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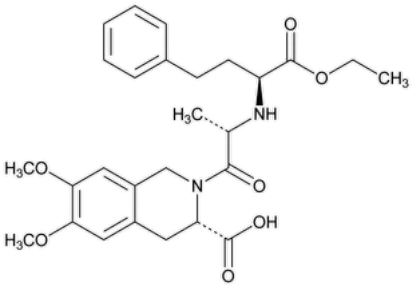
Moexipril Hydrochloride



• HCl

$C_{27}H_{34}N_2O_7 \cdot HCl$ 535.03

3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, monohydrochloride, [3*S*-[2[*R**(*R**)],3*R**]]-;
(3*S*)-2-[(2*S*)-*N*-[(1*S*)-1-Carboxy-3-phenylpropyl]alanyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-3-isoquinolinecarboxylic acid, 2-ethyl ester, monohydrochloride CAS RN®: 82586-52-5; UNII: Q1UMG3UH45.

DEFINITION

Moexipril Hydrochloride contains NLT 98.0% and NMT 102.0% of moexipril hydrochloride ($C_{27}H_{34}N_2O_7 \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

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

• **C.** **Identification Tests—General ⟨191⟩, *Chloride*:** Meets the requirements

ASSAY

• **Procedure**

Buffer: 1.32 g/L of dibasic ammonium phosphate. Adjust with diluted phosphoric acid to a pH of 7.5.

Solution A: Acetonitrile and tetrahydrofuran (95:5)

Mobile phase: *Solution A* and *Buffer* (30:70)

Standard solution: 0.1 mg/mL of USP Moexipril Hydrochloride RS in *Mobile phase*. [Note—Sonication may be necessary for complete dissolution.]

Sample solution: 0.1 mg/mL of Moexipril Hydrochloride in *Mobile phase*. [Note—Sonication may be necessary for complete dissolution.]

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 3.2 times the retention time of moexipril

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of moexipril hydrochloride ($C_{27}H_{34}N_2O_7 \cdot HCl$) in the portion of Moexipril Hydrochloride 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 Moexipril Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Moexipril Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.20%

• **Organic Impurities**

[Note—Use freshly prepared samples for analysis.]

Solution A and **Chromatographic system:** Proceed as directed in the *Assay*.

Solution B: Proceed as directed for the *Buffer* in the *Assay*.

Diluent: *Solution A* and *Solution B* (20:80)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	20	80
5	20	80
35	55	45
65	55	45
70	20	80
80	20	80

Standard solution 1: 4 µg/mL of USP Moexipril Hydrochloride RS in *Diluent*. [Note—Sonication may be necessary for complete dissolution.]

Standard solution 2: 2 mg/mL of USP Moexipril Hydrochloride RS and 3 µg/mL each of USP Moexipril Related Compound A RS, USP Moexipril Related Compound B RS, USP Moexipril Related Compound C RS, USP Moexipril Related Compound D RS, USP Moexipril Related Compound E RS, USP Moexipril Related Compound F RS, and USP Moexipril Related Compound G RS in *Diluent*. [Note—Sonication may be necessary for complete dissolution.]

Sample solution: 2 mg/mL of Moexipril Hydrochloride in *Diluent*. [Note—Sonication may be necessary for complete dissolution.]

System suitability

Samples: *Standard solution 1* and *Standard solution 2*

Suitability requirements

Resolution: NLT 3.5 between moexipril related compound A and moexipril related compound E; NLT 2.5 between moexipril and moexipril related compound G, *Standard solution 2*

Relative standard deviation: NMT 5.0% for moexipril, *Standard solution 1*

Analysis

Samples: *Standard solution 1*, *Standard solution 2*, and *Sample solution*

Calculate the percentage of each specified impurity in the portion of Moexipril Hydrochloride taken:

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

r_U = peak response of each specified impurity from the *Sample solution*

r_S = peak response of the corresponding Reference Standard from *Standard solution 2*

C_S = concentration of each specified impurity in *Standard solution 2* (mg/mL)

C_U = concentration of Moexipril Hydrochloride in the *Sample solution* (mg/mL)

Calculate the percentage of any other individual unspecified impurity in the portion of Moexipril Hydrochloride taken:

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

r_U = peak response of each individual unspecified impurity from the *Sample solution*

r_S = peak response of moexipril from *Standard solution 1*

C_S = concentration of USP Moexipril Hydrochloride RS in *Standard solution 1* (mg/mL)

C_U = concentration of Moexipril Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Moexipril related compound E[a]	0.14	0.15
Moexipril related compound A[b]	0.28	0.2
Moexipril related compound F[c]	0.62	0.15
Moexipril related compound G[d]	0.90	0.15
Moexipril	1.00	—
Moexipril related compound D[e]	1.28	0.15
Moexipril related compound B[f]	1.62	0.2
Moexipril related compound C[g]	2.26	0.15
Any other individual unspecified impurity	—	0.10
Total impurities[h]	—	1.0

[a] (*S*)-6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid.

[b] (3*S*)-2-{(2*S*)-*N*-[(1*S*)-1-Carboxy-3-phenylpropyl]alanyl}-1,2,3,4-tetrahydro-6,7-dimethoxy-3-isoquinolinecarboxylic acid.

[c] (*S*)-2-[(*S*)-1-Ethoxy-1-oxo-4-phenylbutan-2-ylamino]propanoic acid.

[d] (*S*)-6,7-Dimethoxy-2-{(*S*)-2-[(*S*)-1-methoxy-1-oxo-4-phenylbutan-2-ylamino]propanoyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid.

[e] (*S*)-2-{(*S*)-2-[(*S*)-4-Cyclohexyl-1-ethoxy-1-oxobutan-2-ylamino]propanoyl}-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid.

[f] (*S*)-Ethyl 2-{(3*S*,11a*S*)-8,9-dimethoxy-3-methyl-1,4-dioxo-3,4-dihydro-1*H*-pyrazino[1,2-*b*]isoquinolin-2(6*H*,11*H*,11a*H*)-yl}-4-phenylbutanoate.

[g] (*S*)-*tert*-Butyl 2-{(*S*)-2-[(*S*)-1-ethoxy-1-oxo-4-phenylbutan-2-ylamino]propanoyl}-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylate.

[h] Sum of all specified and unspecified impurities.

- **Content of Imidazole**

Mobile phase: Hexane, isopropyl alcohol, and diethyl amine (52:48:0.025)

Standard solution: 0.01 mg/mL of USP Imidazole RS in *Mobile phase*. [Note—Sonication may be necessary for complete dissolution.]

Sample solution: 2 mg/mL of Moexipril Hydrochloride in *Mobile phase*. [Note—Sonication may be necessary for complete dissolution. Use freshly prepared *Sample solution* for analysis.]

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L3

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 3.3 times the retention time of imidazole

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of imidazole in the portion of Moexipril Hydrochloride taken:

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

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

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

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

C_U = concentration of Moexipril Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 0.03%

SPECIFIC TESTS

- **Water Determination ⟨921⟩, *Method I, Method Ia*:** NMT 1.5%
- **Optical Rotation ⟨781S⟩, *Procedures, Specific Rotation***

Sample solution: 0.011 g/mL of Moexipril Hydrochloride in alcohol. Sonicate to dissolve the sample.

Acceptance criteria: +30.0° to +38.0°

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, protected from moisture. Store at room temperature.
- **USP Reference Standards ⟨11⟩**

USP Imidazole RS

USP Moexipril Hydrochloride RS

USP Moexipril Related Compound A RS

(3*S*)-2-{(2*S*)-*N*-[(1*S*)-1-Carboxy-3-phenylpropyl]alanyl}-1,2,3,4-tetrahydro-6,7-dimethoxy-3-isoquinolinecarboxylic acid.

$C_{25}H_{30}N_2O_7$ 470.51

USP Moexipril Related Compound B RS

(*S*)-Ethyl 2-{(3*S*,11a*S*)-8,9-dimethoxy-3-methyl-1,4-dioxo-3,4-dihydro-1*H*-pyrazino[1,2-*b*]isoquinolin-2(6*H*,11*H*,11a*H*)-yl}-4-phenylbutanoate.

$C_{27}H_{32}N_2O_6$ 480.55

USP Moexipril Related Compound C RS

(*S*)-*tert*-Butyl 2-{(*S*)-2-[(*S*)-1-ethoxy-1-oxo-4-phenylbutan-2-ylamino]propanoyl}-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylate.

$C_{31}H_{42}N_2O_7$ 554.67

USP Moexipril Related Compound D RS

(*S*)-2-{(*S*)-2-[(*S*)-4-Cyclohexyl-1-ethoxy-1-oxobutan-2-ylamino]propanoyl}-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid.

$C_{27}H_{40}N_2O_7$ 504.62

USP Moexipril Related Compound E RS

(*S*)-6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid.

$C_{12}H_{15}NO_4$ 237.25

USP Moexipril Related Compound F RS

(*S*)-2-[(*S*)-1-Ethoxy-1-oxo-4-phenylbutan-2-ylamino]propanoic acid.

$C_{15}H_{21}NO_4$ 279.33

USP Moexipril Related Compound G RS

(*S*)-6,7-Dimethoxy-2-{(*S*)-2-[(*S*)-1-methoxy-1-oxo-4-phenylbutan-2-ylamino]propanoyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid.

$C_{26}H_{32}N_2O_7$ 484.54

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

Topic/Question	Contact	Expert Committee
MOEXIPRIL HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 38(3)
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