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# Ceftriaxone for Injection

## DEFINITION

Ceftriaxone for Injection contains an amount of Ceftriaxone Sodium equivalent to NLT 776 µg/mg of ceftriaxone ($C_{18}H_{18}N_8O_7S_3$), calculated on the anhydrous basis, and the equivalent of NLT 90.0% and NMT 115.0% of the labeled amount of ceftriaxone ($C_{18}H_{18}N_8O_7S_3$).

## IDENTIFICATION

***Change to read:***

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

• **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**

Protect solutions containing ceftriaxone sodium from light.

**Solution A:** 9 g/L of monobasic potassium phosphate in water

**Solution B:** 24 g/L of dibasic sodium phosphate, dodecahydrate in water

**Solution C:** 20 g/L of citric acid in water. Adjust with 10 N sodium hydroxide TS to a pH of 5.0 prior to dilution.

**Buffer:** Combine 389 mL of *Solution A* and 611 mL of *Solution B*. Adjust with 10 N sodium hydroxide TS or phosphoric acid to a pH of 7.0.

**Mobile phase:** Dissolve 2.0 g each of tetradecylammonium bromide and tetraheptylammonium bromide in a mixture of 440 mL of water, 55 mL of *Buffer*, 5.0 mL of *Solution C*, and 500 mL of acetonitrile.

**System suitability solution:** 50 µg/mL each of USP Ceftriaxone Sodium RS and USP Ceftriaxone Sodium E-Isomer RS in *Mobile phase*

**Standard solution:** 0.3 mg/mL of USP Ceftriaxone Sodium RS in *Mobile phase*

**Sample solution 1:** Nominally 0.3 mg/mL of ceftriaxone from Ceftriaxone for Injection in *Mobile phase*

**Sample solution 2** (where it is represented as being in a single-dose container)**:** Nominally 0.3 mg/mL of ceftriaxone in *Mobile phase* prepared as follows. Constitute Ceftriaxone for Injection in a volume of water corresponding to the volume of solvent specified in the labeling. Withdraw all of the withdrawable contents using a suitable hypodermic needle and syringe, and transfer to a suitable volumetric flask. Dilute with *Mobile phase* to volume.

**Sample solution 3** (where the label states the quantity of ceftriaxone in a given volume of constituted solution)**:** Nominally 0.3 mg/mL of ceftriaxone in *Mobile phase* prepared as follows. Constitute Ceftriaxone for Injection in a volume of water corresponding to the volume of solvent specified in the labeling, and dilute with *Mobile phase* to final volume.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 254 nm

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

**Flow rate:** 1.5 mL/min

**Injection volume:** 20 µL

**System suitability**

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

[Note—The relative retention times for ceftriaxone and ceftriaxone *E*-isomer are 1.0 and 1.4, respectively.]

**Suitability requirements**

**Resolution:** NLT 3.0 between the ceftriaxone and ceftriaxone *E*-isomer peaks, *System suitability solution*

**Tailing factor:** NMT 2, *Standard solution*

**Relative standard deviation:** NMT 0.7%, *Standard solution*

**Analysis**

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

Calculate the quantity, in µg/mg, of ceftriaxone ($C_{18}H_{18}N_8O_7S_3$) in the portion of Ceftriaxone for Injection taken:

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

$r_U$ = peak response of ceftriaxone from *Sample solution 1*

$r_S$ = peak response of ceftriaxone from the *Standard solution*

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

$C_U$ = nominal concentration of ceftriaxone in *Sample solution 1* (mg/mL)

$P$ = potency of ceftriaxone in USP Ceftriaxone Sodium RS (µg/mg)

**Acceptance criteria:** NLT 776 µg/mg on the anhydrous basis

Calculate the percentage of the labeled amount of ceftriaxone ($C_{18}H_{18}N_8O_7S_3$) in the portion of Ceftriaxone for Injection withdrawn from the container or in the portion of the constituted solution:

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

$r_U$ = peak response of ceftriaxone from *Sample solution 2* or *Sample solution 3*

$r_S$ = peak response of ceftriaxone from the *Standard solution*

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

$C_U$ = nominal concentration of ceftriaxone in *Sample solution 2* or *Sample solution 3* (mg/mL)

$P$ = potency of ceftriaxone in USP Ceftriaxone Sodium RS (µg/mg)

$F$ = conversion factor, 0.001 mg/µg

**Acceptance criteria:** 90.0%–115.0% of the labeled amount of ceftriaxone

## PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

## IMPURITIES

• **Organic Impurities**

Protect solutions containing ceftriaxone sodium from light.

**Solution A, Solution B, Solution C, Buffer, Mobile phase, System suitability solution,** and **Chromatographic system:** Proceed as directed in the *Assay*.

**Standard solution:** 3 µg/mL of USP Ceftriaxone Sodium RS in *Mobile phase*

**Sample solution:** Nominally 0.3 mg/mL of ceftriaxone from Ceftriaxone for Injection in *Mobile phase*

**System suitability**

**Sample:** *System suitability solution*

[Note—The relative retention times for ceftriaxone and ceftriaxone *E*-isomer are listed in *Table 1*.]

**Suitability requirements**

**Resolution:** NLT 3.0 between the ceftriaxone and ceftriaxone *E*-isomer

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

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

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

$r_U$ = peak response of each individual impurity from the *Sample solution*

$r_S$ = peak response of ceftriaxone from the *Standard solution*

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

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

$P$ = potency of ceftriaxone in USP Ceftriaxone Sodium RS (µg/mg)

$F$ = conversion factor, 0.001 mg/µg

**Acceptance criteria:** See *Table 1*. Disregard any peak below 0.1%.

**Table 1**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Deacetylcefotaxime lactone[a] | 0.20 | 0.5 |
| 7-Aminocephalosporanic acid[b] | 0.34 | — |
| Ceftriaxone triazine analog[c] | 0.62 | 1.0 |
| Ceftriaxone benzothiazolyl oxime[d] | 0.72 | 0.2 |
| Deacyl ceftriaxone[e] | 0.78 | 1.0 |
| Ceftriaxone | 1.0 | — |
| Ceftriaxone-3-ene isomer[f] | 1.3 | 0.3 |
| Ceftriaxone *E*-isomer[g] | 1.4 | 1.0 |
| Any individual unspecified impurity | — | 0.2 |
| Total impurities | — | 5.0 |

[a] (*Z*)-2-(2-Aminothiazol-4-yl)-*N*-{(5a*R*,6*R*)-1,7-dioxo-1,3,4,5a,6,7-hexahydroazeto[2,1-*b*]furo[3,4-*d*][1,3]thiazin-6-yl}-2-(methoxyimino)acetamide.

[b] Process impurities that are controlled in the drug substance are not to be reported, are not included in total impurities, and are listed here for information only.

[c] 3-Mercapto-2-methyl-1,2-dihydro-1,2,4-triazine-5,6-dione.

[d] (*Z*)-*S*-Benzothiazol-2-yl 2-(2-aminothiazol-4-yl)-2-(methoxyimino)thioacetate.

[e] (6*R*,7*R*)-7-Amino-3-{[(6-hydroxy-2-methyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)thio]methyl}-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

[f] (6*R*,7*R*)-7-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-(methoxyimino)acetamido]-3-{[(6-hydroxy-2-methyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)thio]methyl}-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylic acid.

[g] (6*R*,7*R*)-7-[(*E*)-2-(2-Aminothiazol-4-yl)-2-(methoxyimino)acetamido]-3-{[(6-hydroxy-2-methyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)thio]methyl}-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

## SPECIFIC TESTS

• **Constituted Solution:** At the time of use, it meets the requirements for *Injections and Implanted Drug Products ⟨1⟩, Product Quality Tests Common to Parenteral Dosage Forms, Specific Tests, Completeness and clarity of solutions*.

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

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

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

• **Crystallinity ⟨695⟩:** Meets the requirements

• **pH ⟨791⟩**

**Sample solution:** 100 mg/mL

**Acceptance criteria:** 6.0–8.0

• **Water Determination ⟨921⟩, *Method I*:** 8.0%–11.0%

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

## ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for constitution*, and protected from light.

• **USP Reference Standards ⟨11⟩**

USP Ceftriaxone Sodium RS

USP Ceftriaxone Sodium E-Isomer RS

(6*R*,7*R*)-7-[(*E*)-2-(2-Aminothiazol-4-yl)-2-(methoxyimino)acetamido]-3-{[(6-hydroxy-2-methyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)thio]methyl}-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, disodium salt.

$C_{18}H_{16}N_8Na_2O_7S_3$ 598.53

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| CEFTRIAXONE FOR INJECTION | Documentary Standards Support | SM12020 Small Molecules 1 |

**Chromatographic Database Information:** Chromatographic Database

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