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Atorvastatin Calcium Tablets

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DEFINITION

Atorvastatin Calcium Tablets contain an amount of atorvastatin calcium [$(C_{33}H_{34}FN_2O_5)_2Ca$], equivalent to NLT 94.5% and NMT 105.0% of the labeled amount of atorvastatin.

IDENTIFICATION

• **A.** The UV absorption spectrum of the major peak of the *Sample solution* corresponds to that 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

• **Procedure**

Buffer: 0.05 M ammonium citrate buffer pH 4.0 prepared as follows. Dissolve 9.62 g of anhydrous citric acid in 950 mL of water, adjust with ammonium hydroxide to a pH of 4.0, and dilute with water to 1000 mL.

Mobile phase: Acetonitrile, stabilizer-free tetrahydrofuran, and *Buffer* (27:20:53)

Solution A: Dissolve 9.62 g of anhydrous citric acid in 900 mL of water, adjust with ammonium hydroxide to a pH of 7.4, and dilute with water to 1000 mL.

Diluent: Acetonitrile and *Solution A* (1:1)

System suitability solution: 0.1 mg/mL of USP Atorvastatin Calcium RS and 0.01 mg/mL of USP Atorvastatin Related Compound H RS in *Diluent*. Shake mechanically for 30 min or until dissolved.

Standard solution: 0.1 mg/mL of USP Atorvastatin Calcium RS in *Diluent*. Shake mechanically for 15 min or until dissolved.

Sample stock solution: Prepare a known nominal concentration of atorvastatin by transferring NLT 10 Tablets to an appropriate volumetric flask. Add *Diluent* to about 50% of the final volume of the flask, and shake the mixture mechanically for 15 min or until dissolved. Dilute with *Diluent* to volume. Centrifuge or pass through a suitable filter of 0.45-µm pore size.

Sample solution: Nominally equivalent to 0.1 mg/mL of atorvastatin in *Diluent* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector

Assay: UV 244 nm

Identification A: Diode array; UV 200–400 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 5.0 between atorvastatin and atorvastatin related compound H, *System suitability solution*

Tailing factor: NMT 1.5 for atorvastatin, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$) 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 atorvastatin from the *Sample solution*

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

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

C_U = nominal concentration of atorvastatin in the *Sample solution* (mg/mL)

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

M_{r1} = molecular weight of atorvastatin, 558.65

M_{r2} = molecular weight of atorvastatin calcium,1155.36

Acceptance criteria: 94.5%–105.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Buffer: 0.05 M phosphate buffer prepared as follows. Dissolve 6.8 g of monobasic potassium phosphate in 900 mL of water. Adjust with 6 N sodium hydroxide to a pH of 6.8 and dilute with water to 1 L.

Medium: *Buffer*; 900 mL

Apparatus 2: 75 rpm

Time: 15 min

Diluent: Acetonitrile and water (50:50)

Standard stock solution: 1 mg/mL of USP Atorvastatin Calcium RS in *Diluent*. Shake mechanically for 10 min or until dissolved.

Standard solution: (*L*/900) mg/mL in *Medium* from *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 or centrifuge prior to analysis.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 244 nm

Cell: See *Table 1* or make appropriate dilutions of the solutions with *Medium* to be within the validated linearity range of the suitable spectrophotometer.

Table 1

Label Claim (mg/Tablet)	Cell (cm)
10	1.0
20 and 40	0.5
80	0.2

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

D = dilution factor for the *Sample solution*, if applicable

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

M_{r1} = molecular weight of atorvastatin, 558.65

M_{r2} = molecular weight of atorvastatin calcium, 1155.36

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L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*. *Dissolution Test 2* is suitable for products labeled to contain 80 mg of atorvastatin.

Medium and **Apparatus 2:** Proceed as directed in *Test 1*.

Time: 30 min

Diluent, Standard solution, Sample solution, Instrumental conditions, and **Blank:** Proceed as directed in *Test 1*.

Tolerances: NLT 85% (Q) of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$) is dissolved.

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

Buffer: Combine 250 mL of 0.2 M monobasic potassium phosphate, 112 mL of 0.2 N sodium hydroxide, and 638 mL of water. Adjust with either 0.02 N sodium hydroxide or phosphoric acid to a pH of 6.8.

Solution A: Acetonitrile, methanol, and 0.1% trifluoroacetic acid (5:5:90)

Solution B: Acetonitrile, methanol, and 0.1% trifluoroacetic acid (45:45:10)

Solution C: Dissolve 50 g of ▲polysorbate 80▲ (RB 1-Sep-2023) in 1 L of *Buffer*.

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0.00	30	70
0.69	30	70
0.74	0	100
2.73	0	100
2.77	30	70
5.00	30	70

Medium: *Solution C* and *Buffer* (6:94); 900 mL

Apparatus 2: 75 rpm

Time: 30 min

Standard stock solution: 0.96 mg/mL of USP Atorvastatin Calcium RS in methanol

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of (L/900) mg/mL, 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 248 nm

Column: 2.1-mm × 5-cm; 2.6-µm packing L1

Column temperature: 40°

Flow rate: 0.7 mL/min

Injection volume: 2 µL

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 atorvastatin ($C_{33}H_{35}FN_2O_5$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

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

M_{r1} = molecular weight of atorvastatin, 558.65

M_{r2} = molecular weight of atorvastatin calcium, 1155.36

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$) is dissolved.

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

Medium: Dissolve 6.8 g of monobasic potassium phosphate and 0.89 g of sodium hydroxide in 1 L of water. Adjust with either 1 N sodium hydroxide or phosphoric acid to a pH of 6.8; 900 mL.

Apparatus 2: 75 rpm

Time: 15 min

Buffer: Dissolve about 6.8 g of monobasic potassium phosphate in 1000 mL of water. Adjust with 0.5 N potassium hydroxide solution to a pH of 6.0.

Mobile phase: Acetonitrile and *Buffer* (55:45)

Standard stock solution: 0.225 mg/mL of atorvastatin from USP Atorvastatin Calcium RS prepared as follows. To a suitable amount of USP Atorvastatin Calcium RS, add 5% of total volume of methanol, sonicate to dissolve, and cool. Dilute with *Medium* to volume.

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of (L/900) mg/mL, 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 248 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

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 atorvastatin ($C_{33}H_{35}FN_2O_5$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

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

M_{r1} = molecular weight of atorvastatin, 558.65

M_{r2} = molecular weight of atorvastatin calcium, 1155.36

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$) is dissolved.

Test 5: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 5*.

Medium: Dissolve 6.8 g of monobasic potassium phosphate and 0.9 g of sodium hydroxide in 1 L of water. Adjust with either sodium hydroxide or phosphoric acid to a pH of 6.8; 900 mL.

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Apparatus 2: 75 rpm

Time: 20 min

Buffer: Dissolve 10.5 g of citric acid in 1000 mL of water. Adjust with ammonium hydroxide to a pH of 4.0.

Mobile phase: Acetonitrile, tetrahydrofuran, and *Buffer* (50:10:40)

Diluent: Acetonitrile and water (50:50)

Standard stock solution: 0.925 mg/mL of USP Atorvastatin Calcium RS in *Diluent*. Sonicate to dissolve.

Standard solution: (*L*/900) mg/mL in *Medium* from *Standard stock solution*, where *L* is the label claim in mg/Tablet. Pass the solution through a suitable filter of 0.45-µm pore size and discard the first few milliliters of the filtrate.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size and discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 244 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Temperatures

Autosampler: 10°

Column: 30°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

Run time: NLT 2 times the retention time of atorvastatin

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 atorvastatin ($C_{33}H_{35}FN_2O_5$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

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

M_{r1} = molecular weight of atorvastatin, 558.65

M_{r2} = molecular weight of atorvastatin calcium, 1155.36

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$) is dissolved.

Test 6: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 6*.

Medium: 0.05 M phosphate buffer, pH 6.8, prepared as follows. Dissolve 6.8 g of monobasic potassium phosphate and 0.89 g of sodium hydroxide in 1 L of water. Adjust with 1 N sodium hydroxide to a pH of 6.8; 900 mL.

Apparatus 2: 100 rpm

Time: 20 min

Buffer: 1.36 g/L of monobasic potassium phosphate in water

Mobile phase: Acetonitrile and *Buffer* (50:50). Adjust with phosphoric acid solution to a pH of 2.8.

Diluent: Acetonitrile and water (50:50)

Standard stock solution: 0.461 mg/mL of USP Atorvastatin Calcium RS in *Diluent*. Sonicate to dissolve.

Standard solution: (*L*/900) mg/mL in *Medium* from *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, and discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

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Detector: UV 238 nm

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

Temperatures

Autosampler: 10°

Column: 30°

Flow rate: 0.8 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of atorvastatin

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 atorvastatin ($C_{33}H_{35}FN_2O_5$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

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

M_{r1} = molecular weight of atorvastatin, 558.65

M_{r2} = molecular weight of atorvastatin calcium, 1155.36

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$) is dissolved.

▲**Test 7:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 7*.

Medium: 0.05 M pH 6.8 phosphate buffer (dissolve 6.8 g of monobasic potassium phosphate in 900 mL of water; adjust with 6 N sodium hydroxide to a pH of 6.8 and dilute with water to 1 L); 900 mL

Apparatus 2: 60 rpm

Time: 30 min

Diluent: Acetonitrile and water (50:50)

Standard stock solution: 1 mg/mL of USP Atorvastatin Calcium RS in *Diluent*. Shake mechanically for 10 min or until dissolved.

Standard solution: (L/900) mg/mL of atorvastatin, contained in USP Atorvastatin Calcium RS, from *Standard stock solution* in *Medium*, where L is the label claim of atorvastatin in mg/Tablet. [NOTE—The *Standard solution* may be stable for 6 h at room temperature.]

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.8-µm pore size, discarding the first 3 mL of the filtrate. [NOTE—The *Sample solution* may be stable for 6 h at room temperature.]

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 244 nm

Cell

For Tablets labeled to contain 10 mg: 1 cm

For Tablets labeled to contain 20 or 40 mg: 0.5 cm

For Tablets labeled to contain 80 mg: 0.2 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times [M \times (Mr_1/Mr_2)] \times (1/L) \times 100$$

A_U = absorbance of atorvastatin from the *Sample solution*

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A_S = absorbance of atorvastatin from the *Standard solution*

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

V = volume of *Medium*, 900 mL

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

Mr_1 = molecular weight of atorvastatin, 558.65

Mr_2 = molecular weight of atorvastatin calcium, 1155.36

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$) is dissolved.▲ (RB 1-Sep-2023)

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

IMPURITIES

• **Organic Impurities**

Rinse glassware with *Diluent* before preparing solutions containing atorvastatin calcium.

Buffer: 5.75 g/L of monobasic ammonium phosphate in water. Adjust with dilute acetic acid (10% v/v) or dilute ammonium hydroxide (10% v/v) to a pH of 4.3 ± 0.05.

Solution A: Acetonitrile and stabilizer-free tetrahydrofuran (925:75)

Solution B: *Solution A* and *Buffer* (42:58)

Solution C: Methanol, *Solution A*, and *Buffer* (60:20:20)

Diluent: *N*,*N*-Dimethylformamide

System suitability solution: 60 µg/mL of USP Atorvastatin Calcium RS, 50 µg/mL of USP Atorvastatin Related Compound B RS, 10 µg/mL of USP Atorvastatin Related Compound H RS, and 0.5 µg/mL of USP Atorvastatin Related Compound D RS in *Diluent*

Standard solution: 5 µg/mL of USP Atorvastatin Calcium RS in *Diluent*. Sonication may be necessary for complete dissolution.

Sample solution: Nominally equivalent to 1 mg/mL of atorvastatin, prepared as follows. Crush and finely powder NLT 20 Tablets. Transfer the amount of powder, equivalent to about 50 mg of atorvastatin, to a 50-mL volumetric flask. Add 30 mL of *Diluent* and shake mechanically for 15 min. Dilute with *Diluent* to volume and pass the solution through a suitable filter of 0.45-µm pore size, discarding the first few mL of the filtrate.

Mobile phase: See *Table 3*.

Table 3

Time (min)	Solution B (%)	Solution C (%)	Flow Rate (mL/min)
0	100	0	1.8
30	100	0	1.8
45	25	75	1.5
50	25	75	1.5
55	20	80	1.5
58	100	0	1.8
65	100	0	1.8

For the *Standard solution*, the run time is only 30 min. For the *System suitability solution* and *Sample solution*, the run time is 65 min.

Chromatographic system

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

Mode: LC

Detector: UV 244 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Temperatures

Autosampler: 10°

Column: 30°

Flow rate: See *Table 3*.

Injection volume: 20 µL

System suitability

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Sample: *System suitability solution*

[NOTE—The relative retention times of all peaks eluting before atorvastatin related compound H as given in *Table 4* are calculated with respect to the atorvastatin peak. The relative retention times for all peaks eluting after atorvastatin related compound H are calculated with respect to atorvastatin related compound H.]

Suitability requirements

Resolution: NLT 1.4 between atorvastatin related compound B and atorvastatin

Tailing factor: NMT 1.5 for the atorvastatin peak

Relative standard deviation: NMT 5% for the atorvastatin peak

Signal-to-noise ratio: NLT 10 for atorvastatin related compound D

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity 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 each impurity from the *Sample solution*

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

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

C_U = nominal concentration of atorvastatin in the *Sample solution* (mg/mL)

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

M_{r1} = molecular weight of atorvastatin, 558.65

M_{r2} = molecular weight of atorvastatin calcium, 1155.36

F = relative response factor (see *Table 4*)

Acceptance criteria: See *Table 4*.

Table 4

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Atorvastatin amide[a,b]	0.44	—	—
Atorvastatin related compound A[b,c]	0.84	—	—
Atorvastatin pyrrolidone analog[d]	0.88	0.68	0.5
Atorvastatin related compound B[b,e]	0.94	—	—
Atorvastatin	1.00	—	—
Atorvastatin related compound C[b,f]	1.09	—	—
Atorvastatin pyrrolidone lactone[b,g]	1.62	—	—
Atorvastatin related compound H[h]	1.00	1.18	1.0
Atorvastatin epoxy pyrrolooxazin 6-hydroxy analog[i]	1.06	0.53	0.5

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Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Atorvastatin methyl ester[b,j]	1.12	—	—
Atorvastatin epoxy pyrrolooxazin 7-hydroxy analog, if present[k]	1.14	0.53	1.0
Atorvastatin epoxy THF analog[l,m]	1.20	1.12	1.0
Atorvastatin related compound D[n]	1.27	1.12	0.5
Atorvastatin *tert*-butyl ester[b,o]	1.49	—	—
Any other unspecified degradation product	—	1.00	0.2
Total degradation products	—	—	4.0

[a] (3*R*,5*R*)-7-{(3*R*,5*R*)-7-[2-(4-Fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-1*H*-pyrrol-1-yl]-3,5-dihydroxyheptanamido}-3,5-dihydroxyheptanoic acid.

[b] Process impurity included in the table for identification only. Process impurities are controlled in the drug substance, and are not to be reported or included in the total impurities for the drug product.

[c] (3*R*,5*R*)-7-[2-Isopropyl-4,5-diphenyl-3-(phenylcarbamoyl)-1*H*-pyrrol-1-yl]-3,5-dihydroxyheptanoic acid.

[d] (3*R*,5*R*)-7-[5-(4-Fluorophenyl)-3-isopropyl-2-oxo-4-phenyl-3-(phenylcarbamoyl)-2,3-dihydro-1*H*-pyrrol-1-yl]-3,5-dihydroxyheptanoic acid.

[e] (3*S*,5*R*)-7-[2-(4-Fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-1*H*-pyrrol-1-yl]-3,5-dihydroxyheptanoic acid.

[f] (3*R*,5*R*)-7-[2,3-Bis(4-fluorophenyl)-5-isopropyl-4-(phenylcarbamoyl)-1*H*-pyrrol-1-yl]-3,5-dihydroxyheptanoic acid.

[g] 5-(4-Fluorophenyl)-1-{2-[(2*R*,4*R*)-4-hydroxy-6-oxotetrahydro-2*H*-pyran-2-yl]ethyl}-3-isopropyl-2-oxo-*N*,4-diphenyl-2,3-dihydro-1*H*-pyrrole-3-carboxamide.

[h] 5-(4-Fluorophenyl)-1-{2-[(2*R*,4*R*)-4-hydroxy-6-oxotetrahydro-2*H*-pyran-2-yl]ethyl}-2-isopropyl-*N*,4-diphenyl-1*H*-pyrrole-3-carboxamide.

[i] 4-{6-(4-Fluorophenyl)-7,8-epoxy-6-hydroxy-8a-isopropyl-7-phenyl-8-(phenylcarbamoyl)hexahydro-2*H*-pyrrolo[2,1-*b*][1,3]oxazin-2-yl}-3-hydroxybutanoic acid.

[j] (3*R*,5*R*)-Methyl 7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanoate.

[k] (3*R*)-4-(1b-(4-Fluorophenyl)-7-hydroxy-7-isopropyl-1a-phenyl-7a-(phenylcarbamoyl)hexahydro-1a*H*-oxireno[2',3':3,4]pyrrolo[2,1-*b*][1,3]oxazin-3-yl)-3-hydroxybutanoic acid.

[l] 4-(4-Fluorophenyl)-2,4-dihydroxy-2-isopropyl-*N*,5-diphenyl-3,6-dioxabicyclo[3.1.0]hexane-1-carboxamide.

[m] Atorvastatin related compound D can undergo transformation equilibrium to the atorvastatin epoxy THF analog. The equilibrium can be shifted under slightly acidic conditions and therefore some products could have a combined specification reported under atorvastatin related compound D.

[n] 3-(4-Fluorobenzoyl)-2-isobutyryl-*N*,3-diphenyloxirane-2-carboxamide.

[o] (3*R*,5*R*)-*tert*-Butyl 7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanoate.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Atorvastatin Calcium RS

USP Atorvastatin Related Compound B RS

Calcium (3*S*,5*R*)-7-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-1*H*-pyrrol-1-yl]-3,5-dihydroxyheptanoate (1:2).
$C_{66}H_{68}CaF_2N_4O_{10}$ 1155.36

USP Atorvastatin Related Compound D RS

3-(4-Fluorobenzoyl)-2-isobutyryl-*N*,3-diphenyloxirane-2-carboxamide.
$C_{26}H_{22}FNO_4$ 431.46

USP Atorvastatin Related Compound H RS

5-(4-Fluorophenyl)-1-{2-[(2*R*,4*R*)-4-hydroxy-6-oxotetrahydro-2*H*-pyran-2-yl]ethyl}-2-isopropyl-*N*,4-diphenyl-1*H*-pyrrole-3-carboxamide.

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$C_{33}H_{33}FN_2O_4$	540.64

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

Topic/Question	Contact	Expert Committee
ATORVASTATIN CALCIUM TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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