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Fluvastatin Capsules

DEFINITION

Fluvastatin Capsules contain fluvastatin sodium ($C_{24}H_{25}FNNaO_4$) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of fluvastatin ($C_{24}H_{26}FNO_4$).

IDENTIFICATION

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

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ *(USP 1-Aug-2019)*

ASSAY

Change to read:

• **Procedure**

▲[Note—Protect all solutions from light.]▲ (USP 1-Aug-2019)

Buffer: Prepare a solution containing 40 mL of 25% aqueous tetramethylammonium hydroxide in 1 L of water. Adjust with approximately 4.5 mL of phosphoric acid to a pH of 7.2.

Solvent mixture: Methanol and acetonitrile (60:40)

Solution A: *Solvent mixture* and *Buffer* (12.5:87.5)

Solution B: *Solvent mixture* and *Buffer* (87.5:12.5)

Mobile phase: See *Table 1*. ▲▲ (USP 1-Aug-2019)

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	54	46
6	54	46
17	17	83
20	17	83
20.1	54	46
26.1	54	46

Diluent: *Solvent mixture* and *Buffer* (46:54)

System suitability solution: 0.42 mg/mL of fluvastatin sodium from USP Fluvastatin for System Suitability RS in *Diluent*

Standard solution: 0.42 mg/mL of USP Fluvastatin Sodium RS, equivalent to 0.4 mg/mL of fluvastatin, in *Diluent*

Sample stock solution: Nominally 1.0 mg/mL of fluvastatin from Capsules prepared as follows. Transfer the contents and the empty shells of ▲a suitable number of▲ (USP 1-Aug-2019) Capsules, equivalent to 200 mg of fluvastatin, to a 200-mL volumetric flask. Add 100 mL of methanol, and stir with a magnetic or mechanical stirrer for 45 min. Centrifuge a portion of this solution at 4000 rpm for 20 min.

Sample solution: Nominally 0.4 mg/mL of fluvastatin from *Sample stock solution* in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 305 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-Aug-2019)

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

Flow rate: 2.0 mL/min

Injection volume: 25 µL

▲▲ (USP 1-Aug-2019)

System suitability

Samples: *System suitability solution* ▲and *Standard solution*▲ *(USP 1-Aug-2019)*

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

Suitability requirements

Resolution: NLT 1.4 between fluvastatin anti-isomer and fluvastatin, *System suitability solution*

▲▲ (USP 1-Aug-2019)

Relative standard deviation: NMT 1.5%, ▲*Standard solution*▲ (USP 1-Aug-2019)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fluvastatin ($C_{24}H_{26}FNO_4$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of fluvastatin from the *Sample solution*

r_S = peak response of fluvastatin from the *Standard solution*

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

C_U = nominal concentration of fluvastatin in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of fluvastatin, ▲411.47▲ (USP 1-Aug-2019)

M_{r2} = molecular weight of fluvastatin sodium, 433.45

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **DISSOLUTION** ⟨711⟩

Medium: Water; 500 mL

Apparatus 2: 50 rpm, sinkers not used

Time: 30 min

▲▲ (USP 1-Aug-2019)

Buffer: 1.534 g of monobasic ammonium phosphate in 800 mL of water. Adjust with phosphoric acid or ammonium hydroxide to a pH of 3.5.

Mobile phase: Methanol and *Buffer* (7:3)

Standard solution:▲ (0.002 × *L*) mg/mL of USP Fluvastatin Sodium RS in *Medium*, where *L* is the label claim in mg/Capsule▲ (USP 1-Aug-2019)

[NOTE—A volume of methanol, not exceeding 2% of the final volume of solution, may be used to aid in dissolving USP Fluvastatin Sodium RS.]

Sample solution: Pass a portion of the solution under test through a suitable filter, discarding the first 2 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Columns

Guard: ▲3.2-mm × 1.5-cm;▲ (USP 1-Aug-2019) 7-µm packing L1

Analytical: 4.6-mm × 10-cm; 5-µm packing L1

Flow rate: 2.0 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

▲Calculate the percentage of the labeled amount of fluvastatin ($C_{24}H_{26}FNO_4$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of fluvastatin from the *Sample solution*

r_S = peak response of fluvastatin from the *Standard solution*

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

V = volume of *Medium*, 500 mL

L = label claim (mg/Capsule)

M_{r1} = molecular weight of fluvastatin, 411.47

M_{r2} = molecular weight of fluvastatin sodium, 433.45

▲ (USP 1-Aug-2019)

Tolerances: NLT 80% (*Q*) of the labeled amount of fluvastatin ($C_{24}H_{26}FNO_4$) is dissolved.

Change to read:

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements ▲▲ (USP 1-Aug-2019)

IMPURITIES

Change to read:

• **Organic Impurities**

▲▲ (USP 1-Aug-2019)

Buffer, Solvent mixture, Solution A, Solution B, Mobile phase, Diluent, System suitability solution, Standard solution, and **Sample solution:** Prepare as directed in the *Assay*.

▲**Sensitivity solution:** 0.21 µg/mL of USP Fluvastatin Sodium RS in *Diluent*, from *Standard solution*▲ (USP 1-Aug-2019)

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

Detector

UV 365 nm: For 3-hydroxy-5-keto fluvastatin

UV 305 nm: For all the other impurities

System suitability

Samples: *System suitability solution*, ▲*Standard solution*, and *Sensitivity solution*▲ (USP 1-Aug-2019)

Suitability requirements

Resolution: NLT 1.4 between fluvastatin anti-isomer and fluvastatin, *System suitability solution*

Relative standard deviation: NMT 1.5%, ▲*Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*▲ (USP 1-Aug-2019)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each ▲degradation product▲ (USP 1-Aug-2019) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

r_U = peak response of each ▲degradation product▲ (USP 1-Aug-2019) from the *Sample solution*

r_S = peak response of fluvastatin from the *Standard solution*

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

C_U = nominal concentration of fluvastatin in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of fluvastatin, ▲411.47▲ (USP 1-Aug-2019)

M_{r2} = molecular weight of fluvastatin sodium, 433.45

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

▲▲ (USP 1-Aug-2019)

Acceptance criteria: ▲See *Table 2*. The reporting threshold is 0.05%.▲ (USP 1-Aug-2019)

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
▲Fluvastatin	1.0	—	—▲ (USP 1-Aug-2019)
Fluvastatin *anti*-isomer[▲a▲] (USP 1-Aug-2019)	1.2	1.0	1.5
3-Hydroxy-5-keto fluvastatin[▲b▲] (USP 1-Aug-2019)	1.6	27.0[c]	1.0
Fluvastatin hydroxydiene[▲d▲] (USP 1-Aug-2019)	2.2	0.92	1.0
Fluvastatin short-chain aldehyde[▲e▲] (USP 1-Aug-2019)	3.2	1.4	0.5
▲Any unspecified degradation product	—	1.0	0.5▲ (USP 1-Aug-2019)
▲Total degradation products	—	—	4.0▲ (USP 1-Aug-2019)

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

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

[c] At 365 nm.

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

[e] 3-(4-Fluorophenyl)-1-(methylethyl)-1*H*-indole-2-carboxaldehyde.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, protected from moisture and from light. Store in a cool place or at controlled room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Fluvastatin Sodium RS

USP Fluvastatin for System Suitability RS

▲Fluvastatin sodium, containing 1%–2% of the fluvastatin sodium *anti*-isomer.▲ (USP 1-Aug-2019)

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

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

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