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Ciprofloxacin Injection

DEFINITION

Ciprofloxacin Injection is a sterile solution of Ciprofloxacin or Ciprofloxacin Hydrochloride in Water for Injection, in 5% Dextrose Injection, or in 0.9% Sodium Chloride Injection prepared with the aid of Lactic Acid. It contains NLT 90.0% and NMT 110.0% of the labeled amount of ciprofloxacin ($C_{17}H_{18}FN_3O_3$).

IDENTIFICATION

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: 0.5 mg/mL of USP Ciprofloxacin Hydrochloride RS in *Mobile phase*

System suitability solution: 0.025 mg/mL of USP Ciprofloxacin Ethylenediamine Analog RS in *Mobile phase*. Transfer 1.0 mL of this solution to a 10-mL volumetric flask, and dilute with *Standard solution* to volume.

Sample solution: Equivalent to 0.5 mg/mL of Ciprofloxacin from Injection diluted with *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 278 nm

Column: 4.6-mm × 25-cm; packing L1

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 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 6 between the ciprofloxacin ethylenediamine analog peak and the ciprofloxacin peak

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 the labeled amount of $C_{17}H_{18}FN_3O_3$ from the portion of Ciprofloxacin Injection taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response 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%

OTHER COMPONENTS

• **Lactic Acid Content**

Mobile phase: Acetonitrile and 0.005 N sulfuric acid (3:17)

Standard solution: 0.8 mg/mL of USP Sodium Lactate RS in water or 4 mg/mL where the Injection is labeled as being a concentrated form

Sample solution: Use the undiluted Injection.

Chromatographic system

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

Mode: LC

Detector: UV 208 nm

Column: 7.8-mm × 30-cm; packing L17

Temperature: 40 ± 1°

Flow rate: 0.6 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for the analyte peak

Relative standard deviation: NMT 2.0%

[Note—After each analysis, rinse the column with a mixture of 0.01 N sulfuric acid and acetonitrile to elute the ciprofloxacin from the column. Promptly regenerate the column with 0.01 N sulfuric acid, and the column may be reused or stored.]

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration of lactic acid ($C_3H_6O_3$) in mg/mg of ciprofloxacin:

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

r_U = peak response of lactic acid from the *Sample solution*

r_S = peak response of lactic acid from the *Standard solution*

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

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

M_{r1} = molecular weight of lactic acid, 90.08

M_{r2} = molecular weight of sodium lactate, 112.07

Acceptance criteria: 0.288–0.352 mg of lactic acid for each mg of ciprofloxacin claimed on the label, except that where the Injection is labeled as being a concentrated form, it contains 0.335–0.409 mg of lactic acid for each mg of ciprofloxacin claimed on the label

• **Dextrose Content** (if present)

Sample solution: Undiluted Injection

Analysis: Determine the angular rotation in a suitable polarimeter tube (see *Optical Rotation ⟨781⟩*).

Calculate the percentage (g/100 mL) of dextrose ($C_6H_{12}O_6 \cdot H_2O$) in the portion of Injection taken:

$$\text{Result} = A \times R \times (M_{r1}/M_{r2}) \times (100/F)$$

A = 100 mm divided by the length of the polarimeter tube (mm)

R = observed rotation (degrees)

M_{r1} = molecular weight of dextrose monohydrate, 198.17

M_{r2} = molecular weight of anhydrous dextrose, 180.16

F = midpoint of the specific rotation range for anhydrous dextrose, 52.9°

Acceptance criteria: 4.75–5.25 g/100 mL

• **Sodium Chloride Content** (if present)

Sample solution: Injection

Analysis: Transfer 10.0 mL of *Sample solution* to a suitable container, dilute with water to 150 mL, add 1.5 mL of potassium chromate TS, and titrate with 0.1 N silver nitrate TS. Each mL of 0.1 N silver nitrate is equivalent to 5.844 mg of sodium chloride (NaCl).

Acceptance criteria: 85.5–94.5 mg

IMPURITIES

Organic Impurities

• **Procedure: Limit of Ciprofloxacin Ethylenediamine Analog**

Mobile phase, System suitability solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Sample: *Sample solution*

Calculate the percentage of ciprofloxacin ethylenediamine analog from the portion of Ciprofloxacin Injection taken:

$$\text{Result} = [F \times r_A/(F \times r_A + r_C)] \times 100$$

F = correction factor for ciprofloxacin ethylenediamine analog, 0.7

r_A = ciprofloxacin ethylenediamine analog peak response

r_C = peak response of ciprofloxacin

Acceptance criteria: NMT 0.5%

SPECIFIC TESTS

• **Particulate Matter in Injections ⟨788⟩:** Meets the requirements

• **pH ⟨791⟩:** 3.5–4.6, except that where the Injection is labeled as being a concentrated form, its pH is 3.3–3.9

• **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 0.50 USP Endotoxin Unit/mg of ciprofloxacin.

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

• **Color and Achromicity ⟨631⟩** (where it is labeled as being a concentrated form)**:** It has no more color than a solution prepared by diluting 5.0 mL of *Matching Fluid O* with 95.0 mL of 0.12 N hydrochloric acid.

• **Other Requirements:** It meets the requirements for *Container Content for Injections ⟨697⟩*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose containers, preferably of Type I glass, and store in a cool place or at controlled room temperature. Avoid freezing and exposure to light.

• **Labeling:** The label indicates whether the vehicle is Sterile Water for Injection, 5% Dextrose Injection, or 0.9% Sodium Chloride Injection. Label the Injection that has Sterile Water for Injection as the vehicle to indicate that it is a concentrated form that must be diluted to appropriate strength (1–2 mg/mL) with 5% Dextrose Injection or 0.9% Sodium Chloride Injection before administration, and that the resulting solution is stable for up to 14 days when stored in a cool place or at controlled room temperature.

• **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

USP Sodium Lactate RS

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

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

Chromatographic Database Information: Chromatographic Database

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