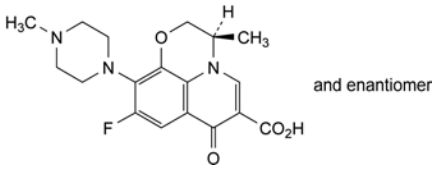
01/2011:1455

OFLOXACIN

Ofloxacinum



$C_{18}H_{20}FN_3O_4$ M_r 361.4
[82419-36-1]

DEFINITION

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

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

CHARACTERS

Appearance: pale yellow or bright yellow, crystalline powder.

Solubility: slightly soluble in water, soluble in glacial acetic acid, slightly soluble or soluble in methylene chloride, slightly soluble in methanol.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *ofloxacin CRS*.

TESTS

Optical rotation (*2.2.7*): – 0.10° to + 0.10°.

Dissolve 0.300 g in a mixture of 10 volumes of *methanol R* and 40 volumes of *methylene chloride R* and dilute to 10.0 mL with the same mixture of solvents.

Absorbance (*2.2.25*): maximum 0.25 at 440 nm.

Dissolve 0.5 g in *0.1 M hydrochloric acid* and dilute to 100.0 mL with the same acid.

Impurity A. Thin-layer chromatography (*2.2.27*).

Solvent mixture: *methanol R, methylene chloride R* (10:40 *V/V*).

Test solution. Dissolve 0.250 g of the substance to be examined in the solvent mixture and dilute to 5.0 mL with the solvent mixture.

Reference solution. Dissolve 10.0 mg of *ofloxacin impurity A CRS* in the solvent mixture and dilute to 100.0 mL with the solvent mixture.

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

Mobile phase: *glacial acetic acid R, water R, ethyl acetate R* (10:10:20 *V/V/V*).

Application: 10 µL.

Development: over 2/3 of the plate.

Drying: in air.

Detection: examine in ultraviolet light at 254 nm.

Limit:

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

Related substances. Liquid chromatography (*2.2.29*). *Prepare the solutions immediately before use.*

Solvent mixture: *acetonitrile R, water R* (10:60 *V/V*).

Test solution. Dissolve 10 mg of the substance to be examined in the solvent mixture and dilute to 50.0 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 10 mg of *ofloxacin impurity E CRS* in the solvent mixture and dilute to 100.0 mL with the solvent mixture. Mix 10 mL of the solution and 5 mL of the test solution and dilute to 50.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 50.0 mL with the solvent mixture.

Column:

– *size*: *l* = 0.15 m, Ø = 4.6 mm;
– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm);
– *temperature*: 45 °C.

Mobile phase: dissolve 4.0 g of *ammonium acetate R* and 7.0 g of *sodium perchlorate R* in 1300 mL of *water R*; adjust to pH 2.2 with *phosphoric acid R* and add 240 mL of *acetonitrile R*.

Flow rate: adjust so that a retention time of about 20 min is obtained for ofloxacin.

Detection: spectrophotometer at 294 nm.

Injection: 10 µL.

Run time: 2.5 times the retention time of ofloxacin.

Identification of impurities: use the chromatogram obtained with reference solution (b) to identify the peak due to impurity E.

Relative retention with reference to ofloxacin (retention time = about 20 min): impurity B = about 0.3; impurity C = about 0.5; impurity D = about 0.7; impurity E = about 0.9; impurity F = about 1.6.

System suitability: reference solution (b):

– *resolution*: minimum 2.0 between the peaks due to impurity E and ofloxacin.

Limits:

– *impurities B, C, D, E, F*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);
– *unspecified impurities*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);
– *total*: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);
– *disregard limit*: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Heavy metals (*2.4.8*): maximum 10 ppm.

2.0 g complies with test C. Prepare the reference solution using 2 mL of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 0.2 per cent, determined on 1.000 g by drying at 105 °C for 4 h.

Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.300 g in 100 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

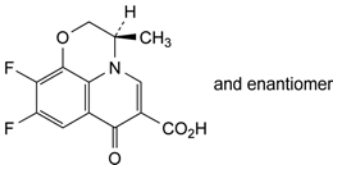
1 mL of *0.1 M perchloric acid* is equivalent to 36.14 mg of $C_{18}H_{20}FN_3O_4$.

STORAGE

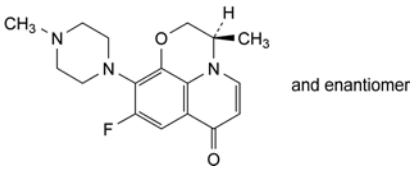
In an airtight container, protected from light.

IMPURITIES

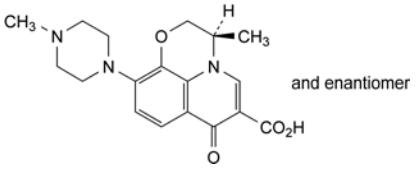
Specified impurities: A, B, C, D, E, F.



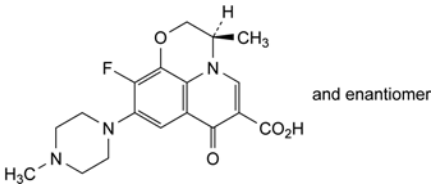
A. (*3RS*)-9,10-difluoro-3-methyl-7-oxo-2,3-dihydro-7*H*-pyrido-[1,2,3-*de*]-1,4-benzoxazine-6-carboxylic acid (FPA),



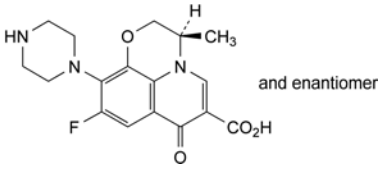
B. (3*RS*)-9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-2,3-dihydro-7*H*-pyrido[1,2,3-*de*]-1,4-benzoxazin-7-one,



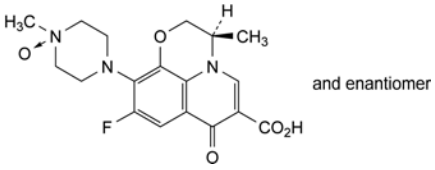
C. (3*RS*)-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7*H*-pyrido[1,2,3-*de*]-1,4-benzoxazine-6-carboxylic acid,



D. (3*RS*)-10-fluoro-3-methyl-9-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7*H*-pyrido[1,2,3-*de*]-1,4-benzoxazine-6-carboxylic acid,



E. (3*RS*)-9-fluoro-3-methyl-7-oxo-10-(piperazin-1-yl)-2,3-dihydro-7*H*-pyrido[1,2,3-*de*]-1,4-benzoxazine-6-carboxylic acid,



F. 4-[(3*RS*)-6-carboxy-9-fluoro-3-methyl-7-oxo-2,3-dihydro-7*H*-pyrido[1,2,3-*de*]-1,4-benzoxazin-10-yl]-1-methylpiperazine 1-oxide.

01/2008:0799

OLEIC ACID

Acidum oleicum

[112-80-1]

DEFINITION

(*Z*)-Octadec-9-enoic acid ($C_{18}H_{34}O_2$; M_r 282.5), together with varying amounts of saturated and other unsaturated fatty acids. A suitable antioxidant may be added.

Content: 65.0 per cent to 88.0 per cent of $C_{18}H_{34}O_2$.

CHARACTERS

Appearance: clear, yellowish or brownish, oily liquid.

Solubility: practically insoluble in water, miscible with alcohol and with methylene chloride.

Relative density: about 0.892.

IDENTIFICATION

A. Acid value (see Tests).

B. Iodine value (see Tests).

C. Composition of fatty acids (see Tests).

Margaric acid: maximum 0.2 per cent for oleic acid of vegetable origin and maximum 4.0 per cent for oleic acid of animal origin.

TESTS

Appearance. The substance to be examined is not more intensely coloured than reference solution Y_1 or BY_1 (*2.2.2, Method I*).

Acid value (*2.5.1*): 195 to 204, determined on 0.5 g.

Iodine value (*2.5.4*): 89 to 105.

Peroxide value (*2.5.5*): maximum 10.0.

Composition of fatty acids. Gas chromatography (*2.4.22, Method C*).

Test solution. Prepare as described in the method but omitting the initial hydrolysis.

Composition of the fatty acid fraction of the substance:

- *myristic acid*: maximum 5.0 per cent,
- *palmitic acid*: maximum 16.0 per cent,
- *palmitoleic acid*: maximum 8.0 per cent,
- *stearic acid*: maximum 6.0 per cent,
- *oleic acid*: 65.0 per cent to 88.0 per cent,
- *linoleic acid*: maximum 18.0 per cent,
- *linolenic acid*: maximum 4.0 per cent,
- *fatty acids of chain length greater than C_{18}*: maximum 4.0 per cent.

Total ash (*2.4.16*): maximum 0.1 per cent, determined on 2.00 g.

STORAGE

In an airtight, well-filled container, protected from light.

LABELLING

The label states the origin of oleic acid (animal or vegetable).

01/2008:1249

OLEOYL MACROGOLGLYCERIDES

Macrogolglyceridorum oleates

DEFINITION

Mixtures of monoesters, diesters and triesters of glycerol and monoesters and diesters of macrogols.

They are obtained by partial alcoholysis of an unsaturated oil mainly containing triglycerides of oleic (*cis*-9-octadecenoic) acid, using macrogol with a mean relative molecular mass between 300 and 400, or by esterification of glycerol and macrogol with unsaturated fatty acids, or by mixing glycerol esters and condensates of ethylene oxide with the fatty acids of this unsaturated oil.

CHARACTERS

Appearance: amber oily liquid, which may give rise to a deposit after prolonged periods at 20 °C.

Solubility: practically insoluble but dispersible in water, freely soluble in methylene chloride.

Viscosity: about 35 mPa·s at 40 °C.

Relative density: about 0.95 at 20 °C.