Mobile phase: Mix 0.366 g of diethylamine with water to make 1000 mL, and add 60 mL of acetonitrile and 5 mL of acetic acid (100).

Flow rate: Adjust the flow rate so that the retention time of cefozopran is about 9 minutes.

System suitability—

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

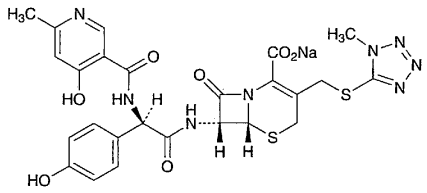
System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of cefozopran to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Hermetic containers.

Storage—Light-resistant.

Cefpiramide Sodium

セフピラミドナトリウム



$C_{25}H_{23}N_8NaO_7S_2$: 634.62

Monosodium (6*R*,7*R*)-7-{(2*R*)-2-[(4-hydroxy-6-methylpyridine-3-carbonyl)amino]-2-(4-hydroxyphenyl)acetylamino}-3-(1-methyl-1*H*-tetrazol-5-ylsulfanylmethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate [*74849-93-7*]

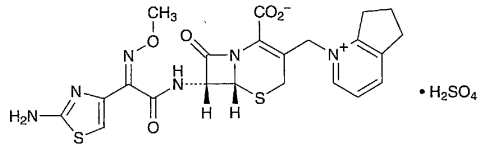
Cefpiramide Sodium conforms to the requirements of Cefpiramide Sodium in the Requirements for Antibiotic Products of Japan.

Description Cefpiramide Sodium occurs as a white to yellowish white powder.

It is freely soluble in water, sparingly soluble in methanol, slightly soluble in ethanol (95), and practically insoluble in diethyl ether.

Cefpirome Sulfate

硫酸セフピロム



$C_{22}H_{22}N_6O_5S_2.H_2SO_4$: 612.66

(6*R*,7*R*)-7-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-methoxyiminoacetylamino]-3-(6,7-dihydro-5*H*-cyclopenta[*b*]pyridinium-1-ylmethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate monosulfate [*98753-19-6*]

Cefpirome Sulfate contains not less than 760 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefpirome Sulfate is expressed as mass (potency) of cefpirome ($C_{22}H_{22}N_6O_5S_2$: 514.58).

Description Cefpirome Sulfate occurs as a white to pale yellowish white crystalline powder, and has a slight, characteristic ordor.

It is soluble in water, and practically insoluble in ethanol (95).

It is hygroscopic.

Identification **(1)** Dissolve 0.01 g of Cefpirome Sulfate in 2 mL of water, add 3 mL of hydroxylammonium hydrochloride-ethanol TS, allow to stand for 5 minutes, add 1 mL of acidic ammonium iron (III) sulfate TS, and shake: a red-brown color develops.

(2) Dissolve 1 mg of Cefpirome Sulfate in 4 mL of water, add 1 mL of dilute hydrochloric acid while cooling in ice, add 1 mL of a freshly prepared solution of sodium nitrite (1 in 100), and allow to stand for 2 minutes. Add 1 mL of ammonium amidosulfuric acid TS while cooling in ice bath, allow to stand for 1 minute, and add 1 mL of a solution of *N*-1-naphthylethylene dihydrochloride (1 in 1000): a purple color develops.

(3) Take 5 mg of Cefpirome Sulfate, dissolve in 1 mL of ethanol (95) and 1 mL of water, add 100 mg of 1-chloro-2,4-dinitrobenzene, and heat on a water bath for 5 minutes. After cooling, add 2 or 3 drops of a solution of sodium hydroxide (1 in 10) and 3 mL of ethanol (95): a red-brown color develops.

(4) Determine the absorption spectra of solutions of Cefpirome Sulfate and Cefpirome Sulfate Reference Standard in 0.01 mol/L hydrochloric acid TS (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectra: both spectra exhibit similar intensities of absorption at the same wavelengths.

(5) Determine the spectrum of a solution of Cefpirome Sulfate in heavy water for nuclear magnetic resonance spectroscopy (1 in 25) 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 4.1 ppm, a double signal B at around δ 5.9 ppm, a single signal C at around δ 7.1 ppm, and a multiple signal D at around δ 7.8 ppm. The ratio of integrated intensity of each signal, A:B:C:D, is about 3:1:1:1.

(6) A solution of Cefpirome Sulfate (1 in 250) responds to the Qualitative Test (1) for sulfate salt.

Absorbance $E^{1\%}_{1\,cm}$ (270 nm): 405 – 435 (0.05 g calculated on the anhydrous basis, 0.01 mol/L hydrochloric acid TS, 2500 mL).

Optical rotation $[\alpha]^{20}_D$: −27 – −33° (0.5 g calculated on the anhydrous basis, a solution prepared by addition of water to 25 mL of actonitrile to make 50 mL, 20 mL, 100 mm).

pH Dissolve 0.1 g of Cefpirome Sulfate in 10 mL of water: the pH of the solution is between 1.6 and 2.6.

Purity **(1)** Clarity and color of solution—Being specified separately.

(2) Heavy metals—Proceed with 1.0 g of Cefpirome Sulfate 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—Being specified separately.

(4) Related substances—Being specified separately.

(5) Residual solvents—Being specified separately.

Water Not more than 2.5% (0.5 g, volumetric titration, direct titration).

Residue on ignition Being specified separately.

Bacterial endotoxins Less than 0.10 EU/mg (potency).

Assay Weigh accurately an amount of Cefpirome Sulfate equivalent to about 0.05 g (potency), dissolve in water to make exactly 100 mL. Pipet 5 mL of this solution, add water to make exactly 20 mL, and use this solution as the sample solution. Separately, weigh accurately an amount of Cefpirome Sulfate Reference Standard equivalent to about 0.05 g (potency), dissolve in water to make exactly 100 mL. Pipet 5 mL of this solution, add water to make exactly 20 mL, and use this solution as the standard solution. Perform the test with 20 μL of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the peak areas, A_T and A_S, of cefpirome of each solution.

$$\text{Amount } [\mu\text{g (potency)}] \text{ of cefpirome } (C_{22}H_{22}N_6O_5S_2) = \text{amount [mg (potency)] of Cefpirome Sulfate Reference Standard} \times \frac{A_T}{A_S} \times 1000$$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 270 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 (5 μm in particle diameter).

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

Mobile phase: Dissolve 3.45 g of ammonium dihydrogenphosphate in 1000 mL of water, and adjust the pH to 3.3 with phosphoric acid. To 800 mL of this solution add 100 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of cefpirome is about 7.5 minutes.

System suitability—

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, the number of theoretical steps of the peak of cefpirome is not less than 3600.

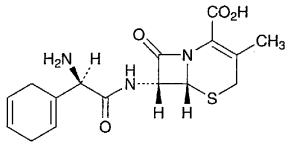
System repeatability: When the test is repeated 5 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of cefpirome is not more than 1.0%.

Containers and storage Containers—Hermetic containers.

Storage—At a temperature between 2 and 8°C.

Cefradine

セフラジン



$C_{16}H_{19}N_3O_4S$: 349.40

(6*R*,7*R*)-7-[(2*R*)-2-Amino-2-cyclohexa-1,4-dienylacetylamino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid [*38821-53-3*]

Cefradine contains not less than 900 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefradine is expressed as mass (potency) of cefradine ($C_{16}H_{19}N_3O_4S$).

Description Cefradine occurs as a white to light yellowish white crystalline powder.

It is freely soluble in trifluoroacetic acid, sparingly soluble in water, slightly soluble in methanol, very slightly soluble in ethanol (95), and practically insoluble in acetonitrile.

Melting point: about 192°C (with decomposition).

Identification **(1)** Determine the absorption spectrum of a solution of Cefradine (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Cefradine Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

(2) Determine the infrared absorption spectrum of Cefradine as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Cefradine Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers. If any difference appears between the spectra, dissolve the sample and the Reference Standard in methanol separately, then evaporate methanol to dryness, and perform the test with these residues.

(3) Determine the spectrum of a solution of Cefradine in trifluoroacetic acid 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 three single signals, A, B and C, at around δ 2.3 ppm, at around δ 2.8 ppm, and at around δ 6.3 ppm. The ratio of integrated intensity of each signal, A, B and C is about 3:4:1.

Optical rotation $[\alpha]_D^{20}$: +80 – +90° (1 g calculated on the anhydrous basis, water, 100 mL, 100 mm).

Purity **(1)** Heavy metals—Proceed with 2.0 g of Cefradine according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(2) Arsenic—Prepare the test solution with 2.0 g of Cefradine according to Method 4, and perform the test using Apparatus B (not more than 1 ppm).

(3) Related substances—Take exactly 0.10 g of Cefra-