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Ciprofloxacin Tablets

General Notices

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

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Notes:	**REVISED** Dissolution, Related Substances and Assay updated **NOTE: Related substances limits revised** If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.

Action and use

Fluoroquinolone antibacterial.

DEFINITION

Ciprofloxacin Tablets contain Ciprofloxacin Hydrochloride.

The tablets comply with the requirements stated under Tablets 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

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.

(1) Add a quantity of the powdered tablets containing the equivalent of 2 g of ciprofloxacin to 750 mL of *water*, mix with the aid of ultrasound for 20 minutes, add sufficient *water* to produce 1000 mL and mix. Filter a portion of the resulting suspension (Whatman GF/C filter paper is suitable) and dilute the filtrate with sufficient *water* to produce a solution containing the equivalent of 0.05% w/v of ciprofloxacin.

(2) 0.058% w/v of *ciprofloxacin hydrochloride BPCRS* in *water*.

(3) Mix 1 volume of solution (1) and 1 volume of solution (2).

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}* (Merck silica gel 60 F_{254} HPTLC plates are suitable).

(b) Use the mobile phase as described below.

(c) Apply 10 µL of each solution, as bands.

(d) Develop the plate to 15 cm.

(e) After removal of the plate, allow it to dry in air for 15 minutes and examine under *ultraviolet light (254 nm* and *365 nm)*.

MOBILE PHASE

10 volumes of *acetonitrile*, 20 volumes of 13.5M *ammonia*, 40 volumes of *dichloromethane* and 40 volumes of *methanol*.

CONFIRMATION

The principal band in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2). The principal band in the chromatogram obtained with solution (3) appears as a single, compact band.

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is the same as that of the principal 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 2, rotating the paddle at 50 revolutions per minute.

(b) Use 900 mL of *water*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 30 minutes withdraw a 10 mL sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with *water*, if necessary, at the maximum at 276 nm, Appendix II B, using dissolution medium in the reference cell.

(2) Measure the *absorbance* of a suitable solution of *ciprofloxacin hydrochloride BPCRS* in *water* at the maximum at 276 nm using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of ciprofloxacin, $C_{17}H_{18}FN_3O_3$, in the medium from the absorbances obtained and from 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 $C_{17}H_{18}FN_3O_3$.

LIMITS

The amount of ciprofloxacin 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.

(1) Add a quantity of the powdered tablets containing the equivalent of 200 mg of ciprofloxacin to 75 mL of the mobile phase, mix with the aid of ultrasound for 20 minutes, add sufficient mobile phase to produce 100 mL and mix. Filter a portion of the resulting suspension (Whatman GF/C filter is suitable) and dilute the filtrate 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 the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

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

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in the mobile phase.

(1) Add a quantity of the powdered tablets containing the equivalent of 200 mg of ciprofloxacin to 75 mL of the mobile phase, mix with the aid of ultrasound for 20 minutes, add sufficient mobile phase to produce 100 mL and mix. Filter a portion of the resulting suspension (Whatman GF/C filter is suitable) and dilute a suitable quantity of the filtrate with sufficient mobile phase 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 tablets 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 $C_{17}H_{18}FN_3O_3$.

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 Hydrochloride.