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Levofloxacin Tablets

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

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Notes:	**New monograph** If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.

Action and use

Fluoroquinolone Antibacterial

DEFINITION

Levofloxacin Tablets contain Levofloxacin Hemihydrate.

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

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

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Dissolve an amount of powdered tablets containing 0.3g of Levofloxacin in dichloromethane. Wash with 2 x 10 mL of water and filter (GF/C filter is suitable). The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the reference spectrum of Levofloxacin. *(RS XXX)*

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 100 revolutions per minute.

(b) Use 900 mL of 0.01M hydrochloric acid, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 30 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium, if necessary, to produce a solution containing of 0.005% w/v of Levofloxacin, at the maximum at 293nm, Appendix II B, using dissolution medium in the reference cell.

(2) Measure the *absorbance* of a 0.005% w/v solution of *levofloxacin BPCRS* in the dissolution medium using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of Levofloxacin, $C_{18}H_{20}FN_3O_4$, in the medium from the absorbances obtained and using the declared content of $C_{18}H_{20}FN_3O_4$, in *levofloxacin BPCRS*.

LIMITS

The amount of Levofloxacin released is not less than 75% (Q) of the stated amount.

Related substances

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

Solution A: 20% v/v *acetonitrile*.

(1) Mix a quantity of the powdered tablets containing 0.5 g of Levofloxacin with 75 mL of solution A. Dilute to produce 100 mL and filter (0.45-µm pore size is suitable). Dilute 1 volume to 25 volumes with the mobile phase.

(2) 0.2% w/v of *levofloxacin BPCRS* in solution A, dissolved with the aid of ultrasound if necessary. Dilute 1 volume to 10 volumes with the mobile phase.

(3) 0.0001% w/v of *levofloxacin impurity B BPCRS* in mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Inertsil ODS is suitable).

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

(c) Use a flow rate of 0.8 mL per minute.

(d) Use a column temperature of 45°.

(e) Use a detection wavelength of 360 nm.

(f) Inject 25 µL of each solution.

(g) Allow the chromatography to proceed for twice the retention time of levofloxacin.

MOBILE PHASE

0.0874% w/v cupric sulfate, 0.0918% w/v L-isoleucineand 0.594% w/v *ammonium acetate* in a mixture containing 3 volumes of *methanol* and 7 volumes of *water*.

SYSTEM SUITABILITY

For system suitability, use solution (2):

the *symmetry factor* is not more than 1.8.

CALCULATION OF IMPURITIES

For each unspecified impurity, use the concentration of levofloxacin in solution (1).

For the reporting threshold, use the concentration of levofloxacin in solution (1).

Levofloxacin retention time: about [X] minutes.

Relative retention: impurity E (decarboxy), about 0.38; impurity B, about 0.47; impurity 1 (diamine derivative), about 0.52; impurity C (N-oxide), about 0.63; and impurity A (dextro-), about 1.23.

LIMITS

Identify any peaks corresponding to impurities 1 and E in the chromatogram obtained with solution (1), and multiply the areas of these peaks by the corresponding correction factors: impurity 1, 1.2; impurity E, 1.6.

— impurity A: not more than 0.5%;

— unspecified impurities: for each impurity, not more than 0.2%;

— total impurities: not more than 1.0%;

— reporting threshold: 0.1%.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Prepare solution A as described under Related Substances.

(1) Disperse a quantity of the whole tablets containing 2.5 g of Levofloxacin in 375 mL of solution A. Dilute to produce 500 mL and filter (0.45-µm pore size is suitable). Dilute 1 volume to 25 volumes with the mobile phase.
(2) 0.2% w/v of *levofloxacin BPCRS* in solution A, dissolved with the aid of ultrasound if necessary. Dilute 1 volume to 10 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

DETERMINATION OF CONTENT

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

LABELLING

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

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B, C and E listed under *Levofloxacin Hemihydrate* and:

 1. (S)-9-Fluoro-2,3-dihydro-3-methyl-10-[2-(methylamino)ethylamino]-7-oxo-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid (diamine derivative)

1. (S)-9-Fluoro-2,3-dihydro-3-methyl-10-[2-(methylamino)ethylamino]-7-oxo-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid (diamine derivative)