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Lovastatin Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-lovastatin-tabs-20210528.

DEFINITION

Lovastatin Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of lovastatin ($C_{24}H_{36}O_5$).

IDENTIFICATION

- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay.*
- **B.** 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**

Buffer: Dissolve 3.45 g of monobasic sodium phosphate in 900 mL of water. Adjust with phosphoric acid to a pH of 4.0, and dilute with water to 1000 mL.

Mobile phase: Acetonitrile, methanol, and *Buffer* (50:10:30)

Solution A: Mix 3.0 mL of glacial acetic acid with 900 mL of water in a 1-L beaker, and adjust with 20% sodium hydroxide solution to a pH of 4.0. Transfer the contents of the beaker to a 1000-mL volumetric flask, and dilute with water to volume.

Diluent: Acetonitrile and *Solution A* (80:20)

Standard solution: 40 µg/mL of USP Lovastatin RS in *Diluent*

Sample stock solution: Nominally 0.2 mg/mL of lovastatin prepared as follows. Weigh and finely powder NLT 20 Tablets. Transfer a portion of the powder, equivalent to 40 mg of lovastatin, to a 200-mL volumetric flask. Add 150 mL of *Diluent*, and sonicate for 20 min. Cool to room temperature, and allow the solution to stand for 30 min. Dilute with *Diluent* to volume. Centrifuge a portion of this solution, and use the supernatant.

Sample solution: Nominally 40 µg/mL of lovastatin in *Diluent* from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

Run time: NLT 2.5 times the retention time of lovastatin

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lovastatin ($C_{24}H_{36}O_5$) in the portion of Tablets taken:

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

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

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

C_S = concentration of USP Lovastatin RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of lovastatin in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 1.38 g of monobasic sodium phosphate and 20 g of sodium lauryl sulfate in 900 mL of water. Adjust with 1 N sodium hydroxide to a pH of 7.0, and dilute with water to 1000 mL; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Mobile phase: Proceed as directed in the *Assay*.

Standard solution: Weigh 44 mg of USP Lovastatin RS into a 500-mL volumetric flask, and dissolve in NMT 20 mL of methanol. Dilute with *Medium* to volume. Further dilute this solution with *Medium* to obtain a final concentration of *L*/900 mg/mL, where *L* is the label claim in mg/Tablet.

Sample solution: Pass the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

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

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Capacity factor, *k'*: NLT 2.0

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lovastatin ($C_{24}H_{36}O_5$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

L = label claim of lovastatin (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of lovastatin ($C_{24}H_{36}O_5$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

• **Organic Impurities**

Buffer, Mobile phase, Solution A, Diluent, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 4 µg/mL of USP Mevastatin RS and 4 µg/mL of USP Lovastatin RS in *Diluent*

Sensitivity solution: 0.08 µg/mL of USP Lovastatin RS in *Diluent* from the *Standard solution*

System suitability

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

Suitability requirements

Resolution: NLT 2.0, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lovastatin acid and any unspecified degradation product in the portion of Tablets taken:

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

r_U = peak response of lovastatin acid or any unspecified degradation product from the *Sample solution*

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

C_S = concentration of USP Lovastatin RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of lovastatin in the *Sample solution* (µg/mL)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Butylated hydroxyanisole[a]	0.45	—	—
Lovastatin acid[b]	0.61	0.91	▲1.5▲ (RB 1-Jun-2021)
Mevastatin[c]	0.78	—	—
Lovastatin	1.00	—	—
Any unspecified degradation product	—	1.0	0.2
Total degradation products[d]	—	—	2.5

[a] Preservative in the formulation; if present, not included in the calculation.

[b] (3*R*,5*R*)-7-[(1*S*,2*S*,6*R*,8*S*,8a*R*)-2,6-Dimethyl-8-{[(*S*)-2-methylbutanoyl]oxy}-1,2,6,7,8,8a-hexahydronaphthalen-1-yl]-3,5-dihydroxyheptanoic acid.

[c] For resolution measurement only.

[d] Total degradation products is the sum of all related compounds except lovastatin acid.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers. Protect from light, and store either in a cool place or at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Lovastatin RS

USP Mevastatin RS

(1*S*,7*S*,8*S*,8a*R*)-8-{2-[(2*R*,4*R*)-4-Hydroxy-6-oxotetrahydro-2*H*-pyran-2-yl]ethyl}-7-methyl-1,2,3,7,8,8a-hexahydronaphthalen-1-yl (*S*)-2-methylbutanoate.

$C_{23}H_{34}O_5$ 390.52

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

Topic/Question	Contact	Expert Committee
LOVASTATIN TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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