Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2021
Document Type: USP Monographs
DocId: GUID-8FA69715-A1F2-468C-BA6E-399B1AAA2B38_8_en-US
DOI: https://doi.org/10.31003/USPNF_M3575_08_01
DOI Ref: dxd5q

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Amlodipine Besylate Tablets

DEFINITION

Change to read:

Amlodipine Besylate Tablets contain ▲an amount of amlodipine besylate equivalent to▲ (USP 1-May-2021) NLT 90% and NMT 110% of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$).

IDENTIFICATION

Change to read:

• **A.** ▲The UV spectra of the major peak of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2021)

• **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**

Buffer: Add 7.0 mL of triethylamine into a 1000-mL flask containing 900 mL of water. Adjust the solution with phosphoric acid to a pH of 3.0.▲▲ (USP 1-May-2021) Dilute with water to volume, and mix well.

Mobile phase: Methanol, acetonitrile, and *Buffer* (35:15:50)

Standard solution: 0.0275 mg/mL of USP Amlodipine Besylate RS and 0.0025 mg/mL of USP Amlodipine Related Compound A RS in *Mobile phase*

Sample solution: Nominally 0.02 mg/mL of amlodipine in *Mobile phase* prepared as follows. Place Tablets (NLT 5) in a suitable volumetric flask, and add a sufficient quantity of *Mobile phase* to disintegrate the Tablets. Shake for 30 min, and dilute with *Mobile phase* to volume. Pass the sample through a syringe tip filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 237 nm. ▲For *Identification A*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-May-2021)

Column: 3.9-mm × 15-cm; ▲4- or▲ (USP 1-May-2021) 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: NLT 3 times the retention ▲time▲ (USP 1-May-2021) of amlodipine

System suitability

Sample: *Standard solution*

[Note—The relative retention times for amlodipine related compound A and amlodipine are about 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 8.5 between amlodipine related compound A and amlodipine

Tailing factor: NMT 2.0 for amlodipine related compound A and amlodipine

Relative standard deviation: NMT 5.0% for amlodipine related compound A ▲and NMT 2.0% for amlodipine▲ (USP 1-May-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) in the portion of Tablets taken:

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

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

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

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

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

M_{r1} = molecular weight of amlodipine, 408.88

M_{r2} = molecular weight of amlodipine besylate, 567.05

Acceptance criteria: 90%–110% ▲▲ (USP 1-May-2021)

PERFORMANCE TESTS

Change to read:

• **Dissolution ⟨711⟩**

[Note—Do not expose any of the solutions to stainless steel because of the degradation of amlodipine.]

▲**Test 1**▲ (USP 1-May-2021)

Medium: 0.01 N hydrochloric acid; 500 mL

Apparatus 2: 75 rpm. [Note—Use paddles covered with Teflon or made of any inert material except stainless steel.]

Time: 30 min

Standard solution: ▲(*L*/360) mg/mL of USP Amlodipine Besylate RS in *Medium*, where *L* is the label claim of amlodipine in mg/Tablet. [Note—These solutions are stable for 1 day.]▲ (USP 1-May-2021)

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

Blank: *Medium*

Instrumental conditions

Mode: UV

Analytical wavelength: 239 nm

Cell: 1-cm quartz

Analysis

Samples: *Standard solution* and *Sample solution*

▲▲ (USP 1-May-2021)

Calculate the percentage of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V^{▲▲\text{ (USP 1-May-2021)}} \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

A_U = absorbance of amlodipine from the *Sample solution*

A_S = absorbance of amlodipine from the *Standard solution*

C_S = concentration of ▲USP Amlodipine Besylate RS▲ (USP 1-May-2021) in the *Standard solution* (mg/mL)

V = volume of *Medium*, 500 mL

▲▲ (USP 1-May-2021)

M_{r1} = molecular weight of amlodipine, 408.88

M_{r2} = molecular weight of amlodipine besylate, 567.05

L = label claim (mg/Tablet)

Tolerances: NLT 75% (*Q*) of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) is dissolved.

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

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

Buffer A: Dissolve 1.36 g of potassium phosphate, monobasic in 1000 mL of water. Add 5 mL of triethylamine and adjust the solution with phosphoric acid to a pH of 2.0.

Buffer B: Dilute 7.0 mL of triethylamine in 1000 mL of water. Adjust the solution with phosphoric acid to a pH of 3.0.

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

Diluent: Acetonitrile, methanol, and *Buffer B* (15:35:50)

Standard stock solution: 0.693 mg/mL of USP Amlodipine Besylate RS in *Diluent*

Standard solution: (*L*/361) mg/mL of USP Amlodipine Besylate RS in *Medium*, where *L* is the label claim of amlodipine in mg/Tablet

Sample solution: Centrifuge a portion of the solution under test for 5 min.

Chromatographic system

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

Mode: LC

Detector: UV 237 nm

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

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Temperatures

Autosampler: 5°

Column: 35°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 1.7 times the retention time of amlodipine

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 amlodipine ($C_{20}H_{25}ClN_2O_5$) dissolved:

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

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

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

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

V = volume of *Medium*, 500 mL

M_{r1} = molecular weight of amlodipine, 408.88

M_{r2} = molecular weight of amlodipine besylate, 567.05

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) is dissolved.▲ (USP 1-May-2021)

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

IMPURITIES

Change to read:

• **Organic Impurities**

Buffer, Mobile phase, Standard solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

▲**Sensitivity solution:** 0.55 µg/mL of USP Amlodipine Besylate RS in *Mobile phase*▲ (USP 1-May-2021)

Sample solution: ▲Nominally 0.4 mg/mL of amlodipine in *Mobile phase* prepared as follows.▲ (USP 1-May-2021) Place a suitable number of Tablets in a 25-mL volumetric flask. ▲▲ (USP 1-May-2021) Add about 10 mL of *Mobile phase* to the flask. Swirl to disintegrate the Tablets, then sonicate for 5 min to completely dissolve, and cool to room temperature. Dilute with *Mobile phase* to volume. Stir for an additional 15 min using a magnetic stir bar, and pass the sample through a syringe tip filter of 0.45-µm pore size, discarding the first 5 mL.

System suitability

Samples: *Standard solution*▲ and *Sensitivity solution*▲ (USP 1-May-2021)

Suitability requirements: Proceed as directed in the *Assay*▲except for *Signal-to-noise ratio*.

Signal-to-noise ratio: NLT 10, *Sensitivity solution*▲ (USP 1-May-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amlodipine related compound A ▲(free base)▲ (USP 1-May-2021) in the portion of Tablets taken:

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

r_U = peak response of amlodipine related compound A from the *Sample solution*

r_S = peak response of amlodipine related compound A from the *Standard solution*

C_S = concentration of USP Amlodipine Related Compound A RS in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of amlodipine related compound A ▲(free base),▲ (USP 1-May-2021) 406.86

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M_{r2} = molecular weight of amlodipine related compound A, ▲522.94▲ (USP 1-May-2021)

Calculate the percentage of amlodipine glucose/galactose adduct or amlodipine lactose adduct, if present, and any unspecified degradation product in the portion of Tablets taken:

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

r_U = peak response of amlodipine glucose/galactose adduct, amlodipine lactose adduct, or any unspecified degradation product from the *Sample solution*

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

C_S = concentration of USP Amlodipine Besylate RS from the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of amlodipine, ▲408.88▲ (USP 1-May-2021)

M_{r2} = molecular weight of amlodipine besylate, 567.05

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
▲Benzenesulfonic acid[a]	0.15	—▲ (USP 1-May-2021)
Amlodipine related compound A[b]	0.50	1.0
Amlodipine lactose adduct[c]	0.80	0.5
Amlodipine glucose/galactose adduct[c]	0.90	0.5
Amlodipine ▲▲ (USP 1-May-2021)	1.0	—
Any unspecified degradation product	—	0.2
▲Total impurities	—	1.5▲ (USP 1-May-2021)

▲a This peak is due to the counterion and is not to be reported or included in the total impurities.▲ (USP 1-May-2021)

b 3-Ethyl 5-methyl [2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-6-methyl-3,5-pyridinedicarboxylate]. ▲▲ (USP 1-May-2021)

c Formulation-specific impurities.

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ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

Add the following:

▲• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (USP 1-May-2021)

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Amlodipine Besylate RS

USP Amlodipine Related Compound A RS

3-Ethyl 5-methyl [2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-6-methyl-3,5-pyridinedicarboxylate] fumarate.

$C_{20}H_{23}ClN_2O_5 \cdot C_4H_4O_4$ ▲522.94▲ (USP 1-May-2021)

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Topic/Question	Contact	Expert Committee
AMLODIPINE BESYLATE 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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(4)

Current DocID: GUID-8FA69715-A1F2-468C-BA6E-399B1AAA2B38_8_en-US
DOI: https://doi.org/10.31003/USPNF_M3575_08_01
DOI ref: dxd5q

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