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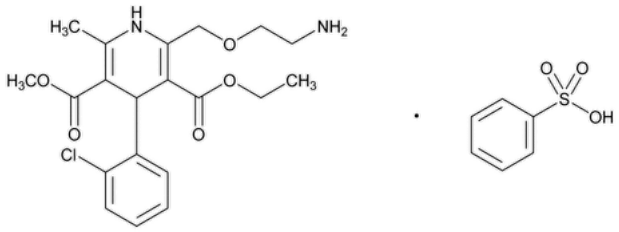
Amlodipine Besylate

Change to read:



$C_{20}H_{25}ClN_2O_5 \cdot C_6H_6O_3S$ 567.05

3,5-Pyridinedicarboxylic acid, 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-, 3-ethyl 5-methyl ester, (±)-, monobenzenesulfonate;

▲3-Ethyl 5-methyl 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate benzenesulfonate▲ (USP 1-Aug-2023) CAS RN®: 111470-99-6; UNII: 864V2Q084H.

Monohydrate

▲$C_{20}H_{25}ClN_2O_5 \cdot C_6H_6O_3S \cdot H_2O$▲ (USP 1-Aug-2023) 585.07 CAS RN®: ▲532929-67-2; UNII: V912825CB9.▲ (USP 1-Aug-2023)

DEFINITION

Amlodipine Besylate is anhydrous or hydrated and contains NLT 97.0% and NMT 102.0% of amlodipine besylate ($C_{20}H_{25}ClN_2O_5 \cdot C_6H_6O_3S$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** ▲197A or▲ (USP 1-Aug-2023) 197M

• **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**

▲[Note—Protect the solutions containing amlodipine besylate from light.]

Solution A: 1.36 g/L of potassium phosphate, monobasic in water prepared as follows. Dissolve 1.36 g of potassium phosphate, monobasic with 950 mL of water. Adjust with phosphoric acid to a pH of 2.5 ± 0.1. Dilute with water to 1 L.

Solution B: Methanol

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
0.5	60	40
8	20	80
9	20	80
10	60	40
11	60	40

Diluent: Methanol and water (50:50)

Standard solution: 0.5 mg/mL of USP Amlodipine Besylate RS in *Diluent*

Sample solution: 0.5 mg/mL of Amlodipine Besylate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 2.1-mm × 5-cm; 1.7-µm packing L1

Column temperature: 40°

Flow rate: 0.5 mL/min

Injection volume: 2 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 0.73%▲ (USP 1-Aug-2023)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amlodipine besylate ($C_{20}H_{25}ClN_2O_5 \cdot C_6H_6O_3S$) in the portion of Amlodipine Besylate 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 = concentration of Amlodipine Besylate in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–102.0% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.2%

Change to read:

• **Organic Impurities**

▲**Solution A, Solution B, Mobile phase, Diluent, Sample solution,** and **Chromatographic system:** Proceed as directed in the *Assay*.

[Note—Protect the solutions containing amlodipine besylate and amlodipine related compounds from light.]

Impurity stock solution: 0.1 mg/mL of USP Amlodipine Related Compound F RS in *Diluent*. Sonicate to dissolve.

System suitability solution: 0.5 mg/mL of USP Amlodipine Besylate RS and 1.5 µg/mL of USP Amlodipine Related Compound F RS in *Diluent* prepared as follows. Transfer an appropriate quantity of USP Amlodipine Besylate RS to a suitable volumetric flask. Add an appropriate volume of the *Impurity stock solution* to the flask. Dilute with *Diluent* to volume.

Sensitivity solution: 0.25 µg/mL of USP Amlodipine Besylate RS in *Diluent*

Standard solution: 0.5 µg/mL of USP Amlodipine Besylate RS in *Diluent*

System suitability

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

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between amlodipine related compound F and amlodipine, *System suitability solution*

Tailing factor: NMT 2.5 for amlodipine, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any specified and unspecified impurity in the portion of Amlodipine Besylate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

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 USP Amlodipine Besylate RS in the *Standard solution* (mg/mL)

C_U = concentration of Amlodipine Besylate in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Benzenesulfonic acid[a]	0.11	—	—
Amlodipine related compound A[b]	0.56	0.56	0.3
Amlodipine related compound F	0.75	1.3	0.15
Amlodipine	1.0	—	—
Amlodipine ethyl analog[c]	1.28	1.4	0.15
Hydroxyethyl phthalyl amlodipine[d]	1.66	1.3	0.10
Amlodipine related compound D[e]	2.31	1.7	0.15
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.50

[a] This peak is due to the counterion and is not to be reported or included in the total impurities.

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

[c] Diethyl 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate.

[d] 3-Ethyl 5-methyl 4-(2-chlorophenyl)-2-{[2-(2-[(2-hydroxyethyl)carbamoyl]benzamido)ethoxy]methyl}-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate.

[e] 3-Ethyl 5-methyl 4-(2-chlorophenyl)-2-{[2-(1,3-dioxoisoindolin-2-yl)ethoxy]methyl}-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate.

▲ (USP 1-Aug-2023)

SPECIFIC TESTS

- **Optical Rotation ⟨781A⟩, *Procedures, Angular Rotation***

  Sample solution: 10 mg/mL of Amlodipine Besylate in methanol

  Acceptance criteria: −0.10° to +0.10°, measured at 20°

- **Water Determination ⟨921⟩, *Method I*:** NMT 0.5% for the anhydrous form. If labeled as the hydrated form, the limit is 3.1%–5.0%.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, protected from light. Store at room temperature.
- **Labeling:** Where it is the hydrated form, the label so indicates.

Change to read:

- **USP Reference Standards ⟨11⟩**

  USP Amlodipine Besylate RS

  ▲ USP Amlodipine Related Compound F RS

Dimethyl 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate maleate.

$C_{19}H_{23}ClN_2O_5 \cdot C_4H_4O_4$ 510.92▲ (USP 1-Aug-2023)

Topic/Question	Contact	Expert Committee
AMLODIPINE BESYLATE	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

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