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Rosuvastatin Tablets

Change to read:

DEFINITION

Rosuvastatin Tablets contain ▲an amount of rosuvastatin calcium [$Ca(C_{22}H_{27}FN_3O_6S)_2$] equivalent to▲ (USP 1-Aug-2024) NLT 90% and NMT 110% of the labeled amount of rosuvastatin ($C_{22}H_{28}FN_3O_6S$).

IDENTIFICATION

Change to read:

• **A.** The UV ▲spectrum▲ (USP 1-Aug-2024) of the ▲major▲ (USP 1-Aug-2024) peak of the *Sample solution* ▲corresponds to that▲ (USP 1-Aug-2024) 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

Change to read:

• **Procedure**

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

Solution A: 1% trifluoroacetic acid in water

Mobile phase: Acetonitrile, *Solution A*, and water (37:1:62)

Diluent: Acetonitrile and water (25:75)

Standard stock solution: 1 mg/mL of USP Rosuvastatin Calcium RS prepared as follows. To a suitable amount of USP Rosuvastatin Calcium RS in a suitable volumetric flask, add water equal to about 50% of the flask volume. Vigorously mix or sonicate the flask to dissolve the material. Add acetonitrile equal to about 25% of the total volume and then dilute with water to volume.

Standard solution: 25 µg/mL of USP Rosuvastatin Calcium RS from the *Standard stock solution*, in *Diluent*

Sample solution: Nominally 25 µg/mL of rosuvastatin prepared as follows. Transfer a suitable number of Tablets, NLT 5 Tablets for 80-mg Tablet strength and NLT 10 Tablets for all other Tablet strengths, into a suitable extraction flask. Add water and vigorously mix to disintegrate the Tablets. Add acetonitrile and mix vigorously. Add more water to obtain a 25:75 composition of acetonitrile and water. Pass the solution through a suitable filter. Dilute the filtrate with *Diluent*, if necessary, to the desired concentration.

Chromatographic system

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

Mode: LC

Detector: UV 242 nm. For *Identification A*, use a diode array detector in the range of 200–▲400▲ (USP 1-Aug-2024) nm.

Column: 3.2-mm × 25-cm; 5-µm packing L1. [Note—A suitable guard column may be used.]

Column temperature: 40°

Flow rate: 0.75 mL/min

Injection volume: 10 µL

Run time: NLT 1.3 times the retention time of rosuvastatin

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.8

Relative standard deviation: NMT ▲1.0%▲ (USP 1-Aug-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of rosuvastatin ($C_{22}H_{28}FN_3O_6S$) in the portion of Tablets taken:

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

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* (µg/mL)

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

M = number of moles of rosuvastatin per mole of rosuvastatin calcium, 2

M_{r1} = molecular weight of rosuvastatin, 481.54

M_{r2} = molecular weight of rosuvastatin calcium, 1001.14

Acceptance criteria: 90%–110%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

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

Test 1

Medium: Citrate buffer, pH 6.6 (prepare a solution of 14.7 g/L of sodium citrate dihydrate and 0.33 g/L of anhydrous citric acid; adjust if necessary with ▲sodium citrate dihydrate▲ (USP 1-Aug-2024) or citric acid to a pH of 6.6); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Diluent: Acetonitrile and water (25:75)

Mobile phase: ▲Acetonitrile and water (40:60). To each liter, add 1 mL of phosphoric acid.▲ (USP 1-Aug-2024)

Standard stock solution: 1 mg/mL of USP Rosuvastatin Calcium RS in *Diluent*

Standard solution: A solution of concentration similar to the *Sample solution* from the *Standard stock solution*, in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 242 nm

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

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 2.5 times the retention time of rosuvastatin

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of rosuvastatin ($C_{22}H_{28}FN_3O_6S$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times [M \times (M_{r1}/M_{r2})] \times 100$$

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)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

M = number of moles of rosuvastatin per mole of rosuvastatin calcium, 2

M_{r1} = molecular weight of rosuvastatin, 481.54

M_{r2} = molecular weight of rosuvastatin calcium, 1001.14

Tolerances: NLT 75% (Q) of the labeled amount of rosuvastatin ($C_{22}H_{28}FN_3O_6S$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets *Dissolution Test 2*.

Medium: 0.05 M citrate buffer pH 6.6 (to a solution of 10.5 g/L of citric acid monohydrate, add 5.9 g/L of sodium hydroxide and mix; adjust with 0.2 M sodium hydroxide or 0.2 M hydrochloric acid to a pH of 6.6); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Buffer: Dissolve 2.72 g of potassium dihydrogen phosphate in 1 L of water and add 2 mL of triethylamine. Adjust with phosphoric acid to a pH of 2.5.

Mobile phase: Acetonitrile and *Buffer* (30:70)

Standard stock solution: 0.5 mg/mL of USP Rosuvastatin Calcium RS in *Medium*. Sonication may be necessary for complete dissolution.

Standard solution: (L/900) mg/mL of USP Rosuvastatin Calcium RS from the *Standard stock solution*, in *Medium*, ▲where L is the label claim in mg/Tablet▲ (USP 1-Aug-2024)

Sample solution: Pass a portion of 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 240 nm

Column: 4.6-mm × 10-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of rosuvastatin

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 rosuvastatin ($C_{22}H_{28}FN_3O_6S$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times [M \times (M_{r1}/M_{r2})] \times 100$$

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)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

M = number of moles of rosuvastatin per mole of rosuvastatin calcium, 2

M_{r1} = molecular weight of rosuvastatin, 481.54

M_{r2} = molecular weight of rosuvastatin calcium, 1001.14

Tolerances: NLT 80% (Q) of the labeled amount of rosuvastatin ($C_{22}H_{28}FN_3O_6S$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets *Dissolution Test 3*.

Medium: 0.05 M citrate buffer pH 6.6 (▲10.5 g/L of citric acid monohydrate and 5.9 g/L of sodium hydroxide in water;▲ (USP 1-Aug-2024) adjust if necessary with sodium hydroxide or citric acid to a pH of 6.6); 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Standard stock solution: 0.044 mg/mL of USP Rosuvastatin Calcium RS in *Medium*. Sonication may be necessary for complete dissolution.

Standard solution: (*L*/900) mg/mL of USP Rosuvastatin Calcium RS in *Medium* from the *Standard stock solution*, where *L* is the label claim in mg/Tablet. [NOTE—The *Standard stock solution* is the *Standard solution* for 40-mg Tablets.]

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

Instrumental conditions

Mode: UV

Analytical wavelength: 241 nm

Cell: 1.0 cm (for 5-mg and 10-mg Tablets) and 0.2 cm (for 20-mg and 40-mg Tablets)

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of rosuvastatin ($C_{22}H_{28}FN_3O_6S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times [M \times (M_{r1}/M_{r2})] \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

M = number of moles of rosuvastatin per mole of rosuvastatin calcium, 2

M_{r1} = molecular weight of rosuvastatin, 481.54

M_{r2} = molecular weight of rosuvastatin calcium, 1001.14

Tolerances: NLT 80% (*Q*) of the labeled amount of rosuvastatin ($C_{22}H_{28}FN_3O_6S$) is dissolved.

Test 4: If the product complies with this test, the labeling indicates that it meets *Dissolution Test 4*.

Medium: 0.05 M sodium citrate buffer pH 6.6 (prepare a solution of 14.7 g/L of sodium citrate dihydrate and 0.33 g/L of anhydrous citric acid; adjust if necessary with 10% w/v sodium citrate dihydrate solution or 10% w/v anhydrous citric acid solution to a pH of 6.6); 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Solution A: Acetonitrile and water (25:75)

Mobile phase: ▲Acetonitrile and water (40:60). To each liter, add 1 mL of phosphoric acid.▲ (USP 1-Aug-2024)

Standard stock solution: 1.04 mg/mL of USP Rosuvastatin Calcium RS in *Solution A*. Sonication may be necessary for complete dissolution.

Standard solution: (*L*/900) mg/mL of USP Rosuvastatin Calcium RS in *Medium* from the *Standard stock solution*, where *L* is the label claim in mg/Tablet

Sample solution: Pass a portion of 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 242 nm

Column: 4.6-mm × 5-cm; 3.5-µm packing L1

Flow rate: 1▲▲ (USP 1-Aug-2024) mL/min

Injection volume: 20 µL

Run time: NLT 3.5 times the retention time of rosuvastatin

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of rosuvastatin ($C_{22}H_{28}FN_3O_6S$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times [M \times (M_{r1}/M_{r2})] \times 100$$

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)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

M = number of moles of rosuvastatin per mole of rosuvastatin calcium, 2

M_{r1} = molecular weight of rosuvastatin, 481.54

M_{r2} = molecular weight of rosuvastatin calcium, 1001.14

Tolerances: NLT 80% (*Q*) of the labeled amount of rosuvastatin ($C_{22}H_{28}FN_3O_6S$) is dissolved.

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

IMPURITIES

Change to read:

• **Organic Impurities**

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

▲**Solution A,**▲ (USP 1-Aug-2024) **Mobile phase,** and **Diluent:** Prepare as directed in the *Assay*.

▲▲ (USP 1-Aug-2024)

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

Standard solution: 10 µg/mL of USP Rosuvastatin Calcium RS in *Diluent*

▲**Sensitivity solution:** 1 µg/mL of USP Rosuvastatin Calcium RS from *Standard solution*, in *Diluent*▲ (USP 1-Aug-2024)

Sample solution: Nominally 1 mg/mL of rosuvastatin prepared as follows. Transfer a number of Tablets per *Table 1* into a suitable extraction flask. Add water, and mix vigorously to disintegrate the Tablets. Add acetonitrile and mix vigorously followed by an additional amount of water to obtain a final composition of acetonitrile and water (25:75). Pass the solution through a suitable filter.

Table 1

Tablet Strength (mg)	Number of Tablets	Volumetric Flask Size (mL)	Water (mL)	Acetonitrile (mL)
2.5	40	100	50	25
5	20	100	50	25
10	10	100	50	25
20	10	200	100	50
40	12	500	250	125

Tablet Strength (mg)	Number of Tablets	Volumetric Flask Size (mL)	Water (mL)	Acetonitrile (mL)
80	6	500	250	125

Chromatographic system

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

Mode: LC

Detector: UV 242 nm

Column: 3.2-mm × 25-cm; 5-µm packing L1. [NOTE—A suitable guard column may be used.]

Column temperature: 40°

Flow rate: 0.75 mL/min

Injection volume: 10 µL

Run time: NLT 2.5 times the retention time of rosuvastatin

System suitability

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

[NOTE—See *Table 2* for the relative retention times.]▲ (USP 1-AUG-2024)

Suitability requirements

Resolution: NLT 1.5 between rosuvastatin and rosuvastatin diastereomers, *System suitability solution*

Tailing factor: NMT 1.8, *Standard solution*

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ▲any specified or unspecified degradation product▲ (USP 1-Aug-2024) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times [M \times (M_{r1}/M_{r2})] \times (1/F) \times 100$$

r_U = peak response of ▲any specified or unspecified degradation product▲ (USP 1-Aug-2024) 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 = nominal concentration of rosuvastatin in the *Sample solution* (mg/mL)

M = number of moles of rosuvastatin per mole of rosuvastatin calcium, 2

M_{r1} = molecular weight of rosuvastatin, 481.54

M_{r2} = molecular weight of rosuvastatin calcium, 1001.14

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

Acceptance criteria: See *Table 2*. ▲The reporting threshold is 0.1%.▲ (USP 1-Aug-2024)

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Rosuvastatin related compound A▲[a,b]▲ (USP 1-Aug-2024)	0.9	—	—

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Rosuvastatin	1.0	—	—
Rosuvastatin diastereomers [b,c]	1.1	—	—
Rosuvastatin ketone[d]	1.6	0.71	2.1
Rosuvastatin lactone[e]	2.3	1.0	1.5
Rosuvastatin ethyl ester (if present)[f]	3.8	1.0	0.5
Any unspecified degradation product	—	1.0	0.2
Total degradation products	—	—	3.6

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

[b] Process impurity controlled in the drug substance monograph. Provided for information only; the content is not calculated, not reported, and not included in the total ▲degradation products.▲ (USP 1-Aug-2024)

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

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

[e] *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.

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

ADDITIONAL REQUIREMENTS

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

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Rosuvastatin Calcium RS

▲ 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 TABLETS	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

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