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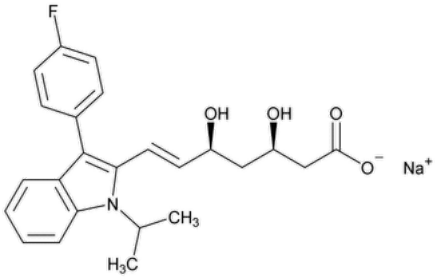
Fluvastatin Sodium



$C_{24}H_{25}FNNaO_4$ 433.45

6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methyl ethyl)-1*H*-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [*R**,*S**-(*E*)]-(±)-;

Sodium (±)-(3*R**,5*S**,6*E*)-7-[3-(*p*-fluorophenyl)-1-iso propylindol-2-yl]-3,5-dihydroxy-6-heptenoate CAS RN®: 93957-55-2; UNII: PYF7O1FV7F.

DEFINITION

Fluvastatin Sodium contains NLT 98.0% and NMT 102.0% of fluvastatin sodium ($C_{24}H_{25}FNNaO_4$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K▲ (CN 1-May-2020)

If a difference appears in the IR spectra of the analyte and the Standard, dissolve equal portions of the sample specimen and the USP Reference Standard in equal volumes of methanol. Evaporate the solutions to dryness on a steam bath, protecting the solutions from light, and dry at 105° for 30 min. Repeat the test on the residues.

• **B.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Sodium*:** Meets the requirements of test *A*

• **C.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: Add 20 mL of 25% aqueous tetramethylammonium hydroxide solution to 880 mL of water. Adjust with about 2.3 mL of phosphoric acid to a pH of 7.2 ± 0.2. Add 100 mL of a mixture of methanol and acetonitrile (60:40).

Solution B: Add 20 mL of 25% aqueous tetramethylammonium hydroxide solution and 80 mL of water to 900 mL of a mixture of methanol and acetonitrile (60:40). Adjust with about 2.3 mL of phosphoric acid to a pH of 7.2 ± 0.2.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
6	60	40
20	18	82
20.1	60	40
25.1	60	40

System suitability solution: 0.5 mg/mL of fluvastatin sodium from USP Fluvastatin for System Suitability RS, dissolved first in *Solution B*, using 40% of the final volume, then diluted with *Solution A* to volume

Standard solution: 0.5 mg/mL of USP Fluvastatin Sodium RS, dissolved first in *Solution B*, using 40% of the final volume, then diluted with *Solution A* to volume

Sample solution: 0.5 mg/mL of Fluvastatin Sodium, dissolved first in *Solution B*, using 40% of the final volume, then diluted with *Solution A* to volume

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 305 nm

Column: 4.6-mm × 5-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 3 mL/min

Injection volume: 20 µL

[NOTE—Adjust the start time of the gradient step and the equilibration time for each instrument.]

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for fluvastatin and fluvastatin *anti*-isomer are about 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 1.6 between fluvastatin *anti*-isomer and fluvastatin, *System suitability solution*

Tailing factor: NMT 3.0 for the fluvastatin peak, *System suitability solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of fluvastatin sodium ($C_{24}H_{25}FNNaO_4$) in the portion of Fluvastatin Sodium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Fluvastatin Sodium RS in the *Standard solution* (mg/mL)

C_U = concentration of Fluvastatin Sodium in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

• **ORGANIC IMPURITIES**

[NOTE—Protect all solutions from light, and use amber autosampler vials and low-actinic glassware.]

Solution A, Solution B, Mobile phase, Standard solution, and **Sample solution:** Prepare as directed in the *Assay*.

System suitability solution A: Prepare as directed for the *System suitability solution* in the *Assay*.

System suitability solution B: 0.1 mg/mL of USP Fluvastatin Related Compound B RS in a mixture of methanol and acetonitrile (60:40). Transfer about 0.5 mL of this solution to a 10-mL volumetric flask, and dilute with *System suitability solution A* to volume. [NOTE—*System suitability solution B* is stable for up to 6 months if stored in a refrigerator.]

Chromatographic system: Proceed as directed in the *Assay*, except for the *Detector*.

Detector

UV 365 nm: 3-Hydroxy-5-keto fluvastatin

UV 305 nm: For all other peaks

System suitability

Samples: *Standard solution* and *System suitability solution B*

Suitability requirements

Resolution: NLT 1.6 between fluvastatin *anti*-isomer and fluvastatin, *System suitability solution B*

Tailing factor: NMT 3.0 for the fluvastatin peak, *System suitability solution B*

Relative standard deviation: NMT 1.0% at 305 nm, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Record the chromatograms at 305 and 365 nm, identify the impurities listed in *Table 2*, and measure the peak responses.

Calculate the percentage of each impurity, except for 3-hydroxy-5-keto fluvastatin, in the portion of Fluvastatin Sodium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response at 305 nm of each impurity from the *Sample solution*

r_S = peak response at 305 nm of fluvastatin from the *Standard solution*

C_S = concentration of USP Fluvastatin Sodium RS in the *Standard solution* (mg/mL)

C_U = concentration of Fluvastatin Sodium in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Calculate the percentage of 3-hydroxy-5-keto fluvastatin in the portion of Fluvastatin Sodium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response at 365 nm of 3-hydroxy-5-keto fluvastatin from the *Sample solution*

r_S = peak response at 365 nm of fluvastatin from the *Standard solution*

C_S = concentration of USP Fluvastatin Sodium RS in the *Standard solution* (mg/mL)

C_U = concentration of Fluvastatin Sodium in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Fluvastatin *N*-ethyl analog[a]	0.7	1.2	0.1
Fluvastatin *anti*-isomer[b]	1.2	1.0	0.8
3-Hydroxy-5-keto fluvastatin[c]	1.5	27.0[d]	0.1
Fluvastatin hydroxydiene[e]	2.0	0.92	0.1
Fluvastatin short-chain aldehyde[f]	3.0	1.4	0.1
Fluvastatin related compound B	3.4	0.94	0.2
Any unspecified impurity	—	1.0	0.1
Total impurities	—	—	1.0

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

[b] [*R**,*R**-*E*]-(±)-7-[3-(4-Fluorophenyl)-1-(methylethyl)-1*H*-indol-2-yl]-3,5-dihydroxy-6-heptenoic acid monosodium salt; also known as Sodium (3*RS*,5*RS*,*E*)-7-(3-(4-fluorophenyl)-1-isopropyl-1*H*-indol-2-yl)-3,5-dihydroxyhept-6-enoate.

[c] Sodium (*E*)-7-[3-(4-fluorophenyl)-1-isopropyl-1*H*-indol-2-yl]-3-hydroxy-5-oxohept-6-enoate.

[d] At 365 nm.

[e] Sodium (4*E*,6*E*)-7-[3-(4-fluorophenyl)-1-isopropyl-1*H*-indol-2-yl]-3-hydroxyhepta-4,6-dienoate.

[f] 3-(4-Fluorophenyl)-1-isopropyl-1*H*-indole-2-carbaldehyde.

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 8.0–10.0, in a 10-mg/mL solution. Perform the test immediately after preparation.

• **Water Determination** ⟨921⟩, *Method I***:** NMT 4.0%; if labeled as a hydrated form, NMT 12.0%. [Note—For this monograph, the term "hydrated form" refers to several known forms of fluvastatin sodium that are not stoichiometric hydrates.]

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, protected from moisture. Store at a temperature not exceeding 40°.

• **Labeling:** Where it is a hydrated form, the label so indicates.

• **USP Reference Standards** ⟨11⟩

USP Fluvastatin Sodium RS

USP Fluvastatin Related Compound B RS

Fluvastatin *t*-butyl ester.

[*R**,*S**-*E*]-(±)-7-[3-(4-Fluorophenyl)-1-methylethyl-1*H*-indol-2-yl]-3,5-dihydroxy-6-heptenoic acid 1,1-dimethylethyl ester; also known as *tert*-Butyl (3*RS*,5*SR*,*E*)-7-[3-(4-fluorophenyl)-1-isopropyl-1*H*-indol-2-yl]-3,5-dihydroxyhept-6-enoate.

$C_{28}H_{34}FNO_4$ 467.58

USP Fluvastatin for System Suitability RS

Fluvastatin sodium, containing 1%–2% of the fluvastatin sodium *anti*-isomer.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
FLUVASTATIN SODIUM	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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