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Levofloxacin Infusion

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 Infusion is a sterile solution of Levofloxacin in a suitable vehicle.

The infusion complies with the requirements stated under Parenteral Preparations 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. Shake a volume of the infusion containing 0.1g Levofloxacin 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 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).

IDENTIFICATION

TESTS

Acidity

pH of the infusion, 3.3 to 5.3, Appendix V L.

Related substances

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

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

(1) Shake a volume of the infusion containing 0.1 g of Levofloxacin with 15 mL of solution A. Dilute to produce 20 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 0.8%;

— 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) Shake a volume of the infusion 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.

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 solution for infusion 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)