

Amlodipine and Olmesartan Medoxomil Tablets

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In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 2 Expert Committee has revised the Amlodipine and Olmesartan Medoxomil Tablets monograph. The purpose for the revision is to add *Dissolution Test 4* to accommodate FDA-approved drug products with different dissolution conditions and/or tolerances than the existing dissolution test(s). The revision also necessitates a change in the table numbering in the test for *Organic Impurities*.

- *Dissolution Test 4* was validated using the Thermo Scientific Hypersil BDS C8 brand of column with L7 packing. The typical retention times for amlodipine and olmesartan medoxomil are about 4.9 and 6.6 min, respectively.

The Amlodipine and Olmesartan Medoxomil Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Yanyin Yang, Scientific Liaison (301-692-3623 or yanyin.yang@usp.org).

Amlodipine and Olmesartan Medoxomil Tablets

DEFINITION

Amlodipine and Olmesartan Medoxomil Tablets contain an amount of Amlodipine Besylate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) and NLT 90.0% and NMT 110.0% of the labeled amount of olmesartan medoxomil ($C_{29}H_{30}N_6O_6$).

IDENTIFICATION

- **A.** The UV spectra of the amlodipine and olmesartan medoxomil peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.
- **B.** The retention times of the amlodipine and olmesartan medoxomil peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• PROCEDURE

Solution A: 6.9 g/L of [sodium phosphate, monobasic](#). Adjust with [phosphoric acid](#) to a pH of 2.5.

Solution B: [Acetonitrile](#)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	68	32
12	68	32
15	30	70
21	30	70
23	68	32
25	68	32

Diluent: [Acetonitrile](#) and [water](#) (50:50)

Standard stock solution: 0.28 mg/mL of [USP Amlodipine Besylate RS](#) and 0.8 mg/mL of [USP Olmesartan Medoxomil RS](#) in *Diluent*

Standard solution: 0.056 mg/mL of [USP Amlodipine Besylate RS](#) and 0.16 mg/mL of [USP Olmesartan Medoxomil RS](#) in *Diluent* from *Standard stock solution*

Sample stock solution: Nominal concentrations given in [Table 2](#) are prepared as follows.

For Tablet strength 5/20, transfer NLT 5 Tablets equivalent to 25 mg of amlodipine and 100 mg of olmesartan medoxomil into a suitable volumetric flask. Add [water](#) to 20% of the total volume and sonicate for 5 min. Add [acetonitrile](#) to 20% of the total volume and sonicate for 5 min. Add *Diluent* to 30% of the total volume and sonicate for 15 min. Dilute with *Diluent* to volume. Centrifuge a portion of the solution for 10 min and pass through a filter of 0.45- μ m pore size.

For Tablet strength 5/40, 10/20, or 10/40, transfer NLT 5 Tablets equivalent to 25 mg of amlodipine and 200 mg of olmesartan medoxomil, 50 mg of amlodipine and 100 mg of olmesartan medoxomil, or 50 mg of amlodipine and 200 mg of olmesartan medoxomil into a suitable volumetric flask. Add [water](#) to 10% of the total volume and sonicate for 5 min. Add [acetonitrile](#) to 10% of the total volume and sonicate for 5 min. Add *Diluent* to 30% of the total volume and sonicate for 15 min. Dilute with *Diluent* to volume. Centrifuge a portion of the solution for 10 min and pass through a filter of 0.45- μ m pore size.

Table 2

Tablet Strength Amlodipine/ Olmesartan Medoxomil (mg/mg)	Nominal Concentration of Amlodipine (mg/mL)	Nominal Concentration of Olmesartan Medoxomil (mg/mL)
5/20, 10/40	0.5	2
5/40	0.25	2
10/20	0.5	1

Sample solution: Nominal concentrations in *Diluent* from *Sample stock solution* are given in [Table 3](#).

Table 3

Tablet Strength Amlodipine/ Olmesartan Medoxomil (mg/mg)	Nominal Concentration of Amlodipine (mg/mL)	Nominal Concentration of Amlodipine/ Olmesartan Medoxomil (mg/mL)
5/20, 10/40	0.04	0.16
5/40	0.02	0.16
10/20	0.04	0.08

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm \times 25-cm; 5- μ m packing [L11](#)

Temperatures

Autosampler: 5°

Column: 60°

Flow rate: 2 mL/min

Injection volume: 10 μ L

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for amlodipine and olmesartan medoxomil peaks

Relative standard deviation: NMT 2.0% for amlodipine and olmesartan medoxomil peaks

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)

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

Calculate the percentage of the labeled amount of olmesartan medoxomil ($C_{29}H_{30}N_6O_6$) in the portion of Tablets taken:

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

r_U = peak response of olmesartan medoxomil from the *Sample solution*

r_S = peak response of olmesartan medoxomil from the *Standard solution*

C_S = concentration of [USP Olmesartan Medoxomil RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria

Amlodipine: 90.0%–110.0%

Olmesartan medoxomil: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **DISSOLUTION** (711)

Test 1

Medium: 6.8 g/L of [potassium phosphate, monobasic](#). Adjust with [0.2 N sodium hydroxide solution](#) to a pH of 6.8; 900 mL.

Apparatus 2: 50 rpm

Times

Amlodipine: 30 min

Olmesartan medoxomil: 45 min

Buffer: 4.08 g/L of [potassium phosphate, monobasic](#). Adjust with [phosphoric acid](#) to a pH of 2.5.

Mobile phase: [Acetonitrile](#) and *Buffer* (40:60)

Standard stock solution A: 0.16 mg/mL of [USP Amlodipine Besylate RS](#) in *Mobile phase*

Standard stock solution B: 0.44 mg/mL of [USP Olmesartan Medoxomil RS](#) in *Mobile phase*

Standard solution: 0.016 mg/mL of [USP Amlodipine Besylate RS](#) and 0.044 mg/mL of [USP Olmesartan Medoxomil RS](#) in *Medium* from *Standard stock solution A* and *Standard stock solution B*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size and discard the first 2–3 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm \times 15-cm; 5- μ m packing [L1](#)

Autosampler temperature: 5°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

Run time: NLT 1.4 times the retention time of olmesartan medoxomil

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for amlodipine and olmesartan medoxomil peaks

Relative standard deviation: NMT 2.0% for amlodipine and olmesartan medoxomil peaks

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*, 900 mL

M_{r1} = molecular weight of amlodipine, 408.88

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

L = label claim of amlodipine (mg/Tablet)

Calculate the concentration (C_1 or C_2) of olmesartan medoxomil ($C_{29}H_{30}N_6O_6$) in the sample withdrawn from the vessel at the 30- or 45-min time point:

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

r_U = peak response of olmesartan medoxomil from the *Sample solution* at the 30- or 45-min time point

r_S = peak response of olmesartan medoxomil from the *Standard solution*

C_S = concentration of [USP Olmesartan Medoxomil RS](#) in the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of olmesartan medoxomil ($C_{29}H_{30}N_6O_6$) dissolved:

$$\text{Result} = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

C_2 = concentration of olmesartan medoxomil in the *Sample solution* at the 45-min time point (mg/mL)

V = volume of *Medium*, 900 mL

V_S = volume of the *Sample solution* withdrawn at the 30-min time point (mL)

C_1 = concentration of olmesartan medoxomil in the *Sample solution* at the 30-min time point (mg/mL)

L = label claim of olmesartan medoxomil (mg/Tablet)

Tolerances: NLT 80.0% (Q) of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) at 30 min and NLT 70.0% (Q) of the labeled amount of olmesartan medoxomil ($C_{29}H_{30}N_6O_6$) at 45 min are dissolved.

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

Medium: 6.8 g/L of [potassium phosphate monobasic](#) and 0.9 g/L of [sodium hydroxide](#). Adjust with 10% [sodium hydroxide](#) solution to a pH of 6.8; 900 mL.

Apparatus 2: 50 rpm

Times

Amlodipine: 30 min

Olmesartan medoxomil: 30 min

Buffer: Add 2 mL of [triethylamine](#) in 1000 mL of [water](#). Adjust with [phosphoric acid](#) to a pH of 2.5.

Mobile phase: [Acetonitrile](#) and *Buffer* (30:70)

Standard stock solution A: 0.15 mg/mL of [USP Amlodipine Besylate RS](#) in [methanol](#)

Standard stock solution B: 0.44 mg/mL of [USP Olmesartan Medoxomil RS](#) in [methanol](#)

Standard solution: Known concentrations of [USP Amlodipine Besylate RS](#) and [USP Olmesartan Medoxomil RS](#) in *Medium* from *Standard stock solution A* and *Standard stock solution B*, prepared per [Table 4](#).

Table 4

Tablet Strength Amlodipine/ Olmesartan Medoxomil (mg/mg)	Concentration of USP Am- lodipine Besylate RS (mg/mL)	Concentration of USP Olmesartan Medoxomil RS (mg/mL)
5/20	0.0075	0.022
5/40	0.0075	0.044
10/20	0.015	0.022
10/40	0.015	0.044

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size and discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 236 nm

Column: 4.6-mm \times 5-cm; 5- μ m packing [L1](#)

Temperatures

Autosampler: 5°

Column: 30°

Flow rate: 1.0 mL/min

Injection volume: 10 μ L

Run time: NLT 1.5 times the retention time of olmesartan medoxomil

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for olmesartan, amlodipine, and olmesartan medoxomil are 0.29, 0.68, and 1.00, respectively.]

Suitability requirements

Tailing factor: NMT 2.0 for amlodipine and olmesartan medoxomil peaks

Relative standard deviation: NMT 2.0% for amlodipine and olmesartan medoxomil peaks

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*, 900 mL
 M_{r1} = molecular weight of amlodipine, 408.88
 M_{r2} = molecular weight of amlodipine besylate, 567.05
 L = label claim of amlodipine (mg/Tablet)

Calculate the percentage of the labeled amount of olmesartan medoxomil ($C_{29}H_{30}N_6O_6$) dissolved:

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

- r_U = sum of peak responses of olmesartan and olmesartan medoxomil from the *Sample solution*
 r_S = sum of peak responses of olmesartan and olmesartan medoxomil from the *Standard solution*
 C_S = concentration of [USP Olmesartan Medoxomil RS](#) in the *Standard solution* (mg/mL)
 V = volume of *Medium*, 900 mL
 L = label claim of olmesartan medoxomil (mg/Tablet)

Tolerances: NLT 75.0% (Q) of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) and NLT 70.0% (Q) of the labeled amount of olmesartan medoxomil ($C_{29}H_{30}N_6O_6$) are dissolved.

Test 4: If the product complies with this test, the labeling indicates that it meets *USP Dissolution Test 4*.

Medium: pH 6.8 phosphate buffer (3.4 g/L of [potassium phosphate monobasic](#) and 3.55 g/L of [sodium phosphate, dibasic, anhydrous](#) in [water](#)) and [water](#) (50:50); 900 mL

Apparatus 2: 50 rpm

Times

Amlodipine: 15 min

Olmesartan medoxomil: 45 min

Solution A: Dissolve 2.72 g of [potassium phosphate monobasic](#) in 1000 mL of [water](#). Add 5 mL of [triethylamine](#) and adjust with [phosphoric acid](#) to a pH of 3.0.

Mobile phase: [Acetonitrile](#) and *Solution A* (35:65)

Standard stock solution A: 0.31 mg/mL of [USP Amlodipine Besylate RS](#) in [acetonitrile](#). Sonicate to dissolve if necessary.

Standard stock solution B: 0.90 mg/mL of [USP Olmesartan Medoxomil RS](#) in [acetonitrile](#). Sonicate to dissolve if necessary.

Standard solution: Known concentrations of [USP Amlodipine Besylate RS](#) and [USP Olmesartan Medoxomil RS](#) in *Medium* from *Standard stock solution A* and *Standard stock solution B*, prepared per [Table 5](#)

Table 5

Tablet Strength Amlodipine/ Olmesartan Medoxomil (mg/mg)	Concentration of USP Amlodipine Besylate RS (mg/mL)	Concentration of USP Olmesartan Medoxomil RS (mg/mL)
5/20	0.00775	0.0225
5/40	0.00775	0.045
10/20	0.0155	0.0225
10/40	0.00775	0.0225

Sample solution: At the end of the specified time, withdraw 10 mL of the solution under test, pass through a suitable filter and discard the first 5 mL of the filtrate. Replace the aliquot withdrawn with equal volumes

of pre-equilibrated *Medium*. For Tablets with strengths of 5/20, 5/40, and 10/20 mg/mg, use the filtrate. For Tablets with a strength of 10/40 mg/mg, dilute 5 mL of the filtrate with *Medium* to 10 mL.

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm × 15-cm; 5-μm packing [L7](#)

Temperatures

Autosampler: 5°

Column: 30°

Flow rate: 1.2 mL/min

Injection volume: 20 μL

Run time: NLT 1.5 times the retention time of olmesartan medoxomil

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for olmesartan, amlodipine, and olmesartan medoxomil are 0.32, 0.74, and 1.00, respectively.]

Suitability requirements

Resolution: NLT 3.0 between amlodipine and olmesartan medoxomil

Tailing factor: NMT 2.0 for amlodipine and olmesartan medoxomil

Relative standard deviation: NMT 2.0% for amlodipine and olmesartan medoxomil

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) dissolved at time point 1:

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

r_U = peak response of amlodipine from the *Sample solution* withdrawn at time point 1

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*, 900 mL

D = dilution factor for the *Sample solution* withdrawn at time point 1, if needed

M_{r1} = molecular weight of amlodipine, 408.88

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

L = label claim of amlodipine (mg/Tablet)

Calculate the concentration (C_i) of olmesartan medoxomil ($C_{29}H_{30}N_6O_6$) in the portion of sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (r_i/r_S) \times C_S \times D$$

r_i = peak response of olmesartan medoxomil from the *Sample solution* withdrawn at time point i

r_S = peak response of olmesartan medoxomil from the *Standard solution*

C_S = concentration of [USP Olmesartan Medoxomil RS](#) in the *Standard solution* (mg/mL)

D = dilution factor for the *Sample solution* withdrawn at time point i , if needed

Calculate the percentage of the labeled amount of olmesartan medoxomil ($C_{29}H_{30}N_6O_6$) dissolved at time point 2:

$$\text{Result} = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

- C_i = concentration of olmesartan medoxomil in the portion of sample withdrawn at time point i (mg/mL)
- V = volume of *Medium*, 900 mL
- V_S = volume of the *Sample solution* withdrawn at each time point and replaced with *Medium*, 10 mL
- L = label claim of olmesartan medoxomil (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) and NLT 70% (Q) of the labeled amount of olmesartan medoxomil ($C_{29}H_{30}N_6O_6$) are dissolved. (See [Table 6.](#))

Table 6

Time point (i)	Time (min)
1	15
2	45▲ (RB 1-Apr-2021)

- **UNIFORMITY OF DOSAGE UNITS** (905): Meet the requirements

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**

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

Standard stock solution A: 28 µg/mL of [USP Amlodipine Besylate RS](#) and 80 µg/mL of [USP Olmesartan Medoxomil RS](#) in *Diluent* from *Standard stock solution*

Standard stock solution B: 50 µg/mL of [USP Amlodipine Related Compound A RS](#) in *Diluent*

Standard solution: 1.4 µg/mL of [USP Amlodipine Besylate RS](#), 2.5 µg/mL of [USP Amlodipine Related Compound A RS](#), and 4 µg/mL of [USP Olmesartan Medoxomil RS](#) in *Diluent* from *Standard stock solution A* and *Standard stock solution B*

Sensitivity solution: 0.28 µg/mL of [USP Amlodipine Besylate RS](#), 0.5 µg/mL of [USP Amlodipine Related Compound A RS](#), and 0.8 µg/mL of [USP Olmesartan Medoxomil RS](#) in *Diluent* from *Standard solution*

Sample solution: Use the *Sample stock solution*, prepared as directed in the Assay.

System suitability

Samples: *Standard solution* and *Sensitivity solution*

[NOTE—See ▲[Table 7](#)▲ (RB 1-Apr-2021) for relative retention times.]

Suitability requirements

Tailing factor: NMT 2.0 for amlodipine related compound A, amlodipine, and olmesartan medoxomil peaks, *Standard solution*

Relative standard deviation: NMT 5.0% for amlodipine related compound A, amlodipine, and olmesartan medoxomil peaks, *Standard solution*

Signal-to-noise ratio: NLT 10 for amlodipine related compound A, amlodipine, and olmesartan medoxomil peaks, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amlodipine related compound A free base 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, 406.86
 M_{r2} = molecular weight of amlodipine related compound A, 522.94

Calculate the percentage of any unspecified amlodipine related impurity 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 any unspecified amlodipine related 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 = 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

Calculate the percentage of olmesartan or any unspecified olmesartan medoxomil related 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 olmesartan or any unspecified olmesartan medoxomil related impurity from the *Sample solution*
 r_S = peak response of olmesartan medoxomil from the *Standard solution*
 C_S = concentration of [USP Olmesartan Medoxomil RS](#) in the *Standard solution* (mg/mL)
 C_U = nominal concentration of olmesartan medoxomil in the *Sample solution* (mg/mL)

Acceptance criteria: See [Table 7](#).

Table 7 [▲](#) (RB 1-Apr-2021)

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Benzenesulfonic acid ^a	0.13	—
Olmesartan ^b	0.25	2.0
Amlodipine related compound A ^c	0.36	0.5
Amlodipine	0.47	—
Olmesartan medoxomil	1.0	—
Olmesartan medoxomil related compound A ^{d,e}	1.13	—
Olmesartan olefinic impurity ^{f,e}	1.50	—
Olmesartan <i>N</i> -alkyl impurity ^{g,e}	2.03	—
Any unspecified amlodipine or olmesartan medoxomil related impurity ^h	—	0.2
Total impurities ⁱ	—	2.0

-
- ^a This peak is due to the counterion and is not to be reported or included in the total impurities.
- ^b 1-{[2'-(1*H*-Tetrazol-5-yl)biphenyl-4-yl]methyl}-4-(2-hydroxypropan-2-yl)-2-propyl-1*H*-imidazole-5-carboxylic acid.
- ^c 3-Ethyl 5-methyl [2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-6-methyl-3,5-pyridinedicarboxylate].
- ^d 1-{[2'-(1*H*-Tetrazol-5-yl)biphenyl-4-yl]methyl}-4,4-dimethyl-2-propyl-1*H*-furo[3,4-*d*]imidazol-6(4*H*)-one.
- ^e Process impurity included in the table for identification only. Process impurities are controlled in the drug substance and are not to be reported or included in the total impurities for the drug product.
- ^f (5-Methyl-2-oxo-1,3-dioxol-4-yl)methyl 1-((2'-(1*H*-tetrazol-5-yl)biphenyl-4-yl)methyl)-4-(prop-1-en-2-yl)-2-propyl-1*H*-imidazole-5-carboxylate.
- ^g (5-Methyl-2-oxo-1,3-dioxol-4-yl)methyl 4-(2-hydroxypropan-2-yl)-2-propyl-1-((2'-(2-trityl-2*H*-tetrazol-5-yl)biphenyl-4-yl)methyl)-1*H*-imidazole-5-carboxylate.
- ^h The relative retention times for unspecified amlodipine related impurities are up to 1.0. The relative retention times for unspecified olmesartan medoxomil related impurities are after 1.0 and also at 0.45, 0.60, 0.76, 0.79, and 0.92.
- ⁱ Excluding olmesartan.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, and store at controlled room temperature.
 - **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
 - **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 Olmesartan Medoxomil RS](#)

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