**Loss on drying** (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

**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 50 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 34.64 mg of $C_{22}H_{16}F_2N_2$.

STORAGE

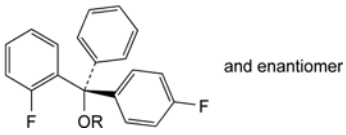
Protected from light.

IMPURITIES

*Specified impurities*: *A, B.*

*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*): *C.*

A. imidazole,



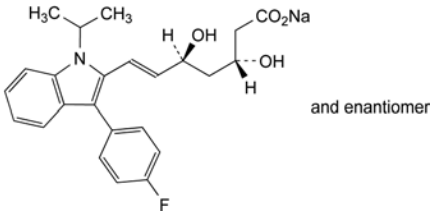

B. R = H: (*RS*)-(2-fluorophenyl)(4-fluorophenyl)phenylmethanol,

C. R = $CH_3$: (*RS*)-(2-fluorophenyl)(4-fluorophenyl)methoxyphenylmethane.

**04/2009:2333**

# FLUVASTATIN SODIUM

## Fluvastatinum natricum




$C_{24}H_{25}FNNaO_4$ $M_r$ 433.5

[93957-55-2]

DEFINITION

Sodium (3*RS*,5*SR*,6*E*)-7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1*H*-indol-2-yl]-3,5-dihydroxyhept-6-enoate.

*Content*: 98.5 per cent to 101.5 per cent (dried substance).

CHARACTERS

*Appearance*: white or almost white, or pale yellow to pale reddish-yellow, very hygroscopic, crystalline powder.

*Solubility*: soluble in water, freely soluble in methanol, practically insoluble in acetonitrile.

It shows polymorphism (*5.9*).

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
*Comparison*: *fluvastatin sodium CRS*.
If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in *methanol R*, evaporate to dryness and record new spectra using the residues.

B. 0.5 mL of solution S (see Tests) gives reaction (a) of sodium (*2.3.1*).

TESTS

**Solution S**. Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 20.0 mL with the same solvent.

**pH** (*2.2.3*): 8.0 to 10.0 for solution S.

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

*Test solution*. Dissolve 25 mg of the substance to be examined in 20 mL of mobile phase B and dilute to 50.0 mL with mobile phase A.

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

*Reference solution (b)*. Dissolve the contents of a vial of *fluvastatin for system suitability CRS* (containing impurities A, B and D) in 1.0 mL of a mixture of equal volumes of mobile phase A and mobile phase B.

*Column*:

– *size*: *l* = 0.10 m, Ø = 4.6 mm;
– *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (3 µm);
– *temperature*: 40 °C.

*Mobile phase*:

– *mobile phase A*: to 880 mL of *water R* add 20 mL of a 250 g/L solution of *tetramethylammonium hydroxide R* and adjust quickly to pH 7.2 with *phosphoric acid R*; mix with 100 mL of a mixture of 40 volumes of *acetonitrile R* and 60 volumes of *methanol R*;
– *mobile phase B*: to 80 mL of *water R* add 20 mL of a 250 g/L solution of *tetramethylammonium hydroxide R* and adjust quickly to pH 7.2 with *phosphoric acid R*; mix with 900 mL of a mixture of 40 volumes of *acetonitrile R* and 60 volumes of *methanol R*;

| Time (min) | Mobile phase A (per cent *V/V*) | Mobile phase B (per cent *V/V*) |
|---|---|---|
| 0 - 3 | 70 | 30 |
| 3 - 23 | 70 → 10 | 30 → 90 |

*Flow rate*: 2.0 mL/min.

*Detection*: spectrophotometer at 305 nm and at 365 nm.

*Injection*: 20 µL.

*Identification of impurities*: use the chromatogram supplied with *fluvastatin for system suitability CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A, B and D.

*Relative retention* with reference to fluvastatin (retention time = about 14 min); impurity A = about 1.05; impurity D = about 1.1; impurity B = about 1.6.

*System suitability*: reference solution (b) at 305 nm:

– *peak-to-valley ratio*: minimum 5, where $H_p$ = height above the baseline of the peak due to impurity A and $H_v$ = height above the baseline of the lowest point of the curve separating this peak from the peak due to fluvastatin.

*Limits*:

– *impurity A at 305 nm*: not more than 4 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.8 per cent);
– *impurity B at 305 nm*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

– *impurity D at 365 nm*: not more than 0.75 times the area of the principal peak in the chromatogram obtained with reference solution (a) at 305 nm (0.15 per cent);
– *unspecified impurities at 305 nm*: not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);
– *sum of impurities at 305 nm*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent);
– *disregard limit at 305 nm*: 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 20 ppm.

Dissolve 1.0 g in a mixture of 15 volumes of *water R* and 85 volumes of *methanol R* and dilute to 20 mL with the same mixture of solvents. 12 mL of the solution complies with test B. Prepare the reference solution using lead standard solution (1 ppm Pb) obtained by diluting *lead standard solution (100 ppm Pb) R* with a mixture of 15 volumes of *water R* and 85 volumes of *methanol R*. For the evaluation of the results, filter the solutions through a membrane filter (nominal pore size 0.45 µm).

**Loss on drying** (*2.2.32*): maximum 4.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

ASSAY

Dissolve 0.325 g in 50 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 43.35 mg of $C_{24}H_{25}FNNaO_4$.

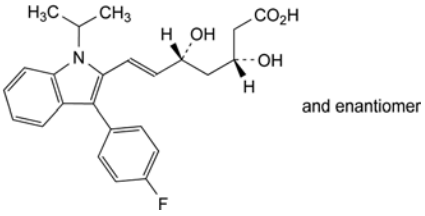
STORAGE

In an airtight container, protected from light.

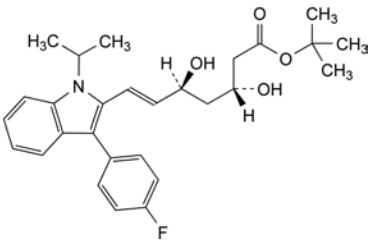
IMPURITIES

*Specified impurities: A, B, D.*

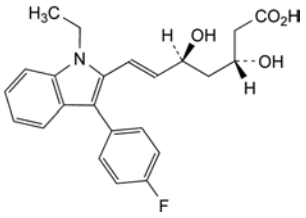
*Other detectable impurities* (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical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



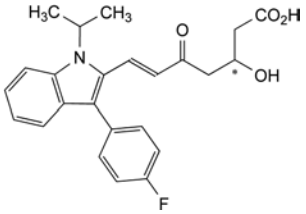

A. (3*RS*,5*RS*,6*E*)-7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1*H*-indol-2-yl]-3,5-dihydroxyhept-6-enoic acid,



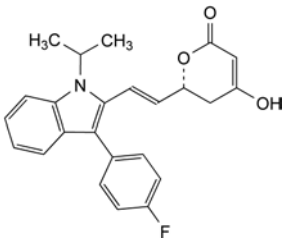
B. 1,1-dimethylethyl (3*R*,5*S*,6*E*)-7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1*H*-indol-2-yl]-3,5-dihydroxyhept-6-enoate,



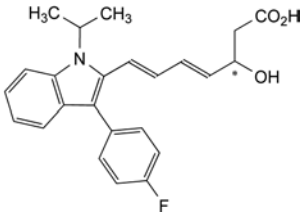
C. (3*R*,5*S*,6*E*)-7-[1-ethyl-3-(4-fluorophenyl)-1*H*-indol-2-yl]-3,5-dihydroxyhept-6-enoic acid,



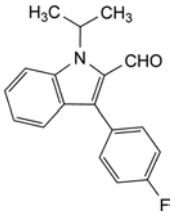
D. (6*E*)-7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1*H*-indol-2-yl]-3-hydroxy-5-oxohept-6-enoic acid,



E. (6*R*)-6-[(*E*)-2-[3-(4-fluorophenyl)-1-(1-methylethyl)-1*H*-indol-2-yl]ethenyl]-4-hydroxy-5,6-dihydro-2*H*-pyran-2-one,



F. (4*E*,6*E*)-7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1*H*-indol-2-yl]-3-hydroxyhepta-4,6-dienoic acid,

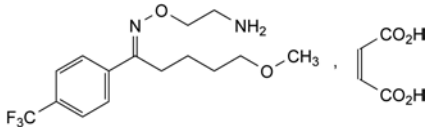


G. 3-(4-fluorophenyl)-1-(1-methylethyl)-1*H*-indole-2-carbaldehyde.

**07/2008:1977**
**corrected 6.3**

# FLUVOXAMINE MALEATE

## Fluvoxamini maleas



$C_{19}H_{25}F_3N_2O_6$ [61718-82-9] $M_r$ 434.4