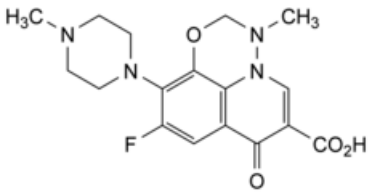
Edition: BP 2025 (Ph. Eur. 11.6 update)

Marbofloxacin

General Notices

(Marbofloxacin for Veterinary Use, Ph. Eur. monograph 2233)



$C_{17}H_{19}FN_4O_4$ 362.4 *115550-35-1*

Action and use

Fluoroquinolone antibacterial.

Ph Eur

DEFINITION

9-Fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7*H*-pyrido[3,2,1-*ij*][4,1,2]benzoxadiazine-6-carboxylic acid.

Content

99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance

Light yellow, crystalline powder.

Solubility

Slightly soluble in water, sparingly soluble or slightly soluble in methylene chloride, very slightly soluble in ethanol (96 per cent).

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison marbofloxacin CRS.

TESTS

Absorbance (2.2.25)

Maximum 0.20, determined at 450 nm. *Prepare the solution immediately before use.*

Dissolve 0.400 g in 0.1 M ammonium carbonate buffer solution pH 10.3 R using sonication and dilute to 10.0 mL with the same buffer solution.

Related substances

Liquid chromatography (2.2.29). *Carry out the test protected from light.*

Solution A A 2.70 g/L solution of sodium dihydrogen phosphate R containing 3.50 g/L of sodium octanesulfonate R, adjusted to pH 2.5 with phosphoric acid R.

Solvent mixture methanol R, water R (23:77 *V/V*).

Test solution To 0.100 g of the substance to be examined add 80 mL of the solvent mixture, sonicate until dissolution and dilute to 100.0 mL with the solvent mixture.

Reference solution (a) Dilute 1.0 mL of the test solution to 50.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Reference solution (b) Dissolve the contents of a vial of marbofloxacin impurity mixture A CRS (containing impurities C, D and E) in 1 mL of the test solution.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: end-capped polar-embedded octadecylsilyl amorphous organosilica polymer R (3.5 µm);

— *temperature*: 40 °C.

Mobile phase Mix 230 volumes of methanol R and 5 volumes of glacial acetic acid R with 770 volumes of the solution A.

Flow rate 1.2 mL/min.

Detection Spectrophotometer at 315 nm.

Injection 10 µL.

Run time 2.5 times the retention time of marbofloxacin.

Identification of impurities Use the chromatogram supplied with marbofloxacin impurity mixture A CRS and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities C, D and E.

Relative retention With reference to marbofloxacin (retention time = about 33 min): impurity C = about 0.9; impurity D = about 1.3; impurity E = about 1.5.

System suitability:

— signal-to-noise ratio: minimum 30 for the principal peak in the chromatogram obtained with reference solution (a);

— resolution: minimum 1.5 between the peaks due to impurity C and marbofloxacin; minimum 4.0 between the peaks due to marbofloxacin and impurity D in the chromatogram obtained with reference solution (b).

Calculation of percentage contents:

— *correction factor*: multiply the peak area of impurity E by 1.5;

— for each impurity, use the concentration of marbofloxacin in reference solution (a).

Limits:

— *impurity E*: maximum 0.20 per cent;

— *unspecified impurities*: for each impurity, maximum 0.20 per cent;

— *total*: maximum 0.5 per cent;

— *reporting threshold*: 0.10 per cent.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 4 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g in a platinum crucible.

ASSAY

Dissolve 0.300 g in 80 mL of *glacial acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 36.24 mg of $C_{17}H_{19}FN_4O_4$.

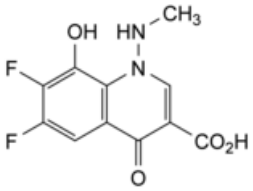
STORAGE

Protected from light.

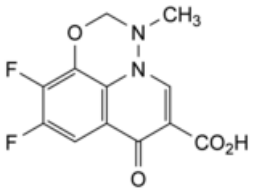
IMPURITIES

Specified impurities *E*.

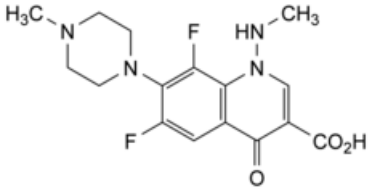
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) *A, B, C, D, F*.



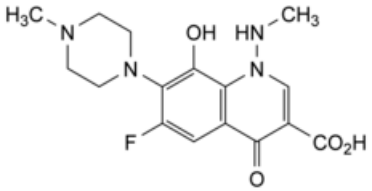
A. 6,7-difluoro-8-hydroxy-1-(methylamino)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



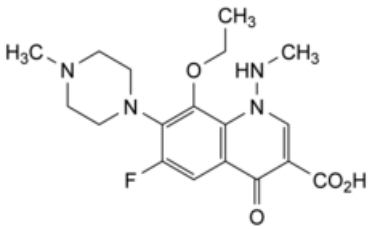
B. 9,10-difluoro-3-methyl-7-oxo-2,3-dihydro-7*H*-pyrido[3,2,1-*ij*][4,1,2]benzoxadiazine-6-carboxylic acid,



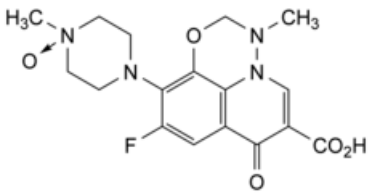
C. 6,8-difluoro-1-(methylamino)-7-(4-methylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



D. 6-fluoro-8-hydroxy-1-(methylamino)-7-(4-methylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



E. 8-ethoxy-6-fluoro-1-(methylamino)-7-(4-methylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



F. 4-[6-carboxy-9-fluoro-3-methyl-7-oxo-2,3-dihydro-7*H*-pyrido[3,2,1-*ij*][4,1,2]benzoxadiazin-10-yl]-1-methylpiperazine 1-oxide.

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