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Cefotaxime for Injection

DEFINITION

Cefotaxime for Injection contains an amount of Cefotaxime Sodium equivalent to NLT 90.0% and NMT 115.0% of the labeled amount of cefotaxime ($C_{16}H_{17}N_5O_7S_2$).

IDENTIFICATION

Where the label indicates that there are no added substances:

Change to read:

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

• **B.** **Identification Tests—General, *Sodium*⟨191⟩:** Meets the requirements

Where the label indicates that there are added substances:

• **C.** The retention time of the major peak of the *Sample solution 1, 2, 3,* or *4* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 7.1 g/L of anhydrous dibasic sodium phosphate in water, adjusted with phosphoric acid to a pH of 6.25

Solution A: Methanol and *Buffer* (14:86). Pass through a filter having a pore size of 0.5 µm or finer, and degas before use.

Solution B: Methanol and *Buffer* (40:60). Pass through a filter having a pore size of 0.5 µm or finer, and degas before use.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
7	100	0
9	80	20
16	80	20
46	0	100
51	0	100
56	100	0

Standard solution: 0.8 mg/mL of USP Cefotaxime Sodium RS in *Solution A*. Use this solution promptly. It may be used within 24 h if stored in a refrigerator.

System suitability solution: Mix 1 mL of *Standard solution*, 7.0 mL of water, and 2.0 mL of methanol. Add 25 mg of sodium carbonate, mix, and allow to stand at room temperature for 10 min, with occasional swirling. Add 3 drops of glacial acetic acid and 1 mL of *Standard solution*.

Sensitivity solution: 1.6 µg/mL of USP Cefotaxime Sodium RS in *Solution A*

Sample solution 1 (for use where the *Weight Variation* test is to be performed)**:** 0.8 mg/mL of Cefotaxime for Injection in *Solution A*. Use this solution promptly. It may be used within 24 h if stored in a refrigerator.

Sample solution 2 (for use in assaying vials and infusion bottles packaged for dispensing)**:** Nominally 0.8 mg/mL of cefotaxime, prepared as follows. Constitute one container of Cefotaxime for Injection with the smallest volume of diluent specified in the labeling. Invert the container, and withdraw all of the withdrawable contents of the container with a hypodermic needle and syringe. Transfer the

contents of the syringe to a 100-mL volumetric flask, dilute with *Solution A* to volume, and mix. Do not rinse the syringe or container. Dilute a suitable aliquot of this solution with *Solution A*. Use this solution promptly. It may be used within 24 h if stored in a refrigerator.

Sample solution 3 (for use in assaying piggyback infusion bottles)**:** Nominally 0.8 mg/mL of cefotaxime, prepared as follows. Constitute one container of Cefotaxime for Injection with the smallest volume of diluent recommended in the labeling, using the directions specified in the labeling. Invert the container, and withdraw all of the withdrawable contents of the container with a hypodermic needle and syringe. Transfer the contents of the syringe to a 100-mL volumetric flask, dilute with *Solution A* to volume, and mix. Do not rinse the syringe or container. Dilute a suitable aliquot of this solution with *Solution A*. Use this solution promptly. It may be used within 24 h if stored in a refrigerator.

Sample stock solution 4 (for use in assaying pharmacy bulk packages where the label states the quantity of cefotaxime in a given volume of constituted solution)**:** Nominally 10 mg/mL of cefotaxime, prepared as follows. Constitute one container of Cefotaxime for Injection with the volume of diluent specified in the labeling. With a hypodermic needle and syringe, withdraw a suitable aliquot of the reconstituted product, transfer to a suitable volumetric flask, dilute with *Solution A* to volume, and mix. Do not rinse the syringe or container.

Sample solution 4: Nominally 0.8 mg/mL of cefotaxime from *Sample stock solution 4* in *Solution A*. Use this solution promptly. It may be used within 24 h if stored in a refrigerator.

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Column: 3.9-mm × 15-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *Standard solution, System suitability solution*, and *Sensitivity solution*. [NOTE—The retention times for desacetylcefotaxime and cefotaxime in the *System suitability solution* are 3.5 min and 14 min, respectively. The retention time for cefotaxime in the *Standard solution* is 12–15 min.]

Suitability requirements

Sensitivity: The response of the cefotaxime peak from the *Sensitivity solution* is between 0.18% and 0.22% of the response of the cefotaxime peak of the *Standard solution*.

Resolution: NLT 20 between desacetylcefotaxime and cefotaxime, *System suitability solution*

Tailing factor: NMT 2, *Standard solution*

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

Analysis

Samples: *Sample solution 1*, or *Sample solution 2*, or *Sample solution 3*, or *Sample solution 4*, and *Standard solution*

Calculate the percentage of the labeled amount of cefotaxime ($C_{16}H_{17}N_5O_7S_2$) withdrawn from the container, or in the portion of Cefotaxime for Injection taken:

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

r_U = peak area of the *Sample solution*

r_S = peak area of the *Standard solution*

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

C_U = nominal concentration of cefotaxime in *Sample solution 1*, *2*, *3*, or *4* (mg/mL)

P = potency of cefotaxime in USP Cefotaxime Sodium RS (µg/mg)

Acceptance criteria: 90.0%–115.0%. Where the test for *Uniformity of Dosage Units* has been peformed using the *Procedure for Content Uniformity*, use the average of these determinations as the *Assay* value.

PERFORMANCE TESTS

• **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meets the requirements

IMPURITIES

• **ORGANIC IMPURITIES**

Mobile phase; Standard solution; System suitability solution; Sample solutions 1, 2, 3 or **4; Chromatographic system;** and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Calculate the percentage of each impurity in the portion of Cefotaxime for Injection taken:

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

r_U = peak area of each individual impurity

r_T = sum of all of the impurity peak areas

r_C = peak area of cefotaxime

Acceptance criteria

Disregard any impurity peak that is less than 0.1%.

Individual impurities: NMT 6.0%

Total impurities: NMT 10.0%

SPECIFIC TESTS

• **Constituted Solution:** At the time of use, it meets the requirements in *Injections and Implanted Drug Products ⟨1⟩, Specific Tests, Completeness and clarity of solutions*.

• **Bacterial Endotoxins Test ⟨85⟩:** NMT 0.20 USP Endotoxin Unit/mg of cefotaxime

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

• **Particulate Matter in Injections ⟨788⟩:** It meets the requirements for small-volume injections.

• **pH ⟨791⟩**

Sample solution: 100-mg/mL solution

Acceptance criteria: 4.5–6.5

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 100°–105° for 3 h.

Acceptance criteria: NMT 3.0%

• **Other Requirements:** It meets the requirements in *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for constitution* .

• **USP Reference Standards ⟨11⟩**

USP Cefotaxime Sodium RS

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

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

Chromatographic Database Information: Chromatographic Database

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