Fluvastatin Capsules

Fluvastatin Sodium Capsules

Fluvastatin Capsules contain fluvastatin sodium equivalent to not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of, $C_{24}H_{26}FNO_4$.

Usual strength. 40 mg; 80 mg.

Identification

In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution (b).

Tests

Dissolution (2.5.2).

Apparatus No.1,
Medium. 500 ml of *water*.
Speed and time. 50 rpm and 30 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Dilute the filtrate, if necessary, with the dissolution medium.

Reference solution. Dissolve a quantity of *fluvastatin sodium RS* in the dissolution medium to obtain a solution of known concentration similar to the expected concentration of the test solution.

NOTE — A volume of methanol, not exceeding 2 per cent of the final volume of solution, may be used to aid in dissolving fluvastatin sodium RS.

Chromatographic system
- a stainless steel column 10 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- mobile phase: a mixture of 30 volumes of buffer solution prepared by dissolving 1.92 g of *monobasic ammonium phosphate* in 1000 ml of *water*, adjusted to pH 3.5 with *orthophosphoric acid* or *ammonium hydroxide* and 70 volumes of *methanol*,
- flow rate: 2 ml per minute,
- spectrophotometer set at 235 nm,
- injection volume: 50 µl.

Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 1.5 per cent

Inject the reference solution and the test solution.

Calculate the content of $C_{24}H_{26}FNO_4$, in the medium.

D. Not less than 80 per cent of the stated amount of $C_{24}H_{26}FNO_4$.

Related substances. Determine by liquid chromatography (2.4.14).

NOTE — Protect all solutions from light.

Buffer solution. A solution containing 40 ml of 25 per cent *aqueous tetramethylammonium hydroxide* in 1000 ml of *water*, adjusted to pH 7.2 with *orthophosphoric acid*.

Solvent mixture (a). 40 volumes of *acetonitrile* and 60 volumes of *methanol*.

Solvent mixture (b). 46 volumes of solvent mixture (a) and 54 volumes of buffer solution.

Reference solution (a). A 0.042 per cent w/v solution of *fluvastatin system suibality RS* in solvent mixture (b).

Reference solution (b). A 0.042 per cent w/v solution of *fluvastatin sodium RS* in solvent mixture (b).

Reference solution (c). Dilute 1.0 ml of reference solution (b) to 100.0 ml with solvent mixture (b).

Reference solution (d). Dilute 1.0 ml of reference solution (b) to 100.0 ml with solvent mixture (b). Dilute 1.0 ml of the solution to 20.0 ml with solvent mixture (b).

Test solution. Disperse a quantity of the mixed contents of the capsules containing about 200 mg of Fluvastatin in 100 ml of *methanol,* stir with a magnetic or mechanical stirrer for 45 minutes and dilute to 200.0 ml with the *methanol*. Centrifuge at 4000 rpm for 20 minutes. Dilute the clear supernatant liquid with the solvent mixture (b) to obtain a solution containing 0.04 per cent w/v of fluvastatin.

Chromatographic system
- a stainless steel column 5 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),

– mobile phase: A. a mixture of 12.5 volumes of solvent mixture (a) and 87.5 volumes of buffer solution,
B. a mixture of 87.5 volumes of solvent mixture (a) and 12.5 volumes of buffer solution,
– a gradient programme using the conditions given below,
– flow rate: 2 ml per minute,
– injection volume: 25 µl,
– spectrophotometer set at 365 nm for 3-hydroxy-5-keto fluvastatin and 305 nm for all other impurities.

Time (in min)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	54	46
6	54	46
17	17	83
20	17	83
20.1	54	46
26.1	54	46

Name	Relative retention time	Correction factor
Fluvastatin	1.0	---
Fluvastatin anti-isomer[1]	1.2	---
3-hydroxy-5-keto fluvastatin[2]	1.6	0.04
Fluvastatin hydroxydiene[3]	2.2	1.09
Fluvastatin short chain aldehyde[4]	3.2	0.71

[1] Sodium (3R,5S,E)-7-[1-ethyl-3-(4-fluorophenyl)-1H-indol-2-yl]-3,5-dihydroxyhept-6-enoate,
[2] Sodium (E)-7-[3-(4-fluorophenyl)-1-isopropyl-1H-indol-2-yl]-3-hydroxy-5-oxohept-6-enoate,
[3] Sodium (4E,6E)-7-[3-(4-fluorophenyl)-1-isopropyl-1H-indol-2-yl]-3-hydroxyhepta-4,6-dienoate,
[4] 3-(4-fluorophenyl)-1-isopropyl-1H-indole-2-carbaldehyde.

Inject reference solution (a), (b) and (d) at 305 nm. The test is not valid unless the resolution between the peaks due to fluvastatin anti-isomer and fluvastatin is not less than 1.4 in the chromatogram obtained with the reference solution (a), the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (c) and the signal to noise ratio for the principal peak is not less than 10.0 in the chromatogram obtained with reference solution (d).

Inject reference solution (c) and the test solution at 305 nm. In the chromatogram obtained with the test solution, the area of any peak corresponding to fluvastatin anti-isomer is not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (1.5 per cent), the area of any peak corresponding to fluvastatin hydroxydiene is not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (1.0 per cent), the area of any peak corresponding to fluvastatin short chain aldehyde is not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.5 per cent). The area of any other secondary peak is not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.5 per cent)

Inject reference solution (c) and the test solution at 365 nm. In the chromatogram obtained with the test solution, the area of any peak corresponding to 3-hydroxy-5 keto fluvastatin is not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (1.0 per cent). The sum of all the impurities is not more than 4.0 per cent.

Assay. Determine by liquid chromatography (2.4.14) as described under Related substances with the following modifications.

NOTE — Protect all the solutions from light.

Chromatographic system
– spectrophotometer set at 305 nm.

The relative retention time with reference to fluvastatin for fluvastatin anti-isomer is about 1.2.

Inject the reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to fluvastatin anti-isomer and fluvastatin peaks is not less than 1.4 in the chromatogram obtained with the reference solution (a) and the relative standard deviation for replicate injections is not more than 1.5 per cent in the chromatogram obtained with the reference solution (b).

Inject the reference solution (b) and the test solution.

Calculate the content of $C_{24}H_{26}FNO_4$ in the capsules.

Storage. Store protected from light and moistures,at a temperature not exceeding 30°.

Labelling. The label states the strength in terms of the equivalent amount of fluvastatin.