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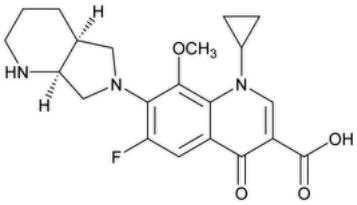
Moxifloxacin Hydrochloride



• HCl

$C_{21}H_{24}FN_3O_4 \cdot HCl$ 437.89

(4a*S*-*cis*)-1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-(octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl)-4-oxo-3-quinolinecarboxylic acid, monohydrochloride;

1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid, monohydrochloride CAS RN®: 186826-86-8; UNII: C53598599T.

DEFINITION

Moxifloxacin Hydrochloride contains NLT 98.0% and NMT 102.0% of moxifloxacin hydrochloride ($C_{21}H_{24}FN_3O_4 \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

• **B.** The 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

• **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 sulfite 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 ($C_{21}H_{24}FN_3O_4 \cdot HCl$) in the portion of Moxifloxacin 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 Moxifloxacin Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = 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.

- **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: 0.05 µg/mL 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:

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

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

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

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

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Moxifloxacin	1.0	—	—
Moxifloxacin related compound A[a]	1.15	1.0	0.1
Moxifloxacin related compound B[b]	1.32	0.71	0.1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Moxifloxacin related compound C[c]	1.48	1.0	0.1
Moxifloxacin related compound D[d]	1.71	1.0	0.1
Moxifloxacin related compound E[e]	1.83	0.29	0.1
Other individual impurity	—	1.0	0.1
Total impurities	—	—	0.5

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

[b] 1-Cyclopropyl-6,8-dimethoxy-1,4-dihydro-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid.

[c] 1-Cyclopropyl-8-ethoxy-6-fluoro-1,4-dihydro-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid.

[d] 1-Cyclopropyl-8-fluoro-6-methoxy-1,4-dihydro-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid.

[e] 1-Cyclopropyl-6-fluoro-8-hydroxy-1,4-dihydro-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid.

• **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* (225:450)

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	100	0
50	100	0
51	0	100
61	0	100
62	100	0
85	100	0

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: 0.8 µg/mL of USP Moxifloxacin Related Compound G RS in *Solution A*

Sample 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:

$$\text{Result} = [r_U/(r_S + r_U)] \times 100$$

r_U = peak response of moxifloxacin related compound G from the *Sample solution*

r_S = peak response of moxifloxacin from the *Sample solution*

Acceptance criteria: NMT 0.15%

SPECIFIC TESTS

- **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩**

  Total aerobic microbial count: NMT 10^3 cfu/g

  Total combined molds and yeasts count: NMT 10^2 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%

ADDITIONAL REQUIREMENTS

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

  USP Moxifloxacin Hydrochloride RS

  USP Moxifloxacin Related Compound A RS

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

  $C_{20}H_{21}F_2N_3O_3$ 389.40

  USP Moxifloxacin Related Compound G RS

  1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4a*R*,7a*R*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid, monohydrochloride.

  $C_{21}H_{24}FN_3O_4 \cdot HCl$ 437.89

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

Topic/Question	Contact	Expert Committee
MOXIFLOXACIN HYDROCHLORIDE	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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