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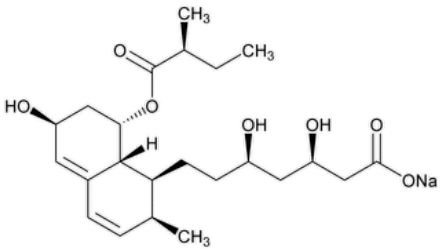
Pravastatin Sodium



$C_{23}H_{35}NaO_7$ 446.52

1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ,6-trihydroxy-2-methyl-8-(2-methyl-1-oxobutoxy)-, monosodium salt, [1*S*-[1α(β*S**,δ*S**),2α,6α,8β(*R**),8aα]]-;

Sodium (β*R*,δ*R*,1*S*,2*S*,6*S*,8*S*,8a*R*)-1,2,6,7,8,8a-hexahydro-β,δ,6,8-tetrahydroxy-2-methyl-1-naphthaleneheptanoate, 8-[(2*S*)-2-methylbutyrate] CAS RN®: 81131-70-6; UNII: 3M8608UQ61.

DEFINITION

Pravastatin Sodium contains NLT 97.5% and NMT 102.0% of pravastatin sodium ($C_{23}H_{35}NaO_7$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**
- **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: 0.08 M phosphoric acid solution. Adjust with a 25% sodium hydroxide solution to a pH of 5.5.

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

Solution C: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution B (%)	Solution C (%)
0	100	0
7.0	90	10
10.0	62.5	37.5
17.0	62.5	37.5
17.1	100	0
20.0	100	0

System suitability solution: 0.25 mg/mL of USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS and 0.001 mg/mL of USP Pravastatin Related Compound A RS in methanol

Standard solution: 0.25 mg/mL of USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS in methanol

Sample solution: 0.2 mg/mL of Pravastatin Sodium in methanol

Chromatographic system

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

Mode: LC

Detector: UV 238 nm

Column: 4.0-mm × 10-cm; 3-µm packing *L1*

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for pravastatin and pravastatin related compound A are about 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 1.2 between pravastatin and pravastatin related compound A

Relative standard deviation: NMT 2.0% for the pravastatin peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of pravastatin sodium ($C_{23}H_{35}NaO_7$) in the portion of Pravastatin Sodium taken:

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

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

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

C_S = concentration of USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of pravastatin sodium, 446.52

M_{r2} = molecular weight of pravastatin 1,1,3,3-tetramethylbutylamine, 553.78

Acceptance criteria: 97.5%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

• **ORGANIC IMPURITIES**

[NOTE—The *Standard solution* and the *Sample solution* are maintained at 15° until injected into the chromatograph.]

Diluent: Methanol and water (50:50)

Solution A: 0.08 M phosphoric acid solution. Adjust with triethylamine to a pH of 7.0.

Solution B: Acetonitrile, *Solution A*, and water (18:30:52)

Solution C: Acetonitrile, *Solution A*, and water (60:30:10)

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution B (%)	Solution C (%)
0	100	0
3.0	100	0
26.5	0	100
26.6	100	0

Time (min)	Solution B (%)	Solution C (%)
30.0	100	0

System suitability solution: 0.6 mg/mL of USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS and 0.001 mg/mL of USP Pravastatin Related Compound A RS in *Diluent*. [NOTE—USP Pravastatin Related Compound A RS is a sodium salt of 3α-hydroxyisocompactin acid.]

Standard solution: 1.25 µg/mL of USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS in *Diluent*

Sample solution: 0.5 mg/mL of Pravastatin Sodium in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 238 nm

Column: 4.6-mm × 7.5-cm; 3.5-µm packing L1.

[NOTE—Alternatively, a 4.0-mm × 10-cm; 3-µm packing L1 can be used.]

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—The relative retention times for pravastatin and pravastatin related compound A are about 1.0 and 1.1, respectively.]

Suitability requirements

Resolution: NLT 2.0 between pravastatin and pravastatin related compound A, *System suitability solution*

Relative standard deviation: NMT 10.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each specified or any unspecified impurity in the portion of Pravastatin Sodium taken:

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

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

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

C_S = concentration of USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of pravastatin sodium, 446.52

M_{r2} = molecular weight of pravastatin 1,1,3,3-tetramethylbutylamine, 553.78

Acceptance criteria: See *Table 3*. The reporting level for impurities is 0.05%.

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
3"-Hydroxypravastatin	0.33	0.2
6'-Epi-pravastatin	0.92	0.3
Pravastatin	1.0	—
Pravastatin related compound A	1.1	0.2
Pentanoyl impurity[a]	1.2	0.2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Pravastatin lactone	1.8	0.2
Compactin	3.1	0.2
Any unspecified impurity	—	0.10
Total impurities	—	0.6

[a] (3*R*,5*R*)-3,5-Dihydroxy-7-[(1*S*,2*S*,6*S*,8*S*,8a*R*)-6-hydroxy-2-methyl-8-[[(2*S*)-2-methylpentanoyl]oxy]-1,2,6,7,8,8a-hexahydronaphthalen-1-yl]heptanoic acid.

SPECIFIC TESTS

• **Limit of Alcohol** (if present)

Standard stock solution 1: Pipet 2 mL of dehydrated alcohol into a 100-mL volumetric flask, and dilute with water to volume.

Standard stock solution 2: Pipet 10 mL of *Standard stock solution 1* into a 100-mL volumetric flask, and dilute with water to volume.

Sample stock solution: Transfer 0.2 g of Pravastatin Sodium to a 20-mL volumetric flask, and dilute with water to volume.

Sample solution: Pipet 5 mL of the *Sample stock solution* into a vial fitted with a septum and a crimp cap, add 1 mL of water, seal the vial, and mix. Heat the sealed vial at 80° for 60 min.

Standard solution: Pipet 1 mL of *Standard stock solution 2* into a vial fitted with a septum and a crimp cap, and calculate the amount of alcohol (W_A) added in grams (the specific gravity of dehydrated alcohol is 0.79 g/mL). Add 5 mL of the *Sample solution* to the same vial, and seal the vial. Heat the sealed vial at 80° for 60 min.

Blank solution: Pipet 6 mL of water into a vial fitted with a septum and a crimp cap, and seal the vial. Heat the sealed vial at 80° for 60 min.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 30-m fused silica capillary; coated with a 3-µm film of stationary phase G43

Temperatures

Transfer line: 85°

Injection port: 140°

Detector: 250°

Column: See *Table 4*.

Table 4

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	0	40	20
40	10	240	—
240	0	240	20

Carrier gas: Helium

Flow rate: Linear velocity of 35 cm/s

Injection volume: 1 mL

Injection type: Split ratio, 1:5

System suitability

Sample: *Blank solution*

Suitability requirement: No interfering peaks are observed.

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of alcohol in the portion of Pravastatin Sodium taken:

$$\text{Result} = [r_U/(r_S - r_U)] \times (W_A/W) \times D \times 100$$

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

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

W_A = amount of alcohol added (g)

W = weight of Pravastatin Sodium taken to prepare the *Sample solution* (g)

D = dilution factor for the *Sample solution*, 4

Acceptance criteria: NMT 3.0%

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 5 mg/mL in water

Acceptance criteria: +150° to +160° (at 20°), calculated on the anhydrous and solvent-free basis

• **pH** ⟨791⟩**:** 7.2–9.0, in a solution (1 in 20)

• **Water Determination** ⟨921⟩, *Method I*: NMT 4.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store as per labeling instructions. Possible storage conditions could include the following, in the presence of stability data supporting the condition: Store under nitrogen in a cold place. Store at room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS

2,4,4-Trimethylpentan-2-amine (3*R*,5*R*)-3,5-dihydroxy-7-[(1*S*,2*S*,6*S*,8*S*,8a*R*)-6-hydroxy-2-methyl-8-{[(*S*)-2-methylbutanoyl]oxy}-1,2,6,7,8,8a-hexahydronaphthalen-1-yl]heptanoate.

$C_{23}H_{36}O_7 \cdot C_8H_{19}N$ 553.78

USP Pravastatin Sodium RS

USP Pravastatin Related Compound A RS

Sodium (3*R*,5*R*)-3,5-dihydroxy-7-[(1*S*,2*R*,3*S*,8*S*,8a*R*)-3-hydroxy-2-methyl-8-[[(2*S*)-2-methylbutanoyl]oxy]-1,2,3,7,8,8a-hexahydronaphthalen-1-yl]heptanoate.

$C_{23}H_{35}NaO_7$ ▲446.52▲ (ERR 1-Jun-2020)

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

Topic/Question	Contact	Expert Committee
PRAVASTATIN SODIUM	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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