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Ciprofloxacin Ophthalmic Ointment

DEFINITION

Ciprofloxacin Ophthalmic Ointment contains an amount of Ciprofloxacin Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of ciprofloxacin ($C_{17}H_{18}FN_3O_3$).

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*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2021)

ASSAY

Change to read:

• **Procedure**

▲**Solution A:** 0.29% (v/v) phosphoric acid in water prepared as follows. Transfer an appropriate volume of phosphoric acid to a suitable volumetric flask containing 90% of the final volume of water. Adjust with triethylamine to a pH of 5.2 and dilute with water to volume.

Mobile phase: Acetonitrile and *Solution A* (12:88)

Diluent: Acetonitrile and *Solution A* (13:87)

Standard solution: 0.1 mg/mL of USP Ciprofloxacin Hydrochloride RS in *Diluent*

Sample solution: Nominally 0.1 mg/mL of ciprofloxacin prepared as follows. Transfer an amount nominally equivalent to 2.5 mg of ciprofloxacin from Ophthalmic Ointment to a suitable volumetric flask. Add 15 mL of hexane, and shake vigorously until the Ophthalmic Ointment is dispersed. Heat in a water bath at 60° for 30 min, with shaking. Add 25.0 mL of *Diluent*, while still warm, and shake vigorously for NLT 3 min. Allow the layers to separate, and use the lower, aqueous layer.

Chromatographic system

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

Mode: LC

Detector: UV 278 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

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

Temperatures

Autosampler: 4°

Column: 39°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%▲ (USP 1-May-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ciprofloxacin ($C_{17}H_{18}FN_3O_3$) in the portion of Ophthalmic Ointment taken:

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

r_U = peak response ▲of ciprofloxacin▲ (USP 1-May-2021) from the *Sample solution*

r_S = peak response ▲of ciprofloxacin▲ (USP 1-May-2021) from the *Standard solution*

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

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

M_{r1} = molecular weight of ciprofloxacin, 331.34

M_{r2} = molecular weight of anhydrous ciprofloxacin hydrochloride, 367.81

Acceptance criteria: 90.0%–110.0%

IMPURITIES

Add the following:

▲• Organic Impurities

Solution A, Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 0.002 mg/mL each of USP Ciprofloxacin Hydrochloride RS and USP Ciprofloxacin Ethylenediamine Analog RS in *Diluent*

Sensitivity solution: 0.2 µg/mL of USP Ciprofloxacin Hydrochloride RS in *Diluent*

Standard solution: 0.001 mg/mL of USP Ciprofloxacin Hydrochloride RS in *Diluent*

Sample solution: Nominally 0.2 mg/mL of ciprofloxacin prepared as follows. Transfer an amount nominally equivalent to 5 mg of ciprofloxacin from Ophthalmic Ointment to a suitable volumetric flask. Add 15 mL of hexane, and shake vigorously until the Ophthalmic Ointment is dispersed. Heat in a water bath at 60° for 30 min, with shaking. Add 25.0 mL of *Diluent*, while still warm, and shake vigorously for NLT 3 min. Allow the layers to separate, and use the lower, aqueous layer.

System suitability

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

Suitability requirements

Resolution: NLT 6.0 between ciprofloxacin ethylenediamine analog and ciprofloxacin, *System suitability solution*

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Ophthalmic Ointment 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 ciprofloxacin from the *Standard solution*

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

C_U = nominal concentration of ciprofloxacin 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[a]	Acceptance Criteria, NMT (%)
Ciprofloxacin ethylenediamine analog	0.7	1.35	0.2
Ciprofloxacin	1.0	—	—
Any unspecified impurity	—	1.0	0.1

Name	Relative Retention Time	Relative Response Factor[a]	Acceptance Criteria, NMT (%)
Total impurities	—	—	0.3▲ (USP 1-May-2021)

[a] *F* values are based on the response of ciprofloxacin hydrochloride.

SPECIFIC TESTS

• **Sterility Tests** ⟨71⟩, *Test for Sterility of the Product to Be Examined, Membrane Filtration*: It meets the requirements.

• **Other Requirements:** It meets the requirements for *Particulate and Foreign Matter* and *Container Contents* in *Ophthalmic Products—Quality Tests* ⟨771⟩, *Drug Product Quality, Universal Tests, Particulate and Foreign Matter* and *Container Contents*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in collapsible ophthalmic ointment tubes. Store at a temperature between 2° and 25°.

• **USP Reference Standards** ⟨11⟩

USP Ciprofloxacin Ethylenediamine Analog RS

1-Cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-[(2-aminoethyl)amino]-3-quinolinecarboxylic acid hydrochloride.

$C_{15}H_{16}FN_3O_3 \cdot HCl$ 341.77

USP Ciprofloxacin Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
CIPROFLOXACIN OPHTHALMIC OINTMENT	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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