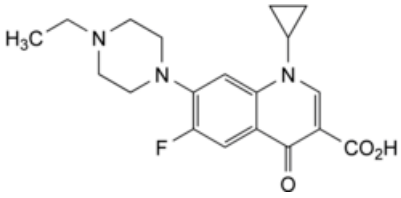
Edition: BP 2025 (Ph. Eur. 11.6 update)

Enrofloxacin

General Notices

(Enrofloxacin for Veterinary Use, Ph. Eur. monograph 2229)



$C_{19}H_{22}FN_3O_3$ 359.4 *93106-60-6*

Action and use

Fluoroquinolone antibacterial (veterinary).

Preparations

Enrofloxacin Concentrate for Oral Solution

Enrofloxacin Injection

Enrofloxacin Oral Solution

Enrofloxacin Oral Suspension

Enrofloxacin Solution for Use in Drinking Water

Enrofloxacin Tablets

Ph Eur

DEFINITION

1-Cyclopropyl-7-(4-ethylpiperazin-1-yl)-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid.

Content

98.5 per cent to 101.5 per cent (dried substance).

CHARACTERS

Appearance

Pale yellowish or light yellow, crystalline powder.

Solubility

Practically insoluble in water, freely soluble in methylene chloride, slightly soluble in methanol.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison *enrofloxacin CRS*.

TESTS

Appearance of solution

The solution is not more opalescent than reference suspension II (2.2.1) and not more intensely coloured than reference solution GY_4 (2.2.2, *Method II*).

To 1.0 g of the substance to be examined add about 0.25 g of *potassium hydroxide R* and 7 mL of *water R*. Sonicate to dissolve and dilute to 10.0 mL with *water R*.

Impurity A

Thin-layer chromatography (2.2.27). *Prepare the solutions immediately before use.*

Solvent mixture *methanol R*, *methylene chloride R* (50:50 *V/V*).

Test solution Dissolve 0.100 g of the substance to be examined in the solvent mixture and dilute to 5.0 mL with the solvent mixture.

Reference solution Dissolve 5.0 mg of *ciprofloxacin impurity A CRS* (enrofloxacin impurity A) in the solvent mixture and dilute to 50.0 mL with the solvent mixture. Dilute 4.0 mL of the solution to 10.0 mL with the solvent mixture.

Plate *TLC silica gel F_{254} plate R* (2-10 µm).

Mobile phase *butanol R*, *water R*, *anhydrous acetic acid R*, *ethyl acetate R* (15:15:20:50 *V/V/V/V*).

Application 10 µL.

Development Over 3/4 of the plate.

Drying In air.

Detection Examine in ultraviolet light at 254 nm.

Results:

— *impurity A*: any spot due to impurity A is not more intense than the spot in the chromatogram obtained with the reference solution (0.2 per cent).

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 50 mg of the substance to be examined in the mobile phase and dilute to 50.0 mL with the mobile phase.

Reference solution (a) Dissolve 10 mg of *enrofloxacin for system suitability CRS* (containing impurities B and C) in the mobile phase and dilute to 10 mL with the mobile phase.

Reference solution (b) Dilute 1.0 mL of the test solution to 50.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: *base-deactivated end-capped octadecylsilyl silica gel for chromatography R* (5 µm);

— *temperature*: 40 °C.

Mobile phase Mix 15 volumes of *methanol R* and 85 volumes of a 2.9 g/L solution of *phosphoric acid R*, previously adjusted to pH 2.3 with *triethylamine R*.

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 270 nm.

Injection 10 µL.

Run time 3 times the retention time of enrofloxacin.

Identification of impurities Use the chromatogram supplied with *enrofloxacin for system suitability CRS* and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities B and C.

Relative retention With reference to enrofloxacin (retention time = about 16 min): impurity C = about 0.6; impurity B = about 0.8.

System suitability Reference solution (a):

— *resolution*: minimum 2.0 between the peaks due to impurity B and enrofloxacin.

Limits:

— *impurity B*: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

— *impurity C*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.20 per cent);

— *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent);

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent).

Loss on drying (*2.2.32*)

Maximum 1.0 per cent, determined on 2.000 g by drying *in vacuo* at 120 °C for 6 h.

Sulfated ash (*2.4.14*)

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

ASSAY

Dissolve 0.250 g in 100 mL of *anhydrous acetic acid R* and 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 35.94 mg of $C_{19}H_{22}FN_3O_3$.

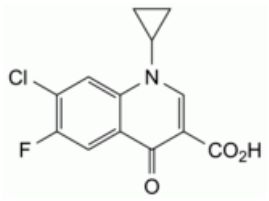
STORAGE

Protected from light.

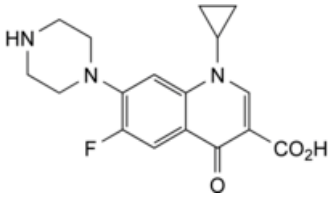
IMPURITIES

Specified impurities A, B, C.

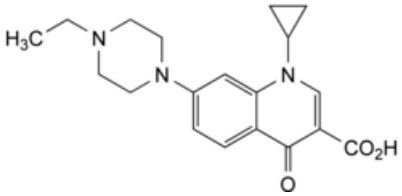
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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) E, F, G.



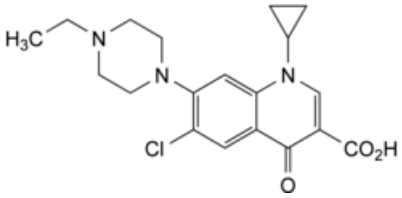
A. 7-chloro-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



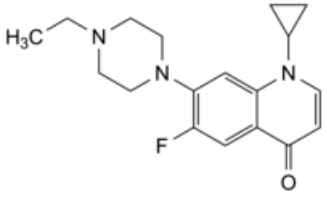
B. ciprofloxacin,



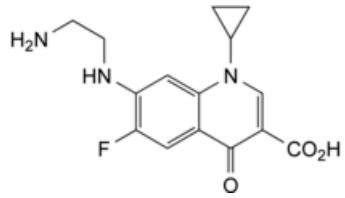
C. 1-cyclopropyl-7-(4-ethylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



E. 6-chloro-1-cyclopropyl-7-(4-ethylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



F. 1-cyclopropyl-7-(4-ethylpiperazin-1-yl)-6-fluoroquinolin-4(1*H*)-one,



G. 7-[(2-aminoethyl)amino]-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid.

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