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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- μ m 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 $\times$ 25-cm; 5- μ m packing [L1](#)

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 20 μ L

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*

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

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- μ m pore size.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 248 nm

Column: 2.1-mm $\times$ 5-cm; 2.6- μ m packing [L1](#)

Column temperature: 40°

Flow rate: 0.7 mL/min

Injection volume: 2 μ L

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*