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.

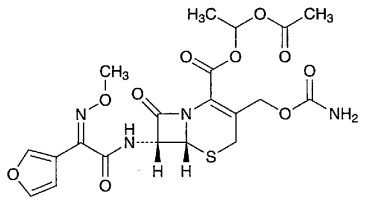
System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of ceftriaxone to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Cefuroxime Axetil

セフロキシムアキセチル



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

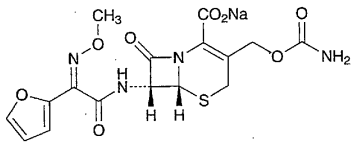
Description Cefuroxime Axetil occurs as a white to yellowish white amorphous powder. It has a faint characteristic odor and a bitter taste.

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

sparingly soluble in ethanol (95), slightly soluble in diethyl ether, and very slightly soluble in water.

Cefuroxime Sodium

セフロキシムナトリウム



$C_{16}H_{15}N_4NaO_8S$: 446.37
Monosodium (6*R*,7*R*)-3-carbamoyloxymethyl-7-[(*Z*)-2-furan-2-yl-2-methoxyiminoacetylamino]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate [*56238-63-2*]

Cefuroxime Sodium contains not less than 875 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefuroxime Sodium is expressed as mass (potency) of cefuroxime ($C_{16}H_{16}N_4O_8S$: 424.39).

Description Cefuroxime Sodium occurs as a white to light yellowish white, crystals or crystalline powder.

It is freely soluble in water, soluble in methanol, and very slightly soluble in ethanol (95).

Identification **(1)** Determine the absorption spectrum of a solution of Cefuroxime Sodium (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Cefuroxime Sodium Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

(2) Determine the infrared absorption spectrum of Cefuroxime Sodium as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Cefuroxime Sodium Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) Determine the spectrum of a solution of Cefuroxime Sodium in heavy water for nuclear magnetic resonance spectroscopy (1 in 10) as directed under the Nuclear Magnetic Resonance Spectroscopy (^{1}H), using sodium 3-trimethylsilylpropanesulfonate for nuclear magnetic resonance spectroscopy as an internal reference compound: it exhibits a single signal A at around δ 4.0 ppm, a quartet signal B at around δ 6.6 ppm, and double signals, C and D, at around δ 6.9 ppm and around δ 7.7 ppm, respectively. The ratio of integrated intensity of each signal, A:B:C:D, is about 3:1:1:1.

(4) Cefuroxime Sodium responds to the Qualitative Test (1) for sodium salt.

Optical rotation $[\alpha]_D^{20}$: +59 – +66° (0.5 g calculated on the anhydrous bases, water, 100 mL, 100 mm).

pH Dissolve 1.0 g of Cefuroxime Sodium in 10 mL of water: the pH of the solution is between 6.0 and 8.5.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Cefuroxime Sodium in 10 mL of water: the solution is clear, and its absorbance at 405 nm is not more than 0.25.

(2) Heavy metals—Proceed with 1.0 g of Cefuroxime Sodium according to Method 2, and perform the test. Prepare the control solution with 3.0 mL of Standard Lead Solution (not more than 30 ppm).

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

(4) Related substances—Dissolve 0.025 g of Cefuroxime Sodium in 25 mL of water, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard 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 cefuroxime from the sample solution is not more than the peak area of cefuroxime from the standard solution, and the total of the peak areas other than cefuroxime from the sample solution is not more than 3 times of the peak area of cefuroxime from the standard solution.

Operating conditions—

Detector, column, column temperature, mobile phase, and flow rate: Proceed as directed in the operating conditions in the Assay.

Time span of measurement: About 4 times as long as the retention time of cefuroxime after the solvent peak.

System suitability—

Test for required detection: Pipet 1 mL of the standard solution, add water to make exactly 10 mL, and confirm that the peak area of cefuroxime obtained from 20 μL of this solution is equivalent to 7 to 13% of that of cefuroxime obtained from 20 μL of the standard solution.

System performance: Proceed as directed in the system suitability in the Assay.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of cefuroxime is not more than 2.0%.

Water Not more than 4.0% (0.4 g, volumetric titration, direct titration).

Assay Weigh accurately an amount of Cefuroxime Sodium and Cefuroxime Sodium Reference Standard, equivalent to about 0.025 g (potency), and dissolve each in water to make exactly 25 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 20 μL each of these solutions as directed under the Liquid Chromatography according to the following conditions, and calculate the peak area, A_T and A_S, of cefuroxime of each solution.

Amount [μg (potency)] of $C_{16}H_{16}N_4O_8S$
= amount [mg (potency)] of Cefuroxime Sodium Reference Standard $\times \frac{A_T}{A_S} \times 1000$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 273 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 125 mm in length, packed with hexasilanized silica gel for liquid chromatography (5 μm in particle diameter).