Amlodipine Besylate Tablets

DEFINITION
Amlodipine Besylate Tablets contain NLT 90% and NMT 110% of the labeled amount of amlodipine ($C_{20}H_{25}N_2O_5Cl$).

IDENTIFICATION
• **A. ULTRAVIOLET ABSORPTION ⟨197U⟩**
Sample solution: Prepare as directed in the test for *Dissolution*.
Standard solution: Prepare as directed in the test for *Dissolution*.
Acceptance criteria: Meet the requirements
• **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: 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 ± 0.1. Dilute with water to volume, and mix well.
Mobile phase: Methanol, acetonitrile, and *Buffer* (35:15:50)
System suitability solution: 0.02 mg/mL of USP Amlodipine Besylate RS and 0.002 mg/mL of USP Amlodipine Related Compound A RS in *Mobile phase*
Standard solution: 0.02 mg/mL of amlodipine prepared from USP Amlodipine Besylate RS in *Mobile phase*
Sample stock solution: Place 5 Tablets into a 500-mL volumetric flask. Add 50 mL of *Mobile phase* to the flask, and swirl to disintegrate the Tablets. Add 300 mL of *Mobile phase*, insert the stopper into the flask, and shake on a reciprocating shaker for 30 min. Dilute with *Mobile phase* to volume, and mix well.
Sample solution: 0.02 mg/mL of amlodipine from *Sample stock solution* in *Mobile phase*. Pass the sample through a 0.45-µm pore size syringe tip filter.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 237 nm
Column: 3.9-mm × 15-cm; 5-µm packing L1
Flow rate: 1 mL/min
Injection size: 50 µL
System suitability
Sample: *System suitability solution*
[NOTE—The run time is about three times the retention of the amlodipine peak.]
Suitability requirements
Resolution: NLT 8.5 between amlodipine and amlodipine related compound A
Tailing factor: NMT 2.0 for both amlodipine and amlodipine related compound A
Relative standard deviation: NMT 1.0% for amlodipine and NMT 5.0% for amlodipine related compound A
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of amlodipine ($C_{20}H_{25}N_2O_5Cl$) in the portion of Tablets taken:

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

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)
C_U = nominal concentration of amlodipine in the *Sample solution* (mg/mL)
Acceptance criteria: 90%–110%

PERFORMANCE TESTS
• **DISSOLUTION ⟨711⟩**
[NOTE—Do not expose any of the solutions to stainless steel because of the degradation of amlodipine.]
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 stock solution A: 0.14 mg/mL of USP Amlodipine Besylate RS prepared by dissolving in methanol (4% of the volume of the flask). Dilute with *Medium* to volume.
Standard stock solution B: Prepare as directed for *Standard stock solution A*.
Standard solution A: Prepare in *Medium* to obtain solutions having concentrations based on Tablet strength as listed in *Table 1*.

Table 1

Tablet Strength	Standard Stock Used	Concentration of USP Amlodipine Besylate RS (µg/mL)
2.5 mg	*Standard stock solution A*	3.5
5 mg	*Standard stock solution A*	7
10 mg	*Standard stock solution A*	14

Standard solution B: Prepare in *Medium* to obtain solutions having concentrations based on Tablet strength as listed in *Table 2*.

Table 2

Tablet Strength	Standard Stock Used	Concentration of USP Amlodipine Besylate RS (µg/mL)
2.5 mg	*Standard stock solution B*	7
5 mg	*Standard stock solution B*	14
10 mg	*Standard stock solution B*	28

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.
Analysis: Determine the amount of amlodipine ($C_{20}H_{25}N_2O_5Cl$) dissolved by employing UV absorption at the wavelength of maximum absorbance at about 237 nm on portions of the *Sample solution* in comparison with the *Standard solutions*, using a 1-cm quartz cell. Calculate the absorptivity:

$$A^{1\%}_{1\text{ cm}}$$

at 237 nm for *Standard solution A* and *Standard solution B*:

$$\text{Result} = (A_S/C_S) \times (1000/100)$$

A_S = absorbance of the *Standard solution*
C_S = concentration of USP Amlodipine Besylate RS in the *Standard solution* (mg/mL)
Calculate the percentage of the labeled amount of amlodipine ($C_{20}H_{25}N_2O_5Cl$) dissolved:

$$\text{Result} = (A_U/\text{mean } A^{1\%}_{1\text{ cm}}) \times (1000/100) \times (V/L) \times (M_{r1}/M_{r2}) \times 100$$

A_U = absorbance of the *Sample solution*
mean $A^{1\%}_{1\,cm}$ = average absorptivity of *Standard solution A* and *Standard solution B*
V = volume of *Medium*, 500 mL
L = label claim (mg/Tablet)
M_{r1} = molecular weight of amlodipine, 408.9
M_{r2} = molecular weight of amlodipine besylate, 567.05

Tolerances: NLT 75% (Q) of the labeled amount of amlodipine ($C_{20}H_{25}N_2O_5Cl$) is dissolved.

- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**

Buffer, Mobile phase, System suitability solution, Chromatographic system, and **System suitability:** Prepare as directed in the *Assay*.

Standard solution: Use the *System suitability solution*.

Sample solution: Place a suitable number of Tablets into a 25-mL volumetric flask to obtain a solution having a final nominal concentration of 0.4 mg/mL of amlodipine. Add about 10 mL of *Mobile phase* to the flask. Swirl to disintegrate the Tablet(s) followed by sonication for 5 min to completely dissolve, and then cool the sample 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 0.45-µm pore size syringe tip filter, discarding the first 5 mL.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amlodipine related compound A 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, 406.86
M_{r2} = molecular weight of amlodipine related compound A fumarate, 522.93

●Calculate the percentage of amlodipine glucose/galactose adduct or amlodipine lactose adduct, if present, 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 the amlodipine glucose/galactose adduct or amlodipine lactose adduct in the *Sample solution*
r_S = peak response of amlodipine in the *Standard solution*
C_S = concentration of USP Amlodipine Besylate 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, 408.9
M_{r2} = molecular weight of amlodipine besylate, 567.05● (RB 1-Feb-2011)

Calculate the percentage of any other individual impurity in the portion of Tablets taken:

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

r_U = peak response of each impurity from the *Sample solution*
r_S = peak response of amlodipine from the *Standard solution*
C_S = concentration of amlodipine in the *Standard solution* (mg/mL)
C_U = nominal concentration of amlodipine in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Amlodipine related compound A [a]	0.50	1.0
●Amlodipine lactose adduct[b]	0.80	0.5● (RB 1-Feb-2011)
●Amlodipine glucose/galactose adduct[b]	0.90	0.5● (RB 1-Feb-2011)
Amlodipine besylate	1.0	—
Any other individual unspecified degradation impurity	—	0.20

[a] 3-Ethyl, 5-methyl [2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-6-methyl-3,5-pyridinedicarboxylate].
●[b] Formulation-specific impurities.● (RB 1-Feb-2011)

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

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.●(RB 1-Feb-2011)
$C_{20}H_{23}ClN_2O_5$● · $C_4H_4O_4$. 522.93●(RB 1-Feb-2011)