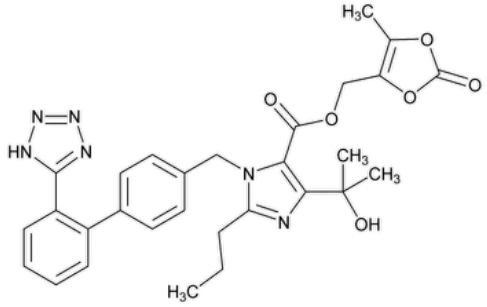
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-539AD1C5-82E6-4E04-8F06-9EC8A1BFA14E_4_en-US
DOI: https://doi.org/10.31003/USPNF_M887_04_01
DOI Ref: 08r3w

Olmesartan Medoxomil



$C_{29}H_{30}N_6O_6$ 558.59

1*H*-Imidazole-5-carboxylic acid, 4-(1-hydroxy-1-methyl ethyl)-2-propyl-1-[[2'-(1*H*-tetrazol-5-yl) [1,1'-biphenyl]-4-yl]methyl]-, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl ester; (5-Methyl-2-oxo-1,3-dioxol-4-yl)methyl 1-{[2'-(1*H*-tetrazol-5-yl)biphenyl-4-yl]methyl}-4-(2-hydroxypropan-2-yl)-2-propyl-1*H*-imidazole-5-carboxylate CAS RN®: 144689-63-4; UNII: 6M97XTV3HD.

DEFINITION

Olmesartan Medoxomil contains NLT 98.5% and NMT 101.5% of $C_{29}H_{30}N_6O_6$, calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **B.** The ratio of the retention time of the major peak to that of the internal standard of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

[Note—The *Standard solution* and *Sample solution* are stable for 24 h at 5°.]

Diluted phosphoric acid: 0.2% phosphoric acid

Buffer: 0.015 M monobasic potassium phosphate. Adjust the solution with *Diluted phosphoric acid* (w/v) to a pH of 3.4.

Mobile phase: Acetonitrile and *Buffer* (17:33)

Diluent 1: Acetonitrile and water (4:1)

Diluent 2: Acetonitrile and water (2:3)

Internal standard solution: 0.5 mg/mL of 4-hydroxybenzoic acid isobutyl ester in *Diluent 2*. [Note—This solution is stable for 1 month at room temperature.]

Standard stock solution: 1 mg/mL of USP Olmesartan Medoxomil RS in *Diluent 1*

Standard solution: 0.05 mg/mL of USP Olmesartan Medoxomil RS from the *Standard stock solution* and 0.025 mg/mL of *p*-hydroxybenzoic acid isobutyl ester from the *Internal standard solution* in *Diluent 2*

Sample stock solution: 1 mg/mL of Olmesartan Medoxomil in *Diluent 1*

Sample solution: 0.05 mg/mL of Olmesartan Medoxomil from the *Sample stock solution* and 0.025 mg/mL of *p*-hydroxybenzoic acid isobutyl ester from the *Internal standard solution* in *Diluent 2*

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

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

Column temperature: 40°

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 4 between olmesartan medoxomil and *p*-hydroxybenzoic acid isobutyl ester

Relative standard deviation: NMT 0.5% for the peak ratio of olmesartan medoxomil and the internal standard

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of olmesartan medoxomil in the portion taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = ratio of the peak areas of olmesartan medoxomil and *p*-hydroxybenzoic acid isobutyl ester from the *Sample solution*

R_S = ratio of the peak areas of olmesartan medoxomil and *p*-hydroxybenzoic acid isobutyl ester from the *Standard solution*

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

C_U = concentration of Olmesartan Medoxomil in the *Sample solution* (mg/mL)

Acceptance criteria: 98.5%–101.5% on the anhydrous and solvent-free basis

IMPURITIES

Inorganic Impurities

• **Residue on Ignition ⟨281⟩:** NMT 0.1%. [Note—The ignition temperature range is 450° to 550°.]

Organic Impurities

• **Procedure**

Buffer: Prepare as directed in the *Assay*.

Solution A: Acetonitrile and *Buffer* (1:4)

Solution B: Acetonitrile and *Buffer* (4:1)

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	75	25
10	75	25
35	0	100
45	0	100

System suitability solution: 0.01 mg/mL each of USP Olmesartan Medoxomil RS and USP Olmesartan Medoxomil Related Compound A RS in acetonitrile

Standard solution: 0.01 mg/mL of USP Olmesartan Medoxomil RS in acetonitrile

Sample solution: 1 mg/mL of Olmesartan Medoxomil in acetonitrile

Chromatographic system

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

[Note—A guard column of 4.6-mm × 5-cm of packing L7 may be used.]

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm × 10-cm; 3.5-µm packing L7

Column temperature: 40°

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

Suitability requirements

Sample: *System suitability solution*

Resolution: NLT 5 between olmesartan medoxomil and olmesartan medoxomil related compound A

Relative standard deviation: NMT 2.0% for the olmesartan medoxomil peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Olmesartan Medoxomil 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 olmesartan medoxomil from the *Standard solution*

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

C_U = concentration of Olmesartan Medoxomil in the *Sample solution* (mg/mL)

F = relative response factor (see the *Impurity Table*)

Acceptance criteria

Individual impurities: See the *Impurity Table*.

Total impurities: NMT 1.3%. [NOTE—Disregard any peak below 0.05%.]

Impurity Table

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Olmesartan[a]	0.2	1.0	0.5
Olmesartan medoxomil related compound A[b]	0.7	1.6	0.1
Olmesartan medoxomil	1.0	1.0	—
Olefinic impurity[c]	1.6	1.0	0.6
N-alkyl impurity[d]	3.4	0.7	0.1
Any other individual unidentified impurity	—	1.0	0.1

[a] 1-{[2'-(1*H*-Tetrazol-5-yl)biphenyl-4-yl]methyl}-4-(2-hydroxypropan-2-yl)-2-propyl-1*H*-imidazole-5-carboxylic acid.

[b] 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.

[c] (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.

[d] (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.

SPECIFIC TESTS

• **LIMIT OF ACETONE (IF PRESENT)**

Internal standard solution: 1% solution of 1-butanol in dimethyl sulfoxide. [NOTE—This solution is stable for 1 month at room temperature.]

Standard solution: 0.37 µL/mL of acetone and 2 µL/mL of 1-butanol from the *Internal standard solution* in dimethylsulfoxide. [NOTE—This solution is stable for 8 h at room temperature.]

Sample solution: 25 mg/mL of Olmesartan Medoxomil and 2 µL/mL of 1-butanol from the *Internal standard solution* in dimethylsulfoxide. [NOTE—This solution is stable for 8 h at room temperature.]

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 30-m × 0.53-mm column bonded with a 1-µm film of phase G14

Column temperature: See the temperature program table below.

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	0	50	5
50	10	180	5

Injection port temperature: 200°

Detector temperature: 200°

Autosampler temperature: 80°

Carrier gas: Helium

Flow rate: 4 mL/min. [NOTE—Adjust the flow rate so that the retention time of acetone is 2.5 min.]

Injection size: 1 mL

Split ratio: 5:1

System suitability

Sample: *Standard solution*. [NOTE—Allow the samples to stand for 30 min in the autosampler at 80°.]

Suitability requirements

Resolution: NLT 60 between the acetone and 1-butanol peaks

Relative standard deviation: NMT 5.0% for the peak area ratio of acetone and 1-butanol

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of acetone in the portion of Olmesartan Medoxomil taken:

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

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

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

C_S = concentration of acetone in the *Standard solution* (mg/mL)

C_U = concentration of Olmesartan Medoxomil in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 0.6%

- **WATER DETERMINATION,** *Method Ic*⟨921⟩**:** NMT 0.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers, protect from moisture, and store below 25°.
- **USP REFERENCE STANDARDS** ⟨11⟩

USP Olmesartan Medoxomil RS

USP Olmesartan Medoxomil Related Compound A RS

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.

$C_{24}H_{24}N_6O_2$ 428.49

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
OLMESARTAN MEDOXOMIL	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. PF 36(5)

Current DocID: GUID-539AD1C5-82E6-4E04-8F06-9EC8A1BFA14E_4_en-US
DOI: https://doi.org/10.31003/USPNF_M887_04_01
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