Assay preparation—Transfer about 50 mg of Amlodipine Besylate, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 237-nm detector and a 3.9-mm × 15-cm column that contains packing L1. The flow rate is about 1.0 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of $C_{20}H_{25}ClN_2O_5 \cdot C_6H_6O_3S$ in the portion of Amlodipine Besylate taken by the formula:

$$100(C_S / C_U)(r_U / r_S)$$

in which C_S and C_U are the concentrations, in mg per mL, of amlodipine besylate in the *Standard preparation* and the *Assay preparation,* respectively; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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**⟩
  Standard solution and **Sample 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 the *Sample stock solution* in *Mobile phase*. Pass the sample through a syringe tip filter of 0.45-µm pore size.
  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 from the *Sample solution*
  r_S = peak response 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% of the labeled amount of amlodipine ($C_{20}H_{25}N_2O_5Cl$)

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 solution: Make appropriate dilutions of USP Amlodipine Besylate RS in *Medium* to obtain the following concentrations: 0.00695 mg/mL for Tablets labeled to contain 2.5 mg; 0.0139 mg/mL for Tablets labeled to contain 5 mg; 0.0278 mg/mL for Tablets labeled to contain 10 mg. These solutions are stable for one day.
  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 using UV absorption at the wavelength of maximum absorbance at about 239 nm on portions of the *Sample solution* in comparison with the *Standard solution,* using a 1-cm quartz cell and the *Medium* as blank.
  Calculate the percentage of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) dissolved:

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

  A_U = absorbance of the *Sample solution*
  A_S = absorbance of the *Standard solution*
  C_S = concentration of the *Standard solution* (mg/mL)
  L = label claim (mg/Tablet)
  D = dilution factor of the *Sample solution*
  M_{r1} = molecular weight of amlodipine, 408.88
  M_{r2} = molecular weight of amlodipine besylate, 567.06
  V = volume of *Medium*, 500 mL
  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

- **ORGANIC IMPURITIES**

Buffer, Mobile phase, System suitability solution, Chromatographic system, and **System suitability:** Proceed 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 syringe tip filter of 0.45-µm pore size, 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

Calculate the percentage of any other individual unspecified degradation product 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 1*.

Table 1

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

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

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers. Store at controlled room temperature.
- **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.
$C_{20}H_{23}ClN_2O_5 \cdot C_4H_4O_4$ 522.93

Aromatic Ammonia Spirit

» Aromatic Ammonia Spirit is a hydroalcoholic solution that contains, in each 100 mL, not less than 1.7 g and not more than 2.1 g of total NH_3, and Ammonium Carbonate corresponding to not less than 3.5 g and not more than 4.5 g of $(NH_4)_2CO_3$.

Packaging and storage—Preserve in tight, light-resistant containers, at a temperature not exceeding 30°.

Alcohol content, *Method I* ⟨611⟩: between 62.0% and 68.0% of C_2H_5OH.

Assay for total NH_3—Transfer 10.0 mL to a 250-mL conical flask containing about 50 mL of water. Add 30.0 mL of 0.5 N sulfuric acid VS, and boil until the solution becomes clear. Cool, add methyl red TS, and titrate the excess acid with 0.5 N sodium hydroxide VS. Perform a blank determination (see *Residual Titrations* under *Titrimetry* ⟨541⟩). Each mL of 0.5 N sulfuric acid is equivalent to 8.515 mg of NH_3.

Assay for ammonium carbonate—Transfer 10.0 mL to a flask of about 300-mL capacity. Add 30 mL of 0.5 N sodium hydroxide, and boil the mixture, replacing the water lost by evaporation, until the vapors no longer turn moistened red litmus paper blue. Cool, dilute with 100 mL of cold, carbon dioxide-free water, add about 6 drops of phenolphthalein TS, then add just enough 0.5 N sulfuric acid VS to discharge the color of the phenolphthalein. Add methyl orange TS, and titrate with 0.5 N sulfuric acid VS. Perform a blank determination (see *Residual Titrations* under *Titrimetry* ⟨541⟩). Each mL of 0.5 N sulfuric acid consumed in the titration with methyl orange TS is equivalent to 48.04 mg of $(NH_4)_2CO_3$.