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Ofloxacin Eye Drops

Details for the public consultation of this monograph are as follows:

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Action and use

Fluoroquinolone antibacterial

DEFINITION

Ofloxacin Eye Drops are a sterile solution of Ofloxacin in a suitable vehicle.

The eye drops comply with the requirements stated under Eye Preparations and with the following requirements.

Content of ofloxacin, $C_{18}H_{20}FN_3O_4$

93.0 to 107.0% of the stated amount.

IDENTIFICATION

Shake a volume of the eye drops containing 0.1g Ofloxacin with an equal volume of *dichloromethane*. Evaporate the bottom layer to dryness. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the reference spectrum of Ofloxacin *(RS XXX)*.

TESTS

Acidity

pH of a 3 mg/ml solution, 6.0 to 6.7, Appendix V L.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 14 volumes of *acetonitrile* and 86 volumes of solution A as the diluent.

Solution A: 3.08 g/L of *ammonium acetate* and 5.38 g/L of *sodium perchlorate*, adjusted to pH 2.2 using orthophosphoric acid.

(1) Dilute a suitable volume of the eye drops with the diluent to form a solution containing 0.04% w/v Ofloxacin.

(2) Dilute 1 volume of solution (1) to 200 volumes.

(3) 0.00008% w/v each of *ofloxacin impurity D EPCRS* and *ofloxacin impurity E EPCRS* and 0.0002% w/v of *ofloxacin BPCRS*.

(4) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (3 µm) (YMC Pack Pro C18 is suitable).

(b) Use gradient elution and the mobile phase described below.

(c) Use a flow rate of 1.0 mL per minute.

(d) Use a column temperature of 38°.

(e) Use a detection wavelength of 294 nm.

(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 16 volumes of *acetonitrile* and 84 volumes of solution A.

Mobile phase B 20 volumes of *methanol*, 30 volumes of *acetonitrile* and 50 volumes of solution A..

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-5	100	0	isocratic
5-10	100→82	0→18	linear gradient
10-15	82→40	18→60	linear gradient
15-30	40	60	isocractic
30-32	40→100	60→100	linear gradient
32-40	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retention(s) with reference to Ofloxacin (retention time about 10 minutes) are: impurity D, about 0.7; impurity E, about 0.9 and impurity A, about 2.8.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (3), the *resolution* between impurity E and ofloxacin is at least 2.0 and;

in the chromatogram obtained with solution (4), the signal-to-noise ratio of the peak due to ofloxacin is not less than 45.

LIMITS

Identify any peak corresponding to impurity D in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3), and multiply the area of this peak by a correction factor of 4.5.

In the chromatogram obtained with solution (1):

the area of no more than 1 *secondary peak* is not greater than 1.6 times the area of the principal peak in the chromatogram obtained with solution (2) (0.8%);

the area of any peak corresponding to impurity D is not greater than twice the area of the principal peak in the chromatogram obtained with solution (4) (0.2%);

the area of any other *secondary peak* is not greater than twice the area of the principal peak in the chromatogram obtained with solution (4) (0.2%);

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

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

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

(1) Dilute a suitable volume of the eye drops to produce a solution containing 0.001% w/v Ofloxacin.
(2) 0.001% w/v of *Ofloxacin BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (3.5 µm) (Symmetry C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 294 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

10 volumes of *acetonitrile* and 90 volumes of a solution containing 27.2 g/L of *potassium dihydrogen phosphate*, previously adjusted to pH 3.3 with orthophosphoric acid.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *symmetry factor* of the principal peak is not less than 0.8 and not greater than 2.0.

DETERMINATION OF CONTENT

Calculate the content of Ofloxacin, $C_{18}H_{20}FN_3O_4$, in the eye drops from the chromatograms obtained and using the declared content of $C_{18}H_{20}FN_3O_4$, in *Ofloxacin BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurity D listed under *Ofloxacin*.