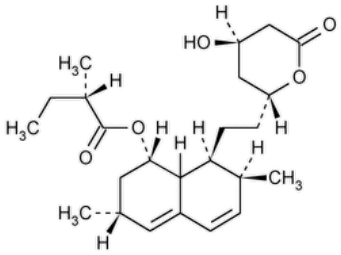
Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-50ACE7BD-C24B-41BD-A564-61C073EA74A3_5_en-US
DOI: https://doi.org/10.31003/USPNF_M45950_05_01
DOI Ref: gbcwo

Lovastatin



$C_{24}H_{36}O_5$ 404.54

Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2*H*-pyran-2-yl)-ethyl]-1-naphthalenyl ester, [1*S*-[1α(*R**),3α,7β,8β(2*S**,4*S**),8aβ]]-.

(*S*)-2-Methylbutyric acid, 8-ester with (4*R*,6*R*)-6-[2-[(1*S*,2*S*,6*R*,8*S*,8a*R*)-1,2,6,7,8,8a-hexahydro-8-hydroxy-2,6-dimethyl-1-naphthyl]ethyl]tetrahydro-4-hydroxy-2*H*-pyran-2-one CAS RN®: 75330-75-5; UNII: 9LHU78OQFD.

» Lovastatin contains not less than 98.5 percent and not more than 101.0 percent of $C_{24}H_{36}O_5$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers under nitrogen in a cold place.

USP Reference standards ⟨11⟩—

USP Lovastatin RS

USP Lovastatin Related Compound A RS

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

$C_{24}H_{38}O_5$ 406.56

Identification—

Change to read:

A: ▲*Spectroscopic Identification Tests* ⟨197⟩*, Infrared Spectroscopy: 197M*▲ (CN 1-May-2020) ·

Change to read:

B: ▲*Spectroscopic Identification Tests* ⟨197⟩*, Ultraviolet-Visible Spectroscopy: 197U*▲ (CN 1-May-2020)

Solution: 10 µg per mL.

Medium: acetonitrile.

Specific rotation ⟨781S⟩**:** between +324° and +338°.

Test solution: 5 mg per mL, in acetonitrile.

Loss on drying ⟨731⟩—Dry it in vacuum at a pressure not exceeding 5 mm of mercury at 60° for 3 hours: it loses not more than 0.3% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.2%.

Limit of lovastatin related compound A—

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile and 0.01 M phosphoric acid (13:7). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

System suitability solution—Dissolve accurately weighed quantities of USP Lovastatin RS and USP Lovastatin Related Compound A RS in acetonitrile, and dilute quantitatively, and stepwise if necessary, to obtain a solution containing 2.0 µg of each per mL.

Standard solution—Dissolve an accurately weighed quantity of USP Lovastatin RS in acetonitrile, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 2.0 µg per mL.

Test solution—Transfer about 25 mg of Lovastatin, accurately weighed, to a 25-mL volumetric flask, dissolve in and dilute with acetonitrile to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 200-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L7. The column temperature is maintained at 40°. The flow rate is about 1.5 mL per minute. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 1.0 for lovastatin and 1.3 for lovastatin related compound A; and the resolution, *R,* between lovastatin and lovastatin related compound A is not less than 6.0. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 5.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure all the peak responses. Calculate the percentage of lovastatin related compound A in the portion of Lovastatin taken by the formula:

$$2.5F(C/W)(r_U/r_S)$$

in which F is the response factor for lovastatin related compound A and is equal to 1.6; C is the concentration, in µg per mL, of USP Lovastatin RS in the *Standard solution;* W is the weight, in mg, of Lovastatin in the *Test solution;* r_U is the peak response for lovastatin related compound A obtained from the *Test solution;* and r_S is the peak response for lovastatin obtained from the *Standard solution:* not more than 0.5% of lovastatin related compound A is found.

Chromatographic purity—

Solution A—Prepare a 0.001 M phosphoric acid solution, adjusted with 1 M sodium hydroxide to a pH of 4.0.

Solution B—Use acetonitrile.

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system.* Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

System suitability solution—Dissolve accurately weighed quantities of USP Lovastatin RS and compactin in acetonitrile, and dilute quantitatively, and stepwise if necessary, with acetonitrile to obtain a solution containing 2.0 µg of each per mL.

Standard solution—Dissolve an accurately weighed quantity of USP Lovastatin RS in acetonitrile, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 2.0 µg per mL.

Test solution—Transfer about 25 mg of Lovastatin, accurately weighed, to a 25-mL volumetric flask, dissolve in and dilute with acetonitrile to volume, and mix.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 238-nm detector and a 4.0-mm × 12.5-cm column that contains 4-µm packing L1. The column temperature is maintained at 40°. The flow rate is about 1.5 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0–2	60	40	isocratic
2–5	60→45	40→55	linear gradient
5–8	45	55	isocratic
8–16	45→10	55→90	linear gradient
16–25	10	90	isocratic
25–27	10→60	90→40	linear gradient
27–35	60	40	isocratic

Chromatograph the *System suitability solution* and the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 1.00 for lovastatin and 0.85 for compactin; the resolution, R, between lovastatin and compactin is not less than 3.5; and the relative standard deviation for replicate injections is not more than 5%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure all the peak responses. Calculate the percentage of each impurity in the portion of Lovastatin taken by the formula:

$$2.5(C/W)(r_i/r_S)F$$

in which C is the concentration, in µg per mL, of USP Lovastatin RS in the *Standard solution;* W is the weight, in mg, of Lovastatin in the *Test solution;* r_i is the peak response for each impurity obtained from the *Test solution;* r_S is the peak response for lovastatin obtained from the *Standard solution;* and F is the response factor for each impurity and is equal to 1.4 for the impurity with a relative retention time of about 0.73 and 1.0 for all other impurities. Disregard any peak with less than 0.04%: not more than 0.2% of any individual impurity is found; and not more than 1.0% of total impurities is found.

Assay—

Dilute phosphoric acid—Transfer 1 mL of phosphoric acid to a 1-L volumetric flask, and dilute with water to volume.

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile and *Dilute phosphoric acid* (65:35). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Dissolve an accurately weighed quantity of USP Lovastatin RS in acetonitrile to obtain a solution having a known concentration of about 0.3 mg per mL.

Assay preparation—Transfer about 30 mg of Lovastatin, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with acetonitrile to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 238-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L7. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 3000 theoretical plates, the tailing factor is not more than 1.4, and the relative standard deviation for replicate injections is not more than 1.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{24}H_{36}O_5$ in the portion of Lovastatin taken by the formula:

$$100C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Lovastatin RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 32(1)

Current DocID: GUID-50ACE7BD-C24B-41BD-A564-61C073EA74A3_5_en-US
Previous DocID: GUID-50ACE7BD-C24B-41BD-A564-61C073EA74A3_4_en-US
DOI: https://doi.org/10.31003/USPNF_M45950_05_01
DOI ref: gbcwo