Ceftizoxime Sodium according to Method 3, and perform the test using Apparatus B (not more than 1 ppm).

(4) Related substances—Dissolve 0.11 g of Ceftizoxime Sodium in 100 mL of 0.1 mol/L phosphate buffer solution, pH 7.0, and use this solution as the sample solution. Perform the test with 5 μL of the sample solution as directed under the Liquid Chromatography according to the following conditions, and calculate the areas of each peak by the automatic integration method: each peak area other than ceftizoxime is not more than 0.5% of the peak area of ceftizoxime, and the total of peak areas other than ceftizoxime is not more than 1.0% of that of ceftizoxime.

Operating conditions—

Detector, column, and column temperature: Proceed as directed in the operating conditions in the Assay.

Mobile phase: Dissolve 2.31 g of disodium hydrogenphosphate 12-water and 1.42 g of citric acid monohydrate in 1000 mL of water, adjust to pH 3.6 with diluted phosphoric acid (1 in 10) or dilute sodium hydroxide TS. To 200 mL of this solution add 10 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of ceftizoxime is about 12 minutes.

Time span of measurement: About 5 times as long as the retention time of ceftizoxime after the solvent peak.

System suitability—

Test for required detection: Pipet 1 mL of the sample solution, add 0.1 mol/L phosphate buffer solution, pH 7.0 to make exactly 100 mL, and use this solution as the solution for test for required detection. Pipet 1 mL of the solution, add 0.1 mol/L phosphate buffer solution, pH 7.0 to make exactly 10 mL, and confirm that the peak area of ceftizoxime obtained from 5 μL of this solution is equivalent to 7 to 13% of that of ceftizoxime obtained from 5 μL of the solution for test for required detection.

System performance: Dissolve about 0.01 g of Ceftizoxime Reference Standard in 100 mL of 0.1 mol/L phosphate buffer solution, pH 7.0, and use this solution as the solution for system suitability test. When the procedure is run with 5 μL of this solution under the above operating conditions, the number of theoretical steps and the symmetry coefficient of the peak of ceftizoxime are not less than 4000 steps and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 5 μL of the solution for system suitability test under the above operating conditions, the relative standard deviation of the peak areas of ceftizoxime is not more than 2.0%.

Water Not more than 8.5% (0.4 g, volumetric titration, direct titration).

Assay Weigh accurately an amount of Ceftizoxime Sodium and Ceftizoxime Reference Standard, equivalent to about 0.1 g (potency), and dissolve each in 0.1 mol/L phosphate buffer solution, pH 7.0 to make exactly 20 mL. Pipet 2 mL each of these solutions, add exactly 10 mL of the internal standard solution, then add 0.1 mol/L phosphate buffer solution, pH 7.0 to make 20 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 5 μL each of these solutions as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of ceftizoxime to that of the internal standard of each solution.

$$\text{Amount [}\mu\text{g (potency)] of } C_{13}H_{13}N_5O_5S_2 = \text{amount [mg (potency)] of Ceftizoxime Reference Standard} \times \frac{Q_T}{Q_S} \times 1000$$

Internal standard solution—A solution of 3-hydroxybenzoic acid in 0.1 mol/L phosphate buffer solution, pH 7.0 (3 in 500).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10 μm in particle diameter).

Column temperature: A constant temperature of about 35°C.

Mobile phase: Dissolve 2.31 g of disodium hydrogenphosphate 12-water and 1.42 g of citric acid monohydrate in 1000 mL of water, and adjust to pH 3.6 with diluted phosphoric acid (1 in 10) or dilute sodium hydroxide TS. To 450 mL of this solution add 50 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of ceftizoxime is about 4 minutes.

System suitability—

System performance: When the procedure is run with 5 μL of the standard solution under the above operating conditions, ceftizoxime and the internal standard are eluted in this order with the resolution between these peaks being not less than 7.0 and the symmetry coefficient of each peak is not more than 2.

System repeatability: When the test is repeated 6 times with 5 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of ceftizoxime to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Ceftriaxone Sodium

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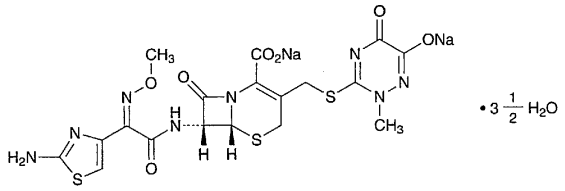

$C_{18}H_{16}N_8Na_2O_7S_3.3\frac{1}{2}H_2O$: 661.60

Disodium (6*R*,7*R*)-7-[(*Z*)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetylamino]-3-(6-hydroxy-2-methyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-ylsulfanylmethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate hemiheptahydrate [*104376-79-6*]

Ceftriaxone Sodium contains not less than 834 μg (potency) per mg, calculated on the anhydrous basis. The potency of Ceftriaxone Sodium is expressed as mass (potency) of ceftriaxone ($C_{18}H_{18}N_8O_7S_3$: 554.58).

Description Ceftriaxone Sodium occurs as a white to yellowish white crystalline powder.

It is freely soluble in water and in dimethylsulfoxide, sparingly soluble in methanol, very slightly soluble in ethanol (99.5), and practically insoluble in acetonitrile.

Identification (1) Determine the absorption spectrum of a solution of Ceftriaxone Sodium (1 in 91,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Ceftriaxone Sodium Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

(2) Determine the spectrum of a solution of Ceftriaxone Sodium in deuterated dimethylsulfoxide for nuclear magnetic resonance spectroscopy (1 in 10), using tetramethylsilane for nuclear magnetic resonance spectroscopy as an internal reference compound, as directed under the Nuclear Magnetic Resonance Spectroscopy (^{1}H): it exhibits single signals, A, B, C and D, at around δ 3.5 ppm, at around δ 3.8 ppm, at around δ 6.7 ppm and at around δ 7.2 ppm, respectively. The ratio of integrated intensity of each signal, A: B: C: D, is about 3:3:1:2. When the signal at around δ 3.5 ppm overlaps with the signal of water, perform the measurement in the probe kept at about 50°C.

(3) Ceftriaxone Sodium responds to the Qualitative Test (1) for sodium salt.

Optical rotation $[\alpha]_D^{20}$: -153 – $-170°$ (0.05 g calculated on the anhydrous basis, water, 2.5 mL, 20 mm).

pH Dissolve 0.6 g of Ceftriaxone Sodium in 5 mL of water: the pH of the solution is between 6.0 and 8.0.

Purity (1) Clarity and color of solution—Dissolve 0.6 g of Ceftriaxone Sodium in 5 mL of water: the solution is clear and light yellow.

(2) Heavy metals—Proceed with 1.0 g of Ceftriaxone Sodium according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(3) Arsenic—Prepare the test solution with 1.0 g of Ceftriaxone Sodium according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

Water Not less than 8.0% and not more than 11.0% (0.15 g, volumetric titration, direct titration).

Assay Weigh accurately an amount of Ceftriaxone Sodium and Ceftriaxone Sodium Reference Standard, equivalent to about 0.1 g (potency), dissolve each in a mixture of water and acetonitrile (11:9) to make exactly 50 mL. Pipet 5 mL of each solution, add exactly 5 mL of the internal standard solution and a mixture of water and acetonitrile (11:9) to make 200 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 10 μL each of these solutions as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of ceftriaxone to that of the internal standard.

$$\text{Amount [}\mu\text{g (potency)] of ceftriaxone } (C_{18}H_{18}N_8O_7S_3) = \text{amount [mg (potency)] of Ceftriaxone Sodium Reference Standard} \times \frac{Q_T}{Q_S} \times 1000$$

Internal standard solution—A solution of diethyl terephthalate in a mixture of water and acetonitrile (11:9) (9 in 5000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10 μm in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: Dissolve 5.796 g of anhydrous disodium hydrogenphosphate and 3.522 g of potassium dihydrogenphosphate in water to make exactly 1000 mL, and use this solution as solution A. Dissolve 20.256 g of citric acid monohydrate and 7.840 g of sodium hydroxide in water to make exactly 1000 mL, and use this solution as solution B. Dissolve 4.00 g of tetra-*n*-heptylammonium bromide in 450 mL of acetonitrile, and add 490 mL of water, 55 mL of solution A, and 5 mL of solution B.

Flow rate: Adjust the flow rate so that the retention time of ceftriaxone is about 7 minutes.

System suitability—

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, ceftriaxone and the internal standard are eluted in this order with the resolution between these peaks being not less than 6.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of ceftriaxone to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Cefuroxime Axetil

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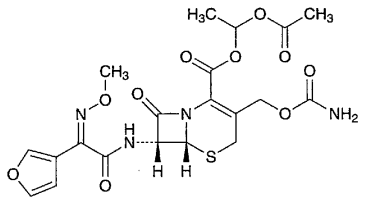

$C_{20}H_{22}N_4O_{10}S$: 510.47

(1*RS*)-1-Acetoxyethyl (6*R*,7*R*)-3-carbamoyloxymethyl-7-[(*Z*)-2-furan-3-yl-2-methoxyiminoacetylamino]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate

[*64544-07-6*]

Cefuroxime Axetil conforms to the requirements of Cefuroxime Axetil in the Requirements for Antibiotic Products of Japan.

Description Cefuroxime Axetil occurs as a white to yellowish white amorphous powder. It has a faint characteristic odor and a bitter taste.

It is freely soluble in 1,4-dioxane, soluble in methanol,