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

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

(3) Determine the spectrum of a solution of Cefadroxil in a mixture of heavy water for nuclear magnetic resonance spectroscopy and deuterated hydrochloric acid (3:1) (1 in 10), using sodium 3-(trimethylsilyl)propionate-$d_4$ for nuclear magnetic resonance spectroscopy as an internal reference compound, as directed under the Nuclear Magnetic Resonance Spectroscopy ($^1$H): it exhibits a single signal A at around $\delta$ 2.1 ppm, a double signal B at around $\delta$ 7.0 ppm, and a double signal C at around $\delta$ 7.5 ppm. The ratio of integrated intensity of each signal, A:B:C, is about 3:2:2.

**Absorbance** $E^{1\%}_{1cm}$ (262 nm): 220 – 240 (0.1 g calculated on the anhydrous basis, water, 5000 mL).

**Optical rotation** $[\alpha]^{25}_D$: +164 – +182° (0.6 g calculated on the anhydrous basis, water, 100 mL, 100 mm).

**pH** Dissolve 1.0 g of Cefadroxil in 200 mL of water: pH of the solution is between 4.0 and 6.0.

**Purity** (1) Heavy metals—Proceed with 1.0 g of Cefadroxil 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).

(2) Related substances—Dissolve 0.1 g of Cefadroxil in 4 mL of a mixture of ethanol (99.5), water and diluted hydrochloric acid (1 in 5) (75:22:3), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a mixture of ethanol (99.5), water and diluted hydrochloric acid (1 in 5) (75:22:3) to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 2 $\mu$L each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop with a mixture of ethyl acetate, water, ethanol (99.5) and formic acid (14:5:5:1) to a distance of about 12 cm, and air-dry the plate. Spray evenly ninhydrin-citric acid-acetic acid TS on the plate, and heat at 100°C for 10 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

**Water** Not less than 4.2% and not more than 6.0% (0.5 g, volumetric titration, direct titration).

**Assay** Weigh accurately an amount of Cefadroxil and Cefadroxil Reference Standard equivalent to about 0.05 g (potency), dissolve each in water to make exactly 500 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 10 $\mu$L each 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 cefadroxil of the solutions.

Amount [$\mu$g (potency)] of $C_{16}H_{17}N_3O_5S$
= amount [mg (potency)] of Cefadroxil Reference Standard $\times \frac{A_T}{A_S} \times 1000$

*Operating conditions*—

Detector: An ultraviolet absorption photometer (wavelength: 262 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 $\mu$m in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: A mixture of a solution of potassium dihydrogenphosphate (17 in 12,500) and methanol (17:3).

Flow rate: Adjust the flow rate so that the retention time of cefadroxil is about 5 minutes.

*System suitability*—

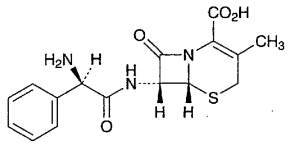
System performance: Dissolve about 5 mg (potency) of Cefadroxil and about 0.01 g (potency) of Propylene Glycol Cefatrizine in 50 mL of water. When the procedure is run with 10 $\mu$L of this solution under the above operating conditions, cefadroxil and cefatrizine are eluted in this order with the resolution between these peaks being not less than 4.

System repeatability: When the test is repeated 6 times with 10 $\mu$L of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of cefadroxil is not more than 1.0%.

**Containers and storage** Containers—Tight containers.

# Cefalexin

セファレキシン




$C_{16}H_{17}N_3O_4S$: 347.39

(6*R*,7*R*)-7-[(2*R*)-2-Amino-2-phenylacetylamino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid [*15686-71-2*]

Cefalexin contains not less than 950 $\mu$g (potency) and not more than 1030 $\mu$g (potency) per mg, calculated on the anhydrous basis. The potency of Cefalexin is expressed as mass (potency) of cefalexin ($C_{16}H_{17}N_3O_4S$).

**Description** Cefalexin occurs as a white to light yellowish white, crystals or crystalline powder.

It is sparingly soluble in water, slightly soluble in methanol, and practically insoluble in ethanol (95) and in *N,N*-dimethylformamide.

It is hygroscopic.

**Identification** (1) Determine the absorption spectrum of a solution of Cefalexin (3 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelength.

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

**(3)** Determine the spectrum of a solution of Cefalexin in heavy water for nuclear magnetic resonance spectroscopy (1 in 200) 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 $\delta$ 1.8 ppm, and a single or a sharp multiple signal B at around $\delta$ 7.5 ppm. The ratio of integrated intensity of these signals, A:B, is about 3:5.

**Optical rotation** $[\alpha]_D^{20}$: +144 – +158° (0.125 g calculated on the anhydrous basis, water, 25 mL, 100 mm).

**Purity** **(1)** Heavy metals—Proceed with 2.0 g of Cefalexin 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 1.0 g of Cefalexin by suspending in 10 mL of *N,N*-dimethylformamide, and perform the test using Apparatus B (not more than 2 ppm).

**(3)** Related substances—Dissolve about 0.025 g of Cefalexin in a solution of potassium dihydrogenphosphate (9 in 500) to make 5 mL, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a solution of potassium dihydrogenphosphate (9 in 500) to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 20 $\mu$L each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and determine the areas of each peak by the automatic integration method. If necessary, correct the change of the base-line due to the potassium dihydrogenphosphate solution by proceeding in the same manner with 20 $\mu$L of a solution of potassium dihydrogenphosphate (9 in 500): each peak area other than cefalexin from the sample solution is not more than the peak area of cefalexin from the standard solution, and the total of the peak areas which are bigger than 1/50 of the peak area of cefalexin from the standard solution and those other than cefalexin from the sample solution is not more than 5 times of 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 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 $\mu$m in particle diameter).

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

Mobile phase A: Dissolve 1.0 g of sodium 1-pentanesulfonate in 1000 mL of water, add 15 mL of triethylamine, and adjust to pH 2.5 with phosphoric acid.

Mobile phase B: Dissolve 1.0 g of sodium 1-pentanesulfonate in 300 mL of water, add 15 mL of triethylamine, and adjust to pH 2.5 with phosphoric acid. To this solution add 350 mL of acetonitrile and 350 mL of methanol.

Flowing of the mobile phase: Control the gradient by mixing the mobile A and B as directed in the following table.

| Time after injection of sample (min) | Mobile phase A (%) | Mobile phase B (%) |
|---|---|---|
| 0 – 1 | 100 | 0 |
| 1 – 34.5 | 100→0 | 0→100 |
| 34.5 – 35.5 | 0 | 100 |

Flow rate: 1.0 mL per minute

Time span of measurement: About 2 times as long as the retention time of cefalexin after the solvent peak.

*System suitability—*

Test for required detection: Pipet 2 mL of the standard solution, add a solution of potassium dihydrogenphosphate (9 in 500) to make exactly 100 mL. Confirm that the peak area of cefalexin obtained from 20 $\mu$L of this solution is equivalent to 1.8 to 2.2% of that of cefalexin obtained from 20 $\mu$L of the standard solution.

System performance: When the procedure is run with 20 $\mu$L of the standard solution under the above operating conditions, the number of theoretical steps and the symmetry coefficient of the peak of cefalexin are not less than 150,000 steps and between 0.8 and 1.3, respectively.

System repeatability: When the test is repeated 3 times with 20 $\mu$L of the standard solution under the above operating conditions, the relative standard deviation of the retention time and the peak areas of cefalexin are not more than 2.0%, respectively.

**Water** Not more than 8.0% (0.2 g, volumetric titration, back titration).

**Assay** Weigh accurately an amount of Cefalexin and Cefalexin Reference Standard, equivalent to about 0.1 g (potency), dissolve each in 0.1 mol/L phosphate buffer solution, pH 4.5 to make exactly 100 mL. Pipet 10 mL of these solutions, add exactly 5 mL of the internal standard solution, then add 0.1 mol/L phosphate buffer solution, pH 4.5 to make 50 mL, and use these solutions as the sample solution and the standard solution. Perform the test with 10 $\mu$L each of the sample solution and the standard solution 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 cefalexin to that of the internal standard.

Amount [$\mu$g (potency)] of $C_{16}H_{17}N_3O_4S$
= amount [mg (potency)] of Cefalexin Reference Standard $\times \frac{Q_T}{Q_S} \times 1000$

*Internal standard solution*—A solution of *m*-hydroxyacetophenone in 0.1 mol/L phosphate buffer solution, pH 4.5 (1 in 1500).

*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 $\mu$m in particle diameter).

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

Mobile phase: Dissolve 6.8 g of potassium dihydrogenphosphate in 1000 mL of water, adjust to pH 3.0 with diluted phosphoric acid (3 in 500). To 800 mL of this solution

add 200 mL of methanol.

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

*System suitability—*

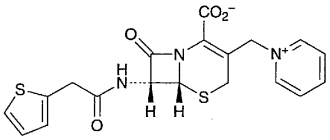
System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, cefalexin and the internal standard are eluted in this order with the resolution between these peaks being not less than 6.

System repeatability: When the test is repeated 5 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 cefalexin to that of the internal standard is not more than 1.0%.

**Containers and storage** Containers—Tight containers.

# Cefaloridine

セファロリジン



$C_{19}H_{17}N_3O_4S_2$: 415.49
(6*R*,7*R*)-8-Oxo-3-(pyridinium-1-ylmethyl)-7-[(thiophen-2-ylacetyl)amino]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate [*50-59-9*]

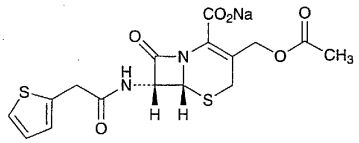
Cefaloridine conforms to the requirements of Cefaloridine in the Requirements for Antibiotic Products of Japan.

**Description** Cefaloridine occurs as a white to light yellowish white crystals or crystalline powder.

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

# Cefalotin Sodium

セファロチンナトリウム



$C_{16}H_{15}N_2NaO_6S_2$: 418.42
Monosodium (6*R*,7*R*)-3-acetoxymethyl-8-oxo-7-[2-(thiophen-2-yl)acetylamino]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate [*58-71-9*]

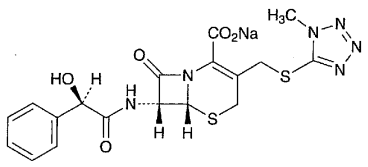
Cefalotin Sodium conforms to the requirements of Cefalotin Sodium in the Requirements for Antibiotic Products of Japan.

**Description** Cefalotin Sodium occurs as a white to yellowish white crystals or crystalline Powder.

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

# Cefamandole Sodium

セファマンドールナトリウム



$C_{18}H_{17}N_6NaO_5S_2$: 484.48
Monosodium (6*R*,7*R*)-7-[(2*R*)-2-hydroxy-2-phenylacetylamino]-3-(1-methyl-1*H*-tetrazol-5-ylsulfanylmethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate [*30034-03-8*]

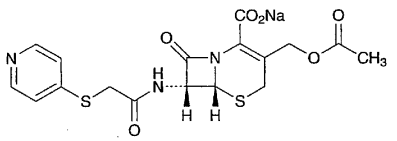
Cefamandole Sodium conforms to the requirements of Cefamandole Sodium in the Requirements for Antibiotic Products of Japan.

**Description** Cefamandole Sodium occurs as a white to light yellowish white crystalline powder. It has a slightly bitter taste.

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

# Cefapirin Sodium

セファピリンナトリウム



$C_{17}H_{16}N_3NaO_6S_2$: 445.45
Monosodium (6*R*,7*R*)-3-acetoxymethyl-8-oxo-7-[2-(pyridin-4-ylsulfanyl)acetylamino]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate [*24356-60-3*]

Cefapirin Sodium contains not less than 865 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefapirin Sodium is expressed as mass (potency) of cefapirin ($C_{17}H_{17}N_3O_6S_2$: 423.47).

**Description** Cefapirin Sodium occurs as a white to yellowish white powder.

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