Moxifloxacin Hydrochloride

Type of Posting  Revision Bulletin
Posting Date  28-Jul-2017
Official Date  01-Aug-2017
Expert Committee  Chemical Medicines Monographs 1
Reason for Revision  Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 1 Expert Committee has revised the Moxifloxacin Hydrochloride monograph. The purpose of the revision is to widen the limit for Moxifloxacin Related Compound G in Enantiomeric Purity test to accommodate products approved by the FDA.

The acceptance criterion in the test for Enantiomeric Purity is revised from NMT 0.10% to NMT 0.15%.

Additionally, minor editorial changes have been made to update the monograph to current USP style.

The Moxifloxacin Hydrochloride Revision Bulletin supersedes the currently official monograph. The Revision Bulletin will be incorporated in to the First Supplement to USP 41–NF 36.

Should you have any questions, please contact Shankari Shivaprasad, Ph.D. Senior Scientific Liaison (301-230-7426 or sns@usp.org).
Moxifloxacin Hydrochloride

C₁₉H₂₀FN₅O₄ · HCl 437.89
(4aR,cis)-1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-(octahydro-6H-pyrrrolo[3,4-b]pyridin-6-yl)-4-oxo-3-quinolinecarboxylic acid, monohydrochloride;
1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-(4aS,7aS)-octahydro-6H-pyrrrolo[3,4-b]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid, monohydrochloride [186826-86-8].

DEFINITION
Moxifloxacin Hydrochloride contains NLT 98.0% and NMT 102.0% of moxifloxacin hydrochloride (C₁₉H₂₀FN₅O₄ · HCl), calculated on the anhydrous basis.

IDENTIFICATION
• A. INFRARED ABSORPTION (197K)
• B. The 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
Sample solution: To a solution (1 in 160) add diluted nitric acid, and filter.
Acceptance criteria: Meets the requirements

ASSAY

Change to read:

• PROCEDURE
  Buffer: Dissolve 0.5 g of tetrabutylammonium hydrogen sulfate and 1.0 g of monobasic potassium phosphate in water, add 2 mL of phosphoric acid, dilute with water to 1000 mL, mix, and pass through a filter of 0.45-μm pore size.
  Mobile phase: Methanol and Buffer (28:72)
  Diluent: Add 20 mg of anhydrous sodium sulfate to 1000 mL of Buffer, mix gently, and pass through a filter of 0.45-μm pore size.
  System suitability solution: 0.1 mg/mL of USP Moxifloxacin Hydrochloride RS and 1 μg/mL of USP Moxifloxacin Related Compound A RS, in Diluent
  Standard solution: 0.1 mg/mL of USP Moxifloxacin Hydrochloride RS in Diluent
  Sample solution: 0.1 mg/mL of Moxifloxacin Hydrochloride in Diluent

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 293 nm
Column: 4.0-mm × 25-cm; 5-μm packing L11
Column temperature: 45°
Flow rate: 0.9 mL/min
Injection volume: 25 μL
System suitability
Samples: System suitability solution and Standard solution
[NOTE—The relative retention times for moxifloxacin and moxifloxacin related compound A are about 1.0 and 1.2, respectively.]

Suitability requirements
Resolution: NLT 1.5 between moxifloxacin and moxifloxacin related compound A, System suitability solution
Tailing factor: NMT 2.0, Standard solution
Relative standard deviation: NMT 0.73%, Standard solution

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of moxifloxacin hydrochloride (C₁₉H₂₀FN₅O₄ · HCl) in the portion of Moxifloxacin Hydrochloride taken:

\[ \text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_U}{C_S} \right) \times 100 \]

\( f_U \) = peak response from the Sample solution
\( f_S \) = peak response from the Standard solution
\( C_U \) = concentration of USP Moxifloxacin Hydrochloride RS in the Standard solution (mg/mL)
\( C_S \) = concentration of Moxifloxacin Hydrochloride in the Sample solution (mg/mL)

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

IMPURITIES
• RESIDUE ON IGNITION (281): NMT 0.1%
• CHLORIDE AND SULFATE (221), Sulfate
Sample: 0.6 g
Acceptance criteria: 0.04%; the Sample shows no more sulfate than corresponds to 0.25 mL of 0.020 N sulfuric acid.

Change to read:

• ORGANIC IMPURITIES
  Protect all solutions containing moxifloxacin from light.
  Mobile phase, Diluent, System suitability solution, and Sample solution: Prepare as directed in the Assay.
  Standard solution: 2 μg/mL of USP Moxifloxacin Hydrochloride RS in Diluent
  Sensitivity solution: Dissolve 0.04 mg of USP Moxifloxacin Hydrochloride RS from the Standard solution in Diluent. Store the Sensitivity solution under refrigeration and protected from light.
  Chromatographic system: Proceed as directed in the Assay with a run time of two times the retention time of moxifloxacin.

System suitability
Samples: System suitability solution, Standard solution, and Sensitivity solution
Suitability requirements
Resolution: NLT 1.5 between moxifloxacin and moxifloxacin related compound A, System suitability solution
Tailing factor: NMT 2.0, Standard solution
Relative standard deviation: NMT 2.0%, Standard solution
Signal-to-noise ratio: NLT 10, Sensitivity solution

Analysis
Samples: Sample solution and Standard solution
Calculate the percentage of each impurity in the portion of Moxifloxacin Hydrochloride taken:

\[ \text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_U}{C_S} \right) \times (1/f) \times 100 \]

\( f_U \) = peak response from the Sample solution

©2017 The United States Pharmacopeial Convention All Rights Reserved.
Moxifloxacin

\[ r_s = \text{peak response of moxifloxacin from the Standard solution} \]
\[ C_1 = \text{concentration of USP Moxifloxacin Hydrochloride RS in the Standard solution (mg/mL)} \]
\[ C_0 = \text{concentration of Moxifloxacin Hydrochloride in the Sample solution (mg/mL)} \]
\[ F = \text{relative response factor (see Table 1)} \]

Acceptance criteria: See Table 1.

### SPECIFIC TESTS

- **Standard solution:** 8 mg/mL of Moxifloxacin Hydrochloride in Solution A

**Chromatographic system**

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

**Mode:** LC

Detector: UV 295 nm

Column: 3.0-mm × 15-cm; 3-μm packing L1

Flow rate: 0.42 mL/min

Injection volume: 1.5 μL

System suitability

Samples: System suitability solution and Sensitivity solution

[NOTE—The relative retention times for moxifloxacin related compound G and moxifloxacin are 0.78 and 1.0, respectively.]

**Suitability requirements**

**Resolution:** NLT 2.0 between moxifloxacin related compound G and moxifloxacin, System suitability solution

**Signal-to-noise ratio:** NLT 5, Sensitivity solution

**Analysis**

Sample: Sample solution

Calculate the percentage of moxifloxacin related compound G in the portion of Moxifloxacin Hydrochloride taken:

\[ \text{Result} = \left( \frac{r_s}{r_1 + r_3} \right) \times 100 \]

- **r_1** = peak response of moxifloxacin related compound G from the Sample solution
- **r_3** = peak response of moxifloxacin from the Sample solution

**Acceptance criteria:** *NMT 0.15% (81-Aug-2017)

### ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at room temperature.

### Change to read:

- **Optical Rotation,** Specific Rotation (7815)

Sample: 10 mg/mL in acetonitrile and water (1:1)

Acceptance criteria: −125° to −138° at 20°

**Microbial Enumeration Tests** (61) and Tests for Specified Microorganisms (62)

Total aerobic microbial count: NMT 10³ cfu/g

Total combined molds and yeasts count: NMT 10² cfu/g

**pH** (791)

Sample solution: 2 mg/mL

Acceptance criteria: 3.9–4.6

**Water Determination** (921), Method I, Method ia: NMT 4.5%

## Table 1

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moxifloxacin</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moxifloxacin related compound A*</td>
<td>1.15</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Moxifloxacin related compound B\ăng</td>
<td>1.32</td>
<td>0.71</td>
<td>0.1</td>
</tr>
<tr>
<td>Moxifloxacin related compound C\ăng</td>
<td>1.48</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Moxifloxacin related compound D\ăng</td>
<td>1.71</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Moxifloxacin related compound E\ăng</td>
<td>1.83</td>
<td>0.29</td>
<td>0.1</td>
</tr>
<tr>
<td>Other individual impurity</td>
<td></td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Total impurities</td>
<td></td>
<td></td>
<td>0.5</td>
</tr>
</tbody>
</table>

*1-Cyclopropyl-6,8-difluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo-3-quinolinocarboxylic acid.

### Change to read:

- **Enantiomeric Purity**

Protect all solutions containing moxifloxacin from light.

**Buffer:** 0.47 g/L of anhydrous cupric sulfate and 1.31 g/L of L-isoleucine in water. Adjust with 0.1 N sodium hydroxide to a pH of 4.50.

**Solution A:** Methanol and Buffer (500:1500)

**Solution B:** Methanol and Buffer (223:450)

**Mobile phase:** See Table 2.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>50</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>51</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>61</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>62</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>85</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>

**System suitability solution:** 8 mg/mL of USP Moxifloxacin Hydrochloride RS and 8 μg/mL of USP Moxifloxacin Related Compound G RS in Solution A

**Sensitivity solution:** 0.5 μg/mL of USP Moxifloxacin Related Compound G RS in Solution A
USP Moxifloxacin Related Compound G RS
1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4aR, 7aR)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid, monohydrochloride.

C₂₁H₂₄F₂N₃O₄ · HCl  437.89 USP40