITIONS

(a) Use a *silica gel GF_{254}* precoated plate (Analtech plates are suitable) which has been previously washed with *methanol* and allowed to dry in air.
(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow it to dry in air and examine under *ultraviolet light* (*254 nm* and *365 nm*).

MOBILE PHASE

8 volumes of *water*, 14 volumes of *diethylamine*, 20 volumes of *toluene*, 40 volumes of *dichloromethane* and 40 volumes of *methanol*.

CONFIRMATION

By each method of visualisation, the principal spot in the chromatogram obtained with solution (1) corresponds in position and size to that in the chromatogram obtained with solution (2).

B. In the Assay, the principal peak in the chromatogram obtained with solution (1) has the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1. Carry out the procedure protected from light.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 750 mL of an acetate buffer solution prepared in the following manner, at a temperature of 37°, as the medium. Add 14.3 mL of *glacial acetic acid* to 4500 mL of *water* and mix. Add slowly, with stirring, 2.5 mL of a 50% w/v solution of *sodium hydroxide* and add sufficient *water* to produce 5000 mL. If necessary, adjust the pH to 4.0 with *glacial acetic acid* or a 50% w/v solution of *sodium hydroxide*.

PROCEDURE

(1) After 30 minutes withdraw a sample of the medium, filter and dilute the filtrate with sufficient of the dissolution medium to give a solution expected to contain about 0.0016% w/v of Norfloxacin. Measure the *absorbance* of this solution, Appendix II B, at 313 nm using dissolution medium in the reference cell.
(2) Measure the *absorbance* of a 0.0016% w/v solution of *norfloxacin BPCRS* in the dissolution medium using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of norfloxacin, $C_{16}H_{18}FN_3O_3$, in the medium from the *absorbances* obtained and using the declared content of $C_{16}H_{18}FN_3O_3$ in *norfloxacin BPCRS*.

LIMITS

The amount of norfloxacin released is not less than 80% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions, in 5 volumes of *acetonitrile* and 95 volumes of *water* previously adjusted to pH 2.0 with *orthophosphoric acid*.

(1) Disperse a quantity of powdered tablets containing 0.2 g of Norfloxacin in 250 mL, sonicate and dilute to 500 mL.
(2) Dilute 1 volume of solution (1) to 100 volumes. Further dilute 1 volume of this solution to 10 volumes.
(3) 0.04% w/v of *norfloxacin for system suitability EPCRS*.
(4) 0.04% w/v of *norfloxacin for peak identification EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped amidohexadecylsilyl silica gel for chromatography* (5 µm) (Supelcosil LC-ABZ is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.4 mL per minute.
(d) Use a column temperature of 60°.
(e) Use a detection wavelength of 265 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A *water* adjusted to pH 2.0 with *orthophosphoric acid*.

Mobile phase B *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-5	95	5	isocratic
5-7	95→93	5→7	linear gradient

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
7-10	93→87	7→13	linear gradient
10-15	87→47	13→53	linear gradient
15-20	47→10	53→90	linear gradient
20-22	10	90	isocratic
22-23	10→95	90→5	linear gradient
23-26	95	5	re-equilibration

Use the chromatogram supplied with *norfloxacin for system suitability EPCRS* and the chromatogram obtained with reference solution (3) to identify the peaks due to impurities A, E and H. Use the chromatogram supplied with *norfloxacin for peak identification EPCRS* and the chromatogram obtained with reference solution (4) to identify the peak due to impurity K.

When the chromatograms are recorded under the prescribed conditions the retentions relative to norfloxacin (retention time, about 11 minutes) are: Impurity K, about 0.6; Impurity E, about 0.97; impurity A, about 1.5; impurity H, about 1.6.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3):

the *resolution* between the peaks due to impurity A and impurity H is at least 3.0;

the *peak-to-valley ratio* is at least 5.0, where *Hp* is the height above the baseline of the peak due to impurity E and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to norfloxacin.

LIMITS

In the chromatogram obtained with solution (1):

the areas of any peaks corresponding to impurities E or K are not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.15% each);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.1%);

the sum of the areas of all the *secondary peaks* is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

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

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, protected from light, using the following solutions.

(1) Add 80 mL of the mobile phase to a quantity of the powdered tablets containing 0.1 g of Norfloxacin and mix with the aid of ultrasound for at least 5 minutes. Add sufficient of the mobile phase to produce 200 mL, mix and dilute 10 volumes of this solution to 25 volumes with the mobile phase.
(2) 0.02% w/v of *norfloxacin BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (30 cm × 3.9 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (10 µm) (Waters µBondapak C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 275 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

150 volumes of *acetonitrile* and 850 volumes of 0.1% v/v *orthophosphoric acid*.

Precondition the column using 0.01M *anhydrous sodium dihydrogen orthophosphate*, adjusted to pH 4.0 with *orthophosphoric acid*, at a flow rate of 0.5 mL per minute for 8 hours. Equilibrate the column with the mobile phase for about 30 minutes before starting the chromatography.

When the chromatograms are recorded under the prescribed conditions, the retention time of norfloxacin is about 5 minutes.

SYSTEM SUITABILITY

The Assay is not valid unless the *symmetry factor* of the principal peak in the chromatogram obtained with solution (2) is less than 2.0.

Inject solution (2) six times. The Assay is not valid unless the relative standard deviation of the area of the principal peak is at most 2.0%.

DETERMINATION OF CONTENT

Calculate the content of $C_{16}H_{18}FN_3O_3$ in the tablets using the declared content of $C_{16}H_{18}FN_3O_3$ in *norfloxacin BPCRS*.

STORAGE

Norfloxacin Tablets should be protected from light and moisture.