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Ciprofloxacin Ear Drops

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

Ciprofloxacin Ear Drops are a solution of ciprofloxacin hydrochloride in a suitable vehicle.

The ear drops comply with the requirements stated under Ear Preparations and with the following requirements.

Content of ciprofloxacin, $C_{17}H_{18}FN_3O_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210-400 nm:

the UV spectrum 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);

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

Acidity

pH, 4.0 to 5.0, Appendix V L.

Related substances

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

(1) Dilute a volume of the ear drops with sufficient mobile phase to produce a solution containing the equivalent of 0.01% w/v of ciprofloxacin.
(2) Dilute 1 volume of solution (1) to 20 volumes with the mobile phase and further dilute 1 volume to 10 volumes with the mobile phase.
(3) 0.01% w/v of *ciprofloxacin impurity standard BPCRS* in the mobile phase.
(4) Dilute 1 volume of solution (2) to 5 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *base-deactivated octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil BDS).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 278 nm.
(f) Inject 25 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for twice the retention time of ciprofloxacin.

MOBILE PHASE

13 volumes of *acetonitrile* and 87 volumes of a 0.245% w/v solution of *orthophosphoric acid* the pH of which has been adjusted to 3.0 with *triethylamine*.

When the chromatograms are recorded under the prescribed conditions the retention time of ciprofloxacin is about 9 minutes. Retention times relative to ciprofloxacin are: impurity E, about 0.4; impurity F, about 0.5; impurity B, about 0.6; impurity C, about 0.7; impurity D, about 1.2.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to ciprofloxacin impurity B and ciprofloxacin impurity C is at least 1.3.

LIMITS

Identify any peaks in the chromatogram obtained with solution (1) corresponding to ciprofloxacin impurities B, C, D and E using solution (2) and multiply the area of these peaks by the following correction factors: 0.7, 0.6, 1.4 and 6.7 respectively.

In the chromatogram obtained with solution (1):

tthe area of any peak corresponding to impurity C is not greater than 0.8 times the area of the principal peak in the chromatogram obtained with solution (2) (0.4%);

the area of any peak corresponding to impurity E is not greater than 0.6 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

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 all the *secondary peaks* is not greater than 1.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.7%).

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 volume of the ear drops to produce a solution containing the equivalent of 0.001% w/v of ciprofloxacin.

(2) 0.001% w/v of *ciprofloxacin hydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions stated under related substances may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_{17}H_{18}FN_3O_3$ in the ear drops using the declared content of $C_{17}H_{18}FN_3O_3$,HCl in *ciprofloxacin hydrochloride BPCRS*. Each mg of $C_{17}H_{18}FN_3O_3$,HCl is equivalent to 0.9010 mg of $C_{17}H_{18}FN_3O_3$.

STORAGE

Ciprofloxacin Ear Drops should be kept in an airtight container and protected from light.

LABELLING

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

IMPURITIES

The impurities limited by the requirements of this monograph include impurities B, C, D, E and F listed under Ciprofloxacin.