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Moxifloxacin Ophthalmic Solution

DEFINITION

Moxifloxacin Ophthalmic Solution is a sterile, self-preserved aqueous solution of Moxifloxacin Hydrochloride. It contains NLT 90.0% and NMT 110.0% of the labeled amount of moxifloxacin ($C_{21}H_{24}FN_3O_4$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV absorption spectra of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Solution A: Dissolve 0.5 g of tetrabutylammonium hydrogen sulfate and 1.0 g of monobasic potassium phosphate in 1000 mL of water. Add 2 mL of phosphoric acid, filter, and degas.

Solution B: Methanol

Mobile phase: See *Table 1*.

Table 1

Time (min)	Flow Rate (mL/min)	Solution A (%)	Solution B (%)
0	0.5	69	31
30	0.5	69	31
31	0.9	60	40
36	0.9	60	40
37	0.5	69	31
42	0.5	69	31

System suitability solution: 0.1 mg/mL of USP Moxifloxacin Hydrochloride RS and 1 µg/mL of USP Moxifloxacin Related Compound A RS in *Solution A*

Standard stock solution: 6 mg/mL of USP Moxifloxacin Hydrochloride RS in water

Standard solution: 0.1 mg/mL of USP Moxifloxacin Hydrochloride RS in *Solution A* from the *Standard stock solution*

Sample solution: Nominally 0.1 mg/mL of moxifloxacin from Ophthalmic Solution in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 293 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.0-mm × 25-cm; 5-µm packing L11

Column temperature: 45°

Flow rate: See *Table 1*.

Injection volume: 25 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between the moxifloxacin and moxifloxacin related compound A peaks, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of moxifloxacin ($C_{21}H_{24}FN_3O_4$) in the portion of Ophthalmic Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of moxifloxacin 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 = nominal concentration of moxifloxacin in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of moxifloxacin, 401.43

M_{r2} = molecular weight of moxifloxacin hydrochloride, 437.89

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• Organic Impurities: Early-Eluting Related Compounds (Relative Retention Less Than 1.8)

Protect the *System suitability solution*, *Sample solution*, and *Standard solution* from light. Analyze the *Sample solution* immediately after preparation.

Solution A, Solution B, Mobile phase, System suitability solution, Standard stock solution, and **Sample solution:** Prepare as directed in the *Assay*.

Blank solution: Use *Solution A*.

Standard solution: 2 µg/mL of USP Moxifloxacin Hydrochloride RS in *Solution A* from the *Standard stock solution*

Sensitivity solution: 0.05 µg/mL of USP Moxifloxacin Hydrochloride RS from the *Standard solution* in *Solution A*. Store the *Sensitivity solution* under refrigeration and protected from light.

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: See *Table 1*.

Injection volume: 25 µL

System suitability

Samples: *System suitability solution*, *Standard solution*, and *Sensitivity solution*

Suitability requirements

Resolution: NLT 2.0 between the moxifloxacin and moxifloxacin related compound A peaks, *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: *Blank solution*, *Standard solution*, and *Sample solution*

[Note—Determine the relative retention values (r) for components listed in *Table 2*, using the time measured at the first baseline deflection of the *Standard solution* chromatogram as the void volume (t_M).]

Calculate the percentage of each impurity in the portion of Ophthalmic Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

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 = nominal concentration of moxifloxacin in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of moxifloxacin, 401.43

M_{r2} = molecular weight of moxifloxacin hydrochloride, 437.89

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention (*r*)	Relative Response Factor	Acceptance Criteria, NMT (%)
Specified unknown impurity #1	0.3	1.0	0.2
Decarboxy moxifloxacin[a]	0.4	0.16	0.3
Specified unknown impurity #2	0.9	1.0	0.3
Moxifloxacin	1.0	—	—
Moxifloxacin related compound A[b]	1.1	—	—
8-Hydroxy[c,d]	1.8	—	—
Any other individual impurity	—	1.0	0.1
Any specified and identified impurity	—	1.0	1.0

[a] 1-Cyclopropyl-6-fluoro-8-methoxy-7-[(4a*S*,7a*S*)-octahydro-pyrrolo[3,4-*b*]pyridin-6-yl]-1*H*-quinolin-4-one.

[b] Disregard this peak because this is a process impurity controlled for the drug substance.

[c] 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.

[d] Disregard this peak because it is quantitated using *Organic Impurities: Late-Eluting Related Compounds (Relative Retention Equal to More Than 1.8)*.

• **Organic Impurities: Late-Eluting Related Compounds (Relative Retention Equal to More Than 1.8)**

Protect the *Standard solution* and *Sample solution* from light. Analyze the *Sample solution* immediately after preparation.

Solution A, Solution B, and **Standard stock solution:** Prepare as directed in the *Assay*.

Mobile phase: *Solution A* and *Solution B* (60:40)

Blank solution: Use *Solution A*.

Standard solution: 2 µg/mL of USP Moxifloxacin Hydrochloride RS in *Solution A* from the *Standard stock solution*

Sensitivity solution: 0.05 µg/mL of USP Moxifloxacin Hydrochloride RS from the *Standard solution* in *Solution A*. Store the *Sensitivity solution* under refrigeration and protected from light.

Sample solution: Nominally 0.1 mg/mL of moxifloxacin from Ophthalmic Solution in *Solution A*. The 8-hydroxy compound is unstable in dilute aqueous solutions.

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

Run time: NLT 5 times the retention time of moxifloxacin peak

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

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: *Blank solution*, *Standard solution*, and *Sample solution*

[NOTE—Determine the relative retention values (r) for components listed in *Table 3*, using the time measured at the first baseline deflection of the *Standard solution* chromatogram as the void volume (t_M).]

Calculate the percentage of each impurity in the portion of Ophthalmic Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

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 = nominal concentration of moxifloxacin in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of moxifloxacin, 401.43

M_{r2} = molecular weight of moxifloxacin hydrochloride, 437.89

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention (r)	Relative Response Factor	Acceptance Criteria, NMT (%)
Moxifloxacin	1.0	—	—
8-Hydroxy	1.8	0.29	0.2
Specified unknown impurity #3	3.4	1.0	0.2
Floxacin amine[a]	3.9	0.42	0.2
Any other individual impurity	—	1.0	0.1

[a] 7-Amino-1-cyclopropyl-6-fluoro-8-methoxy-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid.

Total impurities: NMT 1.5%, sum from both *Organic Impurities* tests

SPECIFIC TESTS

- **STERILITY TESTS ⟨71⟩, *Test for Sterility of the Product to Be Examined, Membrane Filtration*:** Meets the requirements
- **pH ⟨791⟩:** 6.3–7.9
- **OSMOLALITY AND OSMOLARITY ⟨785⟩:** 260–370 mOsmol/kg

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store between 2° and 25°.
- **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

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

Topic/Question	Contact	Expert Committee
MOXIFLOXACIN OPHTHALMIC SOLUTION	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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