

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 μ L 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.

$$\begin{aligned} \text{Amount } [\mu\text{g (potency)}] \text{ of cefpirome (C}_{22}\text{H}_{22}\text{N}_6\text{O}_5\text{S}_2) \\ = \text{amount [mg (potency)] of Cefpirome Sulfate} \\ \text{Reference Standard} \times \frac{A_T}{A_S} \times 1000 \end{aligned}$$

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 μ m 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 μ L of the standard solution under the above operating conditions, the number of theoretical steps of the peak of cefpirome is not less than 3600.

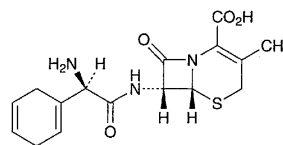
System repeatability: When the test is repeated 5 times with 20 μ L of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of cefpirome is not more than 1.0%.

Containers and storage Containers—Hermetic containers.

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

Cefradine

セフラジン



$\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_4\text{S}$: 349.40

(6*R*,7*R*)-7-[(2*R*)-2-Amino-2-cyclohexa-1,4-dienylacetylami-
no]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-
carboxylic acid [3882I-53-3]

Cefradine contains not less than 900 μ g (potency) per mg, calculated on the anhydrous basis. The potency of Cefradine is expressed as mass (potency) of cefradine ($\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_4\text{S}$).

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 (^1H): 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-

dine, dissolve in the mobile phase to make exactly 50 mL, and use this solution as the sample solution. Separately, take exactly 0.025 g of Cefalexin Reference Standard, dissolve in the mobile phase to make exactly 250 mL, and use this solution as the standard solution. Perform the test with 5 μ L each of these solutions as directed under the Liquid Chromatography according to the following conditions, and calculate the areas of each peak by the automatic integration method: the peak area of cefalexin from the sample solution is not more than the peak area of cefalexin from the standard solution.

Operating conditions—

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

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μ m in particle diameter).

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

Mobile phase: Dissolve 6.8 g of potassium dihydrogenphosphate in 800 mL of water, adjust the pH to 3.0 with diluted phosphoric acid (1 in 10), and add water to make 1000 mL. To 700 mL of this solution add 100 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of cefalexin is about 10 minutes.

System suitability—

System performance: When the procedure is run with 5 μ L of the sample solution under the above operating conditions, cefalexin and cefradine are eluted in this order with the resolution between these peaks being not less than 4.

System repeatability: When the test is repeated 6 times with 5 μ L of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of cefalexin is not more than 2.0%.

Water Not more than 6.0% (0.2 g, volumetric titration, direct titration).

Assay Perform the test according to the Cylinder-plate method as directed under the Microbial Assay for Antibiotics according to the following conditions.

(1) Test organism—*Bacillus subtilis* ATCC 6633

(2) Culture medium—Use the medium i in 1) Medium for test organism [5] under (1) Agar media for seed and base layer. Adjust the pH of the medium so that it will be 6.2 to 6.4 after sterilization.

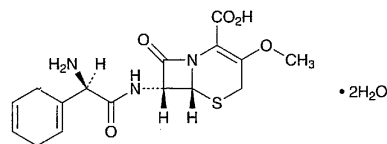
(3) Standard solution—Weigh accurately an amount of Cefradine Reference Standard equivalent to about 0.02 g (potency), dissolve in phosphate buffer solution, pH 6.0 to make exactly 50 mL. Take exactly a suitable amount of this solution, add phosphate buffer solution, pH 6.0 to make solutions so that each mL contains 20 μ g (potency) and 5 μ g (potency), and use these solutions as the high concentration standard solution and the low concentration standard solution, respectively.

(4) Sample solution—Weigh accurately an amount of Cefradine equivalent to about 0.02 g (potency), dissolve in phosphate buffer solution, pH 6.0 to make exactly 50 mL. Take exactly a suitable amount of this solution, add phosphate buffer solution, pH 6.0 to make solutions so that each mL contains 20 μ g (potency) and 5 μ g (potency), and use these solutions as the high concentration sample solution and the low concentration sample solution, respectively.

Containers and storage Containers—Tight containers.

Cefroxadine

セフロキサジン



$C_{16}H_{19}N_3O_5S \cdot 2H_2O$: 401.43

(6*R*,7*R*)-7-[(2*R*)-2-Amino-2-cyclohexa-1,4-dienylacetylami-
no]-3-methoxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-
carboxylic acid dihydrate [51762-05-1, anhydride]

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

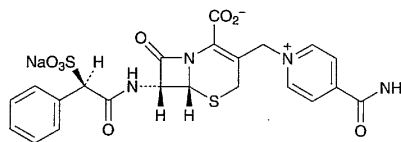
Description Cefroxadine occurs as pale yellowish white to light yellow crumbly, crystalline grains or powder. It has a characteristic odor.

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

It dissolves in 0.1 mol/L hydrochloric acid TS.

Cefsulodin Sodium

セフスロジンナトリウム



$C_{22}H_{19}N_4NaO_8S_2$: 554.53

Monosodium (6*R*,7*R*)-3-(4-carbamoylpyridinium-1-
ylmethyl)-8-oxo-7-[(2*R*)-2-phenyl-2-sulfonatoacetylami-
no]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate
[52152-93-9]

Cefsulodin Sodium contains not less than 864 μ g (potency) per mg, calculated on the anhydrous basis. The potency of Cefsulodin Sodium is expressed as mass (potency) of cefsulodin ($C_{22}H_{20}N_4O_8S_2$: 532.55).

Description Cefsulodin Sodium occurs as white to light yellow, crystals or crystalline powder.

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

It is hygroscopic.

Identification (1) Determine the absorption spectrum of a solution of Cefsulodin Sodium (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum