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Marbofloxacin 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 (veterinary).

DEFINITION

Marbofloxacin Tablets contain Marbofloxacin.

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

Content of marbofloxacin, $C_{17}H_{19}FN_4O_4$

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 220 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with 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

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 0.1M hydrochloric acid, at a temperature of 37°, as the medium.

PROCEDURE

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

(1) After 30 minutes withdraw a sample of the medium and filter (a 0.45 µm nylon syringe filter is suitable). Dilute with the dissolution medium, if necessary, to produce a solution expected to contain the equivalent of 0.00056% w/v of marbofloxacin.
(2) 0.00056% w/v solution of *marbofloxacin EPCRS* in the dissolution medium.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilanized silica gel* (5 µm) (Nucleosil 100-5C 8 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.2 mL per minute.
(d) Use a column temperature of 20°.
(e) Use a detection wavelength of 298 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

5 volumes of *glacial acetic acid*, 230 volumes of *methanol* and 770 volumes of solution A.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *resolution* between the peaks due to marbofloxacin and impurity A is at least 1.5.

DETERMINATION OF CONTENT

Calculate the total content of $C_{17}H_{19}FN_4O_4$ in the medium from the absorbances obtained and using the declared content of $C_{17}H_{19}FN_4O_4$ in *marbofloxacin impurity mixture A EPCRS*.

LIMITS

The amount of marbofloxacin 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 prepared in solution B, protected from light.

Solution A 0.27% w/v solution of *sodium dihydrogen phosphate* containing 0.35% w/v of *sodium octanesulfonate* adjusted to pH 2.5 with *orthophosphoric acid*.

Solution B 23 volumes of *methanol* and 77 volumes of *water*.

(1) Dissolve a quantity of powdered tablets containing 10 mg of Marbofloxacin in 10 mL of solution B.
(2) Dilute 1 volume of solution (1) to 50 volumes with solution B. Further dilute 1 volume to 10 volumes with solution B.
(3) Dissolve 1 vial of *marbofloxacin impurity mixture A EPCRS* in 1 mL of solution (1).
(4) Dilute 1 volume of solution (2) to 2 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped polar-embedded octadecylsilyl amorphous organosilica polymer for chromotography* (3.5 µm) (X-Terra Shield RP18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.2 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 315 nm.
(f) Inject 10 µL of each solution.
(g) Allow the chromatography to proceed for 2.5 times the retention time of marbofloxacin.

MOBILE PHASE

5 volumes of *glacial acetic acid*, 230 volumes of *methanol* and 770 volumes of *Solution A*.

When the chromatograms are recorded under the prescribed conditions, the relative retention times with reference to marbofloxacin (retention time about 28 minutes) are: impurity C = about 0.9; impurity D = about 1.3; impurity E = about 1.5.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (2), the *resolution* between impurity C and marbofloxacin is at least 1.5 and the *resolution* between marbofloxacin and impurity D is at least 4.0.

in the chromatogram obtained with solution (4), the *signal to noise ratio* of the peak due to marbofloxacin is at least 30.

LIMITS

Identify any peak corresponding to impurity E 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 1.5.

In the chromatogram obtained with solution (1):

the area of any peak due to impurities C, D or E are not greater than the area of the principal peak in the chromatogram obtained with solution (2) (2%);

the area of any other *secondary peaks* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (2%);

the sum of the areas of all *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (3%).

Disregard any peaks 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 prepared in solution B, protected from light.

Solution B 23 volumes of *methanol* and 77 volumes of *water*.

(1) Dissolve a quantity of powdered tablets in sufficient amount of solution B to give a 0.01% w/v solution of Marbofloxacin.
(2) 0.01% w/v of *marbofloxacin EPCRS*.
(3) Dissolve 1 vial of *marbofloxacin impurity mixture A EPCRS* in 1 mL of solution (1).

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between impurity C and marbofloxacin is at least 1.0 and the *resolution* between marbofloxacin and impurity D is at least 4.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{17}H_{19}FN_4O_4$ in the tablets from the chromatograms obtained and using the declared content of $C_{17}H_{19}FN_4O_4$ in *marbofloxacin EPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under *Marbofloxacin*.