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Pravastatin Sodium Tablets

» Pravastatin Sodium contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of pravastatin sodium ($C_{23}H_{35}NaO_7$).

Packaging and storage—Preserve in tight containers. Protect from moisture and light. Store at controlled room temperature.

USP Reference standards ⟨11⟩—

USP Pravastatin Related Compound A RS

3-α-Hydroxyisocompactinor sodium (3*R*,5*R*)-3,5-dihydroxy-7-[(1*S*,2*S*,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.

$C_{23}H_{35}NaO_7$ 446.51

USP Pravastatin Related Compound B RS

6′-Epi-pravastatinor sodium (3*R*,5*R*)-3,5-dihydroxy-7-[(1*S*,2*S*,6*R*,8*S*,8a*R*)-6-hydroxy-2-methyl-8-[[(2*S*)-2-methylbutanoyl]oxy]-1,2,6,7,8,8a-hexahydronaph thalen-1-yl]heptanoate.

$C_{23}H_{35}NaO_7$ 446.51

USP Pravastatin Sodium RS

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

Identification—

A: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Change to read:

B: ▲*Spectroscopic Identification Tests ⟨197⟩, Ultraviolet-Visible Spectroscopy: 197U*▲ (CN 1-May-2020) —Finely powder a number of Tablets, and extract with water a portion equivalent to about 10 mg of pravastatin sodium. The UV absorption spectrum of a solution of pravastatin sodium in water containing about 10 µg per mL exhibits maxima at the same wavelength as that of a similar solution of USP Pravastatin Sodium RS, concomitantly measured between 220 and 340 nm.

Dissolution ⟨711⟩—

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Procedure—Determine the amount of $C_{23}H_{35}NaO_7$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 238 nm on filtered portions of the solution under test, suitably diluted with *Medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS in the same *Medium.*

[Note—To express the concentration of the Standard solution as pravastatin sodium, use the conversion factor of (446.51/553.78), in which 446.51 and 553.78 are the molecular weights of pravastatin sodium and pravastatin 1,1,3,3-tetramethylbutylamine, respectively.]

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{23}H_{35}NaO_7$ is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Related compounds—[Note—Maintain the *Test solution* at 15° until injected into the chromatograph. Without refrigeration, the *Test solution* should be prepared fresh.]

Diluent—Prepare a mixture of methanol and water (1:1).

Buffer pH 7.0—Prepare a 0.08 M phosphoric acid solution, adjust with triethylamine to a pH of 7.0, and mix.

Solution A—Prepare a filtered and degassed mixture of water, *Buffer pH 7.0,* and acetonitrile (52:30:18).

Solution B—Prepare a filtered and degassed mixture of acetonitrile, *Buffer pH 7.0,* and water (60:30:10).

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⟩*).

Standard solution—Dissolve an accurately weighed quantity of USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS in *Diluent,* and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 1.25 µg of pravastatin

1,1,3,3-tetramethylbutylamine per mL.

System suitability solution—Dissolve accurately weighed quantities of USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS and USP Pravastatin Related Compound A RS in *Diluent* to obtain a solution containing about 0.6 mg of USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS and 0.001 mg of USP Pravastatin Related Compound A RS per mL. [NOTE—USP Pravastatin Related Compound A RS is a sodium salt of 3α-hydroxyisocompactin acid.]

Test solution—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 50 mg of pravastatin sodium, to a 100-mL volumetric flask. Add 60 mL of the *Diluent*, sonicate for 15–20 minutes, dilute with *Diluent* to volume, and mix. Pass through a 0.45-µm nylon filter.

Chromatographic system (see *Chromatography* ⟨621⟩—The liquid chromatograph is equipped with a 238-nm detector and a 4.6-mm × 7.5-cm column that contains 3.5-µm packing L1. Alternatively, a 4.0-mm × 10-cm column that contains 3-µm packing L1 can be used. The flow rate is about 1 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0–3.0	100	0	isocratic
3.0–26.5	100→0	0→100	linear gradient
26.5–26.6	0→100	100→0	linear gradient
26.6–30.0	100	0	re-equilibration

Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 1.0 for pravastatin and 1.1 for pravastatin related compound A; and the resolution, *R,* between pravastatin and pravastatin related compound A is not less than 2.0. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 10.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, identify the impurities listed in *Table 1,* and measure the peak responses.

Table 1

Name	Relative Retention Time	Limit (%)
Oxidation impurity[1]	0.61	1
6′-Epipravastatin[2]	0.92	0.3
Pravastatin sodium	1.0	—
Pravastatin lactone	1.8	2
Any other individual impurity	—	0.2
Total impurities	—	3

[1] Sodium (3*R*,5*R*)-3,5-dihydroxy-7-((1*S*,2*S*)-6-hydroxy-2-methyl-1,2-dihydronaphthalen-1-yl)heptanoate.

[2] USP Pravastatin Related Compound B RS.

Calculate the percentage of each impurity in the portion of Tablets taken by the formula:

$$100\times(446.51/553.78)(C_S/C_T)(r_I/r_S)$$

in which 446.51 and 553.78 are the molecular weights of pravastatin sodium and pravastatin 1,1,3,3-tetramethylbu tylamine, respectively; C_S is the concentration, in mg per mL, of pravastatin 1,1,3,3-tetramethylbutylamine in the *Standard solution;* C_T is the nominal concentration, in

mg per mL, of pravastatin sodium in the *Test solution*; r_i is the peak response for each impurity obtained from the *Test solution*; and r_S is the pravastatin peak response obtained from the *Standard solution*. The reporting level for impurities is 0.1%.

Assay—[NOTE—The *Standard preparation*, *Assay stock preparation,* and *Assay preparation* can be stored for up to 7 days at room temperature.]

Mobile phase—Prepare a filtered and degassed mixture of methanol, water, glacial acetic acid, and triethylamine (500:500:1:1). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Diluent 1—Transfer 16.4 g of anhydrous sodium acetate into a 2000-mL volumetric flask. Add 1600 mL of water, adjust with glacial acetic acid to a pH of 5.6, dilute with water to volume, and mix.

Diluent 2—Prepare a mixture of *Diluent 1* and methanol (80:20).

Standard preparation—Transfer an accurately weighed quantity of USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS to a suitable volumetric flask, and dissolve in *Diluent 1* using sonication to obtain a solution having a known concentration of about 0.6 mg of pravastatin 1,1,3,3-tetramethylbutylamine per mL. Dilute 5.0 mL of this solution with *Diluent 2* to 25.0 mL, and mix.

Assay stock preparation—Transfer not fewer than 5 Tablets to a suitable volumetric flask with at least a (*NL*×2)-mL capacity, *N* being the number of Tablets transferred, and *L* being the label claim per Tablet, filled to at least 80% capacity with *Diluent 1*. [NOTE—It is necessary to fill the flask to 80% capacity to maintain the correct pH throughout the preparation.] Shake for at least 1 hour, and sonicate for at least 15 minutes with periodic shaking of the flask by hand, until the Tablets have completely disintegrated. Allow to cool, and dilute with *Diluent 1* to volume. Centrifuge a portion of the solution for 15 minutes at 2000 rpm, or filter.

Assay preparation—Dilute approximately 5 mL of the *Assay stock preparation* with *Diluent 2* to obtain a solution having an expected concentration of about 0.1 mg per mL, based on the label claim.

Resolution solution—Transfer about 2 mg of USP Pravastatin Related Compound B RS to a 10-mL volumetric flask. Dissolve in and dilute with methanol to volume. Transfer 0.1 mL of this solution and 1.0 mL of the *Standard preparation* to a small tube, and mix. [NOTE—Pravastatin related compound B is the 6'-epipravastatin sodium.]

Chromatographic system (see *CHROMATOGRAPHY ⟨621⟩*)—The liquid chromatograph is equipped with a 238-nm detector and a 4.6-mm × 5-cm column than contains endcapped packing L1. Alternatively, a 3.9-mm × 7.5-cm column containing endcapped packing L1 can be used. The flow rate is about 1.0 mL per minute. Chromatograph the *Resolution solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.7 for pravastatin related compound B and 1.0 for pravastatin; the resolution, *R,* between the pravastatin related compound B and the pravastatin peaks is not less than 3.0. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the peak response for pravastatin. Calculate the percentage of pravastatin sodium ($C_{23}H_{35}NaO_7$) in the portion of Tablets taken by the formula:

$$100(446.51/553.78)(CVD/NL)(r_U/r_S)$$

in which 100 is the conversion factor to percentage; 446.51 and 553.78 are the molecular weights of pravastatin sodium and pravastatin 1,1,3,3-tetramethylbutylamine, respectively; *C* is the concentration, in mg per mL, of pravastatin 1,1,3,3-tetramethylbutylamine in the *Standard preparation; V* is the volume, in mL, of the *Assay stock preparation; D* is the dilution factor of the *Assay preparation; N* is the number of Tablets taken to prepare the *Assay stock preparation; L* is the label claim, in mg of pravastatin sodium per Tablet; and r_U and r_S are the pravastatin 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
PRAVASTATIN SODIUM TABLETS	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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