Apparatus 1: 100 rpm.

Time: 30 minutes.

Standard preparation—Dissolve an accurately weighed quantity of USP Cinoxacin RS in *Dissolution Medium* to obtain a solution having a known concentration of about 0.35 mg per mL.

Procedure—Determine the amount of $C_{12}H_{10}N_2O_5$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 270 nm of filtered portions of the solution under test, suitably diluted with 0.1 N sodium hydroxide, in comparison with the *Standard preparation*, similarly diluted.

Tolerances—Not less than 60% *(Q)* of the labeled amount of $C_{12}H_{10}N_2O_5$ is dissolved in 30 minutes.

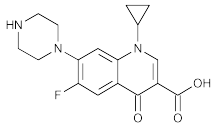
Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—Transfer the contents of not less than 20 Capsules to a suitable tared container, and weigh. T ransfer an accurately weighed portion of the mixed powder, equivalent to about 250 mg of cinoxacin, to a 100-mL volumetric flask. Dilute with 0.1 M sodium borate to volume, and mix. Filter the solution, discarding the first 20 mL of the filtrate, transfer 2.0 mL of the filtrate to a 500-mL volumetric flask, dilute with water to volume, and mix. Concomitantly determine the absorbances of this solution and of a Standard solution of USP Cinoxacin RS in the same medium having a known concentration of about 10 µg per mL, in 1-cm cells at the wavelength of maximum absorbance at about 352 nm, using 2 mL of 0.1 M sodium borate diluted with water to 500 mL as the blank. Calculate the quantity, in mg, of $C_{12}H_{10}N_2O_5$ in the portion of Capsules taken by the formula:

$$25C(A_U / A_S)$$

in which C is the concentration, in µg per mL, of USP Cinoxacin RS in the Standard solution; and A_U and A_S are the absorbances of the solution from the Capsules and the Standard solution, respectively.

Ciprofloxacin



$C_{17}H_{18}FN_3O_3$ 331.34

3-Quinolinecarboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-;

1-Cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid [85721-33-1].

DEFINITION

Ciprofloxacin contains NLT 98.0% and NMT 102.0% of $C_{17}H_{18}FN_3O_3$, calculated on the dried basis.

IDENTIFICATION

- **A. Infrared Absorption:** The IR absorption spectrum of a potassium bromide dispersion of it exhibits maxima at the same wavelengths as that of a similar preparation of USP Ciprofloxacin RS.
- **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**

Solution A: 0.025 M phosphoric acid. Adjust with triethylamine to a pH of 3.0 ± 0.1.

Mobile phase: Acetonitrile and *Solution A* (13:87)

Standard solution: Transfer 12.5 mg of USP Ciprofloxacin RS to a 25-mL volumetric flask. Add 0.1 mL of 7% phosphoric acid, and dilute with *Mobile phase* to volume.

System suitability stock solution: 0.025 mg/mL of USP Ciprofloxacin Ethylenediamine Analog RS in *Mobile phase*

System suitability solution: Transfer 1.0 mL of the *System suitability stock solution* to a 10-mL volumetric flask, and dilute with the *Standard solution* to volume.

Sample solution: Transfer 25 mg of Ciprofloxacin to a 50-mL volumetric flask. Add 0.2 mL of 7% phosphoric acid, and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 278 nm

Column: 4.6-mm × 25-cm; packing L1

Column temperature: 30 ± 1°

Flow rate: 1.5 mL/min

Injection size: 10 µL

System suitability

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

[Note—The relative retention times for ciprofloxacin ethylenediamine analog and ciprofloxacin are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 6 between ciprofloxacin ethylenediamine analog and ciprofloxacin, *System suitability solution*

Column efficiency: NLT 2500 theoretical plates from the ciprofloxacin peak, *Standard solution*

Tailing factor: NMT 2.5 for the ciprofloxacin peak, *Standard solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{17}H_{18}FN_3O_3$ in the portion of Ciprofloxacin taken:

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

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

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

IMPURITIES

Inorganic Impurities

- **Residue on Ignition** ⟨281⟩**:** NMT 0.1%, except that where it is intended for use in preparing Ciprofloxacin for Oral Suspension, it is NMT 0.2%.
- **Chloride**

Standard solution: 8.2 µg/mL of sodium chloride (5 µg/mL of chloride)

Sample solution: Add 30.0 mL of water to 0.5 g of Ciprofloxacin, shake for 5 min, and pass through chloride-free filter paper. Use the filtrate as the *Sample solution*.

Analysis

Samples: *Standard solution* and *Sample solution*

Transfer 15.0 mL of the *Sample solution* to a 50-mL color-comparison tube. Transfer 10.0 mL of the *Standard solution* to a second matched 50-mL color-comparison tube, add 5.0 mL of water, and mix. T o each tube add 1 mL of 2 N nitric acid, mix, add 1 mL of silver nitrate TS, and mix.

Acceptance criteria: The turbidity exhibited by the *Sample solution* does not exceed that of the *Standard solution* (0.02%).

- **Sulfate**

Standard solution: 18.1 µg/mL of potassium sulfate in 30% alcohol (10 µg/mL of sulfate)

Sample solution: Dissolve 0.5 g of Ciprofloxacin in 5.0 mL of 2 N acetic acid and 15.0 mL of water.
Analysis
Samples: *Standard solution* and *Sample solution*
To each of two 50-mL matched color-comparison tubes transfer 1.50 mL of the *Standard solution*. To each tube add, successively and with continuous shaking, 1.0 mL of 250 mg/mL barium chloride solution, and allow to stand for 1 min. To one of the tubes transfer 15.0 mL of the *Standard solution* and 0.5 mL of 30% acetic acid, and mix. To the second tube add 15.0 mL of the *Sample solution* and 0.5 mL of 30% acetic acid, and mix.
Acceptance criteria: The turbidity exhibited in the tube containing the *Sample solution* does not exceed that of the tube containing the *Standard solution* (0.04%).

- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 20 ppm

Organic Impurities

- **PROCEDURE 1: LIMIT OF FLUOROQUINOLONIC ACID**

Standard stock solution: Transfer 5.0 mg of USP Fluoroquinolonic Acid RS to a 50-mL volumetric flask containing 0.05 mL of 6 N ammonium hydroxide, and dilute with water to volume.
Standard solution: Dilute 2.0 mL of the *Standard stock solution* with water to 10.0 mL.
Sample solution: 10.0 mg/mL of Ciprofloxacin in 0.1 N acetic acid
Developing solvent system: Methylene chloride, methanol, acetonitrile, and ammonium hydroxide (4:4:1:2)
Chromatographic system
(See *Chromatography* ⟨621⟩*, Thin-Layer Chromatography*.)
Mode: TLC
Adsorbent: 0.25-mm layer of silica gel mixture
Application volume: 5 µL
Analysis
Samples: *Standard solution* and *Sample solution*
Place the plate in a suitable chamber in which is placed a beaker containing 50 mL of ammonium hydroxide. After 15 min, transfer the plate to a suitable chromatographic chamber, and develop the chromatogram in the *Developing solvent system* until the solvent front has moved three-fourths of the length of the plate. Remove the plate from the chamber, mark the solvent front, and allow the plate to air-dry for about 15 min. Examine the plate under short-wavelength UV light.
Acceptance criteria: Any spot from the *Sample solution*, at an R_F value corresponding to the principal spot from the *Standard solution*, is not greater in size or intensity than the principal spot from the *Standard solution* (0.2%).

- **PROCEDURE 2**

Solution A, Mobile phase, System suitability stock solution, System suitability solution, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.
Analysis
Sample: *Sample solution*
Calculate the percentage of each impurity in the portion of Ciprofloxacin taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = response of each impurity peak
r_T = sum of the responses of all the peaks
Acceptance criteria
Ciprofloxacin ethylenediamine analog or any other individual impurity peak: NMT 0.2%
Total impurities: NMT 0.5%

SPECIFIC TESTS

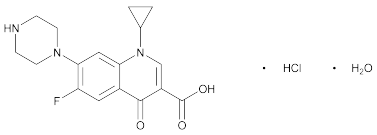
- **CLARITY OF SOLUTION:** Dissolve 0.25 g in 10 mL of 0.1 N hydrochloric acid: a clear to slightly opalescent solution is obtained.
- **MICROBIAL ENUMERATION TESTS** ⟨**61**⟩ and **TESTS FOR SPECIFIED MICROORGANISMS** ⟨**62**⟩**:** Where it is intended for use in preparing Ciprofloxacin for Oral Suspension, the total microbial count does not exceed 1000 cfu/g, and the total combined molds and yeasts count does not exceed 100 cfu/g. It also meets the requirement for absence of *Salmonella* species and *Escherichia coli*.
- **LOSS ON DRYING** ⟨**731**⟩**:** Dry a sample in a vacuum at 120 ° for 6 h: it loses NMT 1.0% of its weight, except that where it is labeled as intended for use in preparing Ciprofloxacin for Oral Suspension, it loses between 10% and 20% of its weight.
- **STERILITY TESTS** ⟨**71**⟩**:** Where the label states that it is sterile, it meets the requirements for *Test for Sterility of the Product to Be Examined, Membrane Filtration*.
- **BACTERIAL ENDOTOXINS TEST** ⟨**85**⟩**:** Where the label states that it is sterile or where the label states that Ciprofloxacin must be subjected to further processing during the preparation of injectable dosage forms, it contains NMT 0.50 USP Endotoxin Unit/mg of ciprofloxacin.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers. Store at 25 °, excursion permitted between 15 ° and 30°, and avoid excessive heat.
- **LABELING:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms. Where it is intended for use in preparing Ciprofloxacin for Oral Suspension, it is so labeled.
- **USP REFERENCE STANDARDS** ⟨**11**⟩

USP Ciprofloxacin RS
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 Endotoxin RS
USP Fluoroquinolonic Acid RS

Ciprofloxacin Hydrochloride



$C_{17}H_{18}FN_3O_3 \cdot HCl \cdot H_2O$ 385.82
3-Quinolinecarboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-, monohydrochloride, monohydrate;
1-Cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid, monohydrochloride, monohydrate [86393-32-0].

DEFINITION
Ciprofloxacin Hydrochloride contains NLT 98.0% and NMT 102.0% of $C_{17}H_{18}FN_3O_3 \cdot HCl$, 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,** *Chloride* ⟨**191**⟩

ASSAY

- **PROCEDURE**

Solution A: 0.025 M phosphoric acid. Adjust with triethylamine to a pH of 3.0 ± 0.1.
Mobile phase: Acetonitrile and *Solution A* (13:87)
Standard solution: 0.5 mg/mL of USP Ciprofloxacin Hydrochloride RS in *Mobile phase*