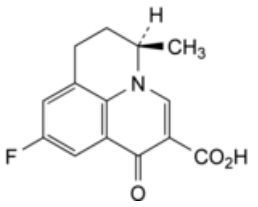
Edition: BP 2025 (Ph. Eur. 11.6 update)

# Flumequine

General Notices

*(Ph. Eur. monograph 1517)*




and enantiomer

$C_{14}H_{12}FNO_3$ 261.3 *42835-25-6*

**Action and use**

Antibacterial.

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## DEFINITION

(*RS*)-9-Fluoro-5-methyl-1-oxo-6,7-dihydro-1*H*,5*H*-benzo[*ij*]quinolizine-2-carboxylic acid.

**Content**

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

## CHARACTERS

**Appearance**

White or almost white, microcrystalline powder.

**Solubility**

Practically insoluble in water, sparingly soluble in methylene chloride, very slightly soluble in methanol. It is freely soluble in dilute solutions of alkali hydroxides.

## IDENTIFICATION

*First identification: A, B.*

*Second identification: B, C, D.*

A. Infrared absorption spectrophotometry (2.2.24).

*Comparison* flumequine CRS.

B. Optical rotation (see Tests).

C. Thin-layer chromatography (2.2.27).

*Test solution* Dissolve 5 mg of the substance to be examined in 10 mL of methylene chloride R.

*Reference solution* Dissolve 5 mg of flumequine CRS in 10 mL of methylene chloride R.

*Plate* TLC silica gel $F_{254}$ plate R.

*Mobile phase* ammonia R, water R, ethanol (96 per cent) R (10:10:90 *V/V/V*).

*Application* 5 µL.

*Development* Over 2/3 of the plate.

*Drying* In air.

*Detection* Examine in ultraviolet light at 254 nm.

*Results* The principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with the reference solution.

D. Mix about 5 mg with 45 mg of heavy magnesium oxide R and ignite in a crucible until an almost white residue is obtained (usually less than 5 min). Allow to cool, add 1 mL of water R, 0.05 mL of phenolphthalein solution R1 and about 2 mL of dilute hydrochloric acid R to render the solution colourless. Filter and add to the filtrate a freshly prepared mixture of 0.1 mL of alizarin S solution R and 0.1 mL of zirconyl nitrate solution R. Mix, allow to stand for 5 min and compare the colour of the solution with that of a blank prepared in the same manner. The test solution changes from red to yellow and the blank remains red.

## TESTS

### Solution S

Dissolve 5.00 g in 0.5 M sodium hydroxide and dilute to 50.0 mL with the same solvent.

### Appearance of solution

Solution S is clear (2.2.1) and not more intensely coloured than reference solution $BY_5$ (2.2.2, Method II).

### Optical rotation (2.2.7)

-0.10° to + 0.10°, determined on solution S.

### Related substances

Liquid chromatography (2.2.29).

*Test solution* Dissolve 35.0 mg of the substance to be examined in dimethylformamide R and dilute to 100.0 mL with the same solvent.

*Reference solution (a)* Dissolve the contents of a vial of flumequine impurity B CRS in 2.0 mL of a 50 µg/mL solution of flumequine CRS in dimethylformamide R.

*Reference solution (b)* Dilute 1.0 mL of the test solution to 200.0 mL with dimethylformamide R.

*Column*:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: octadecylsilyl silica gel for chromatography R (5 µm).

*Mobile phase* methanol R, 1.36 g/L solution of potassium dihydrogen phosphate R (49:51 *V/V*).

*Flow rate* 0.8 mL/min.

*Detection* Spectrophotometer at 313 nm.

*Injection* 10 µL; inject dimethylformamide R as a blank.

*Run time* 3 times the retention time of flumequine.

*Relative retention* With reference to flumequine (retention time = about 13 min): impurity A = about 0.67; impurity B = about 0.85.

*System suitability* Reference solution (a):

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

*Limits*:

— *impurities A, B*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

— *unspecified impurities*: for each impurity, not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);

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

— *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 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 3 h.

**Sulfated ash** (*2.4.14*)

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

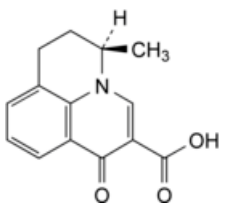
## ASSAY

Dissolve 0.500 g in 50 mL of dimethylformamide R. Titrate with 0.1 M tetrabutylammonium hydroxide, determining the end-point potentiometrically (*2.2.20*).

1 mL of 0.1 M tetrabutylammonium hydroxide is equivalent to 26.13 mg of $C_{14}H_{12}FNO_3$.

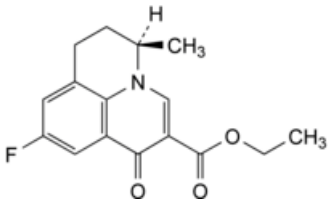
## IMPURITIES

*Specified impurities* *A, B.*




and enantiomer

A. (*RS*)-5-methyl-1-oxo-6,7-dihydro-1*H*,5*H*-benzo[*ij*]quinolizine-2-carboxylic acid (defluoroflumequine),




and enantiomer

B. ethyl (*RS*)-9-fluoro-5-methyl-1-oxo-6,7-dihydro-1*H*,5*H*-benzo[*ij*]quinolizine-2-carboxylate (flumequine ethyl ester).

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