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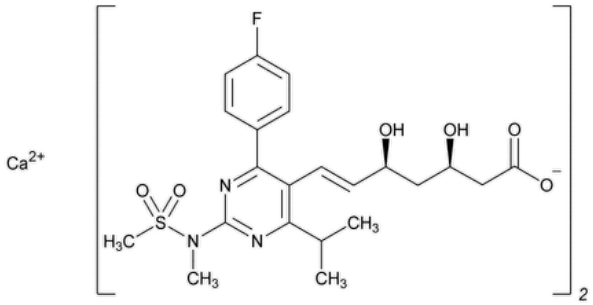
Rosuvastatin Calcium

Change to read:



$Ca(C_{22}H_{27}FN_3O_6S)_2$ 1001.14

6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, calcium salt (2:1), (3*R*,5*S*,6*E*);

[*S*-[*R**,*S**-(*E*)]]-7-[4-(4-Fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-6-heptenoic acid, calcium salt (2:1);

Calcium (3*R*,5*S*,*E*)-7-(4-(4-fluorophenyl)-6-isopropyl-2-(*N*-methylmethylsulfonamido)pyrimidin-5-yl)-3,5-dihydroxyhept-6-enoate salt (1:2) CAS RN®: 147098-20-2; ▲UNII: 83MVU38M7Q.

Rosuvastatin (free acid)

$C_{22}H_{28}FN_3O_6S$ 481.54 CAS RN®: 287714-41-4; UNII: 413KH5ZJ73.▲ (USP 1-Aug-2024)

DEFINITION

Rosuvastatin Calcium contains NLT 97.0% and NMT 103.0% of rosuvastatin calcium [$Ca(C_{22}H_{27}FN_3O_6S)_2$], calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K▲▲ (USP 1-Aug-2024)

Change to read:

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the ▲*Assay*.▲ (USP 1-Aug-2024)

• **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Calcium***

Sample solution: 8 mg/mL of Rosuvastatin Calcium in a mixture of methanol and water (50:50)

Acceptance criteria: Meets the requirements

ASSAY

Change to read:

• **Procedure**

Protect all solutions containing rosuvastatin calcium and its related compounds from light.

Solution A: Acetonitrile, 1% (v/v) aqueous trifluoroacetic acid, and water (29:1:70)

Solution B: Acetonitrile, 1% (v/v) aqueous trifluoroacetic acid, and water (75:1:24)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
30	100	0
50	60	40
60	0	100
70	0	100
71	100	0
80	100	0

Diluent: Acetonitrile and water (25:75)

▲**System suitability stock solution A:** 1 mg/mL of USP Rosuvastatin System Suitability Mixture RS in *Diluent*▲ (USP 1-Aug-2024)

System suitability ▲stock▲ (USP 1-Aug-2024) solution ▲B:▲ (USP 1-Aug-2024) 0.25 mg/mL each of USP Rosuvastatin Related Compound A RS and USP Rosuvastatin Related Compound B RS in a mixture of acetonitrile and water (50:50)

System suitability ▲stock▲ (USP 1-Aug-2024) solution ▲C:▲ (USP 1-Aug-2024) 0.04 mg/mL of USP Rosuvastatin Related Compound C RS in a mixture of acetonitrile and water (50:50)

▲**System suitability solution:** 0.4 mg/mL of USP Rosuvastatin System Suitability Mixture RS, 5 µg/mL of USP Rosuvastatin Related Compound A RS, 5 µg/mL of USP Rosuvastatin Related Compound B RS, and 0.8 µg/mL of USP Rosuvastatin Related Compound C RS prepared as follows. Mix 10 mL of *System suitability stock solution A*, 0.5 mL of *System suitability stock solution B*, and 0.5 mL of *System suitability stock solution C* in a 25 mL-volumetric flask. Bring to volume with *Diluent*.▲ (USP 1-Aug-2024)

Standard solution: 0.7 mg/mL of USP Rosuvastatin Calcium RS in *Diluent*

Sample solution: 0.7 mg/mL of Rosuvastatin Calcium in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 242 nm

Column: 3.0-mm × 15-cm; 3-µm packing L1

Column temperature: 40°

Flow rate: 0.75 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution*▲▲ (USP 1-Aug-2024) and *Standard solution*

[NOTE—▲The relative retention times for rosuvastatin related compound B and rosuvastatin related compound C are 2.2 and 2.6, respectively.▲ (USP 1-Aug-2024) See *Table 2* for ▲the rest of▲ (USP 1-Aug-2024) the relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between rosuvastatin and rosuvastatin diastereomer▲▲ (USP 1-Aug-2024) , *System suitability solution* ▲▲ *(USP 1-Aug-2024)*

Tailing factor: NMT 1.5 ▲▲ (USP 1-Aug-2024) , *Standard solution*

▲**Relative standard deviation:** NMT 1.10%, *Standard solution*▲ (USP 1-Aug-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of rosuvastatin calcium $[Ca(C_{22}H_{27}FN_3O_6S)_2]$ in the portion of Rosuvastatin Calcium taken:

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

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

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

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

C_U = concentration of Rosuvastatin Calcium in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–103.0% on the anhydrous and solvent-free basis

IMPURITIES

Change to read:

• **Organic Impurities**

Protect all solutions containing rosuvastatin calcium and its related compounds from light.

▲**Solution A, Solution B,**▲ (USP 1-Aug-2024) **Mobile phase, Diluent,** ▲**System suitability stock solution A, System suitability stock solution B, System suitability stock solution C,**▲ (USP 1-Aug-2024) **System suitability solution** ▲▲ (USP 1-Aug-2024) **, Sample solution,** and **Chromatographic system**▲▲ (USP 1-Aug-2024) **:** Proceed as directed in the *Assay*.

Standard solution: 1.4 µg/mL of USP Rosuvastatin Calcium RS in *Diluent*

▲**Sensitivity solution:** 0.35 µg/mL of USP Rosuvastatin Calcium RS from the *Standard solution* in *Diluent*

System suitability

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

[Note—The relative retention times for rosuvastatin related compound B and rosuvastatin related compound C are 2.2 and 2.6, respectively. See *Table 2* for the rest of the relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between rosuvastatin and rosuvastatin diastereomers, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*▲ (USP 1-Aug-2024)

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each impurity in the portion of Rosuvastatin Calcium taken:

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

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

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

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

C_U = concentration of Rosuvastatin Calcium in the *Sample solution* (mg/mL)

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

Acceptance criteria: See *Table 2*. ▲The reporting threshold is 0.05%.▲ (USP 1-Aug-2024)

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Rosuvastatin related compound A	0.9	1.00	0.2
Rosuvastatin	1.0	1.00	—
Rosuvastatin diastereomers[a]	1.1	1.00	0.5

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Rosuvastatin ketone[b]	1.5	0.71	0.8
Rosuvastatin lactone ▲▲ (USP 1-Aug-2024)	1.7	1.00	0.15
Rosuvastatin dehydro analog[c]	1.8	1.00	0.15
▲▲ (USP 1-Aug-2024)	▲▲ (USP 1-Aug-2024)	▲▲ (USP 1-Aug-2024)	▲▲ (USP 1-Aug-2024)
▲▲ (USP 1-Aug-2024)	▲▲ (USP 1-Aug-2024)	▲▲ (USP 1-Aug-2024)	▲▲ (USP 1-Aug-2024)
Any unspecified impurity	—	1.00	0.10
Total impurities	—	—	1.5

[a] (3*RS*,5*RS*,*E*)-7-[4-(4-Fluorophenyl)-6-isopropyl-2-(*N*-methylmethylsulfonamido)pyrimidin-5-yl]-3,5-dihydroxyhept-6-enoic acid.

[b] (*R*,*E*)-7-[4-(4-Fluorophenyl)-6-isopropyl-2-(*N*-methylmethylsulfonamido)pyrimidin-5-yl]-3-hydroxy-5-oxohept-6-enoic acid.

[c] (*S*,2*ZE*,6*E*)-7-[4-(4-Fluorophenyl)-6-isopropyl-2-(*N*-methylmethylsulfonamido)pyrimidin-5-yl]-5-hydroxyhepta-2,6-dienoic acid.

Change to read:

• **Enantiomeric Purity**

▲Protect▲ (USP 1-Aug-2024) all solutions containing rosuvastatin calcium and its related compounds ▲from light.▲ (USP 1-Aug-2024)

Mobile phase: Acetonitrile and 0.1% (v/v) trifluoroacetic acid in water (25:75)

Diluent: Acetonitrile and water (25:75)

System suitability solution: 1 mg/mL of USP Rosuvastatin Calcium RS and 0.004 mg/mL of USP Rosuvastatin Enantiomer RS in *Diluent*

Standard solution: 0.005 mg/mL of USP Rosuvastatin Calcium RS in *Diluent*

Sample solution: 1 mg/mL of Rosuvastatin Calcium in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 242 nm

Column: 4.6-mm × 15-cm; 5-µm packing L107

Column temperature: 35°

Flow rate: 0.5 mL/min

Injection volume: 10 µL

▲**Run time:** NLT 2.7 times the retention time of rosuvastatin▲ (USP 1-Aug-2024)

System suitability

Samples: *System suitability solution* ▲and *Standard solution*▲ (USP 1-Aug-2024)

[Note—The relative retention times for rosuvastatin enantiomer and rosuvastatin are about 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between rosuvastatin enantiomer and rosuvastatin▲▲ (USP 1-Aug-2024) , *System suitability solution*

Tailing factor: NMT 1.8, ▲*Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*▲ (USP 1-Aug-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of rosuvastatin enantiomer in the portion of Rosuvastatin Calcium taken:

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

r_U = peak response of rosuvastatin enantiomer from the *Sample solution*

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

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

C_U = concentration of Rosuvastatin Calcium in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 0.15%

Delete the following:

▲• **Limit of Chloride**▲ (USP 1-Aug-2024)

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I, Method Ia* or *Method Ic*: NMT 6%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, protected from light. Store at controlled room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Rosuvastatin Calcium RS

USP Rosuvastatin Enantiomer RS

Calcium (3*S*,5*R*,*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-(*N*-methylmethylsulfonamido)pyrimidin-5-yl]-3,5-dihydroxyhept-6-enoate salt (1:2).

$Ca(C_{22}H_{27}FN_3O_6S)_2$ 1001.14

USP Rosuvastatin Related Compound A RS

Calcium (3*R*,5*S*,*E*)-7-{4-(4-fluorophenyl)-2-[(2-hydroxy-*N*,2-dimethylpropyl)▲sulfonamido▲ (USP 1-Aug-2024)]-6-isopropylpyrimidin-5-yl}-3,5-dihydroxyhept-6-enoate salt (1:2).

$Ca(C_{25}H_{33}FN_3O_7S)_2$ 1117.30

USP Rosuvastatin Related Compound B RS

Calcium (3*R*,5*S*,*E*)-7-(4-(4-fluorophenyl)-2-{2-[4-(4-fluorophenyl)-6-isopropyl-2-(*N*-methylmethylsulfonamido)pyrimidin-5-yl]-2-hydroxy-*N*-methylethylsulfonamido}-6-isopropylpyrimidin-5-yl)-3,5-dihydroxyhept-6-enoate salt (1:2).

$Ca(C_{38}H_{45}F_2N_6O_9S_2)_2$ 1703.93

USP Rosuvastatin Related Compound C RS

tert-Butyl 2-[(4*R*,6*S*)-6-{(*E*)-2-[4-(4-fluorophenyl)-6-isopropyl-2-(*N*-methylmethylsulfonamido)pyrimidin-5-yl]vinyl}-2,2-dimethyl-1,3-dioxan-4-yl]acetate.

$C_{29}H_{40}FN_3O_6S$ 577.71

▲ USP Rosuvastatin System Suitability Mixture RS

Contains a mixture of the following 4 compounds. Other impurities may also be present.

Rosuvastatin calcium.

Rosuvastatin ketone: Calcium (*R*,*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-(*N*-methylmethylsulfonamido)pyrimidin-5-yl]-3-hydroxy-5-oxohept-6-enoate salt (1:2).

$Ca(C_{22}H_{25}FN_3O_6S)_2$ 997.11

Rosuvastatin lactone: *N*-[4-(4-Fluorophenyl)-5-{(*E*)-2-[(2*S*,4*R*)-4-hydroxy-6-oxotetrahydro-2*H*-pyran-2-yl]vinyl}-6-isopropylpyrimidin-2-yl]-*N*-methylmethanesulfonamide.

$C_{22}H_{26}FN_3O_5S$ 463.52

Rosuvastatin diastereomers: Calcium (3*RS*,5*RS*,*E*)-7-(4-(4-fluorophenyl)-6-isopropyl-2-(*N*-methylmethylsulfonamido)pyrimidin-5-yl)-3,5-dihydroxyhept-6-enoate salt (1:2).

$Ca(C_{22}H_{27}FN_3O_6S)_2$ 1001.14▲ (USP 1-Aug-2024)

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

Topic/Question	Contact	Expert Committee
ROSUVASTATIN CALCIUM	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

Most Recently Appeared In:
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