Moexipril Hydrochloride Tablets

Type of Posting	Revision Bulletin
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Expert Committee	Chemical Medicines Monographs 2
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 2 Expert Committee has revised the Moexipril Hydrochloride Tablets monograph. The purpose for the revision is to widen the disregard limit from NMT 0.02% to NMT 0.1% and the any unspecified impurity limit from NMT 0.20% to NMT 0.2% to be consistent with the FDA approved drug product.

Minor editorial changes have been made to update the monograph to the current *USP* style.

The Moexipril Hydrochloride Tablets Revision Bulletin supersedes the currently official Moexipril Hydrochloride Tablets monograph. The Revision Bulletin will be incorporated in the *USP 40–NF 35.*

Should you have any questions, please contact Sujatha Ramakrishna, Ph.D., MBA. Senior Scientific Liaison (301–816–8349 or sxr@usp.org).

Moexipril Hydrochloride Tablets

DEFINITION

Moexipril Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of moexipril hydrochloride ($C_{27}H_{34}N_2O_7 \cdot HCl$).

IDENTIFICATION

- **A. ULTRAVIOLET ABSORPTION ⟨197U⟩**
- **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: 0.01 M potassium dihydrogen phosphate
Diluent: Acetonitrile and water (30:70)
Mobile phase: Acetonitrile and *Buffer* (350:650)
Standard solution: 0.075 mg/mL of USP Moexipril Hydrochloride RS in *Diluent*. Initially fill with *Diluent* to about 70% of the total volume, and sonicate. Further dilute with *Diluent* to volume.
Sample solution: Nominally 0.075 mg/mL of moexipril hydrochloride in *Diluent*, prepared from a sufficient number of crushed Tablets as follows. Add *Diluent* to about 75% of the total volume, and sonicate for 30 min with intermittent shaking. Dilute with *Diluent* to volume, and pass through a suitable filter of 0.45-µm pore size.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 210 nm
Column: 4.6-mm × 15-cm; 5-µm packing L7
Column temperature: 45°
Flow rate: 1.5 mL/min
Injection volume: 20 µL
Run time: 4 times the retention time of the moexipril peak
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of moexipril hydrochloride ($C_{27}H_{34}N_2O_7 \cdot HCl$) 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 Moexipril Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of moexipril hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **DISSOLUTION ⟨711⟩**

Test 1
Buffer, Diluent, Mobile phase, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.
Medium: Water; 900 mL
Apparatus 2: 50 rpm
Time: 15 min
Standard stock solution: 0.16 mg/mL of USP Moexipril Hydrochloride RS in *Diluent*. [NOTE—Sonication may be necessary for complete dissolution.]
Standard solution: 0.016 mg/mL of USP Moexipril Hydrochloride RS in *Medium* from the *Standard stock solution* for 15-mg Tablet strength and 0.008 mg/mL of USP Moexipril Hydrochloride RS in *Medium* from the *Standard stock solution* for 7.5-mg Tablet strength
Sample solution: Pass 10 mL of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 2–3 mL.
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of moexipril hydrochloride ($C_{27}H_{34}N_2O_7 \cdot HCl$) dissolved:

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

r_U = peak response of moexipril from the *Sample solution*
r_S = peak response of moexipril from the *Standard solution*
C_S = concentration of USP Moexipril Hydrochloride RS in the *Standard solution*
L = label claim (mg/Tablet)
V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (*Q*) of the labeled amount of moexipril hydrochloride ($C_{27}H_{34}N_2O_7 \cdot HCl$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.
Buffer, Diluent, Mobile phase, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.
Medium, Apparatus 2, Standard stock solution, Standard solution, Sample solution, and **Analysis:** Proceed as directed in *Test 1*.
Time: 30 min
Tolerances: NLT 80% (*Q*) of the labeled amount of moexipril hydrochloride ($C_{27}H_{34}N_2O_7 \cdot HCl$) is dissolved.

- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements for *Content Uniformity*

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**

Solution A: 0.025% trifluoroacetic acid in water
Solution B: Acetonitrile and tetrahydrofuran (90:10)
Diluent: Acetonitrile and water (30:70)
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
50	30	70
60	95	5
70	95	5

Impurity stock solution: 0.12 mg/mL of USP Moexipril Related Compound G RS in *Diluent*. [NOTE—Sonication may be necessary for complete dissolution.]
System suitability solution: 1.2 mg/mL of USP Moexipril Hydrochloride RS and 2.4 µg/mL of USP Moexipril

Related Compound G RS from the *Impurity stock solution* in *Diluent.* [NOTE—Sonication may be necessary for complete dissolution.]

Standard stock solution: 1.2 mg/mL of USP Moxipril Hydrochloride RS in *Diluent*. Initially add *Diluent* to about 60% of the volume of the flask, and sonicate with intermittent shaking for complete dissolution.

Standard solution: 6 µg/mL each of USP Moxipril Related Compound A RS and USP Moxipril Related Compound B RS, and 1.2 µg/mL of USP Moxipril Hydrochloride RS in *Diluent* from the *Standard stock solution*. [NOTE—Sonication may be necessary for complete dissolution.]

Sample solution: Nominally 1.2 mg/mL of moxipril hydrochloride in *Diluent*, prepared from a sufficient number of crushed Tablets. Initially add *Diluent* to about 60% of the volume of the flask, and sonicate for 20 min with intermittent shaking in ice cold water. Dilute with *Diluent* to volume. Pass through a suitable filter of 0.45-µm pore size.

Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 210 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Column temperature: 30°
Flow rate: 1 mL/min
Injection volume: 10 µL

System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 2.5 between moexipril and moexipril related compound G, *System suitability solution*
Tailing factor: NMT 2.0 for the moexipril peak, *System suitability solution*
Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis
Samples: *System suitability solution*, *Standard solution*, and *Sample solution*
Calculate the percentage of moexipril related compound A and moexipril related compound B in the portion of Tablets taken:

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

r_U = peak response of moexipril related compound A and moexipril related compound B from the *Sample solution*
r_S = peak response of moexipril related compound A and moexipril related compound B from the *Standard solution*
C_S = concentration of USP Moexipril Related Compound A RS and USP Moexipril Related Compound B RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of moexipril hydrochloride in the *Sample solution* (mg/mL)

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 any other individual unspecified degradation product from the *Sample solution*
r_S = peak response of moexipril from the *Standard solution*
C_S = concentration of USP Moexipril Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of moexipril hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard peaks less than •0.1%.• (RB 1-Jun-2016)

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Moexipril related compound E[a]	0.31	—
Moexipril related compound F[a]	0.77	—
Moexipril related compound A[b]	0.85	2.0
Moexipril related compound G[a]	0.94	—
Moexipril	1.00	—
Moexipril related compound D[a]	1.17	—
Moexipril related compound C[a]	1.27	—
Moexipril related compound B[c]	1.43	1.5
Any unspecified degradation product	—	•0.2• (RB 1-Jun-2016)
Total impurities[d]	—	2.0

[a] Process-related impurities controlled in the drug substance.
[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*)-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.
[d] Total impurities do not include moexipril related compound A.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Store at controlled room temperature in tight, well-closed containers, and protect from moisture.
- **LABELING:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  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 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