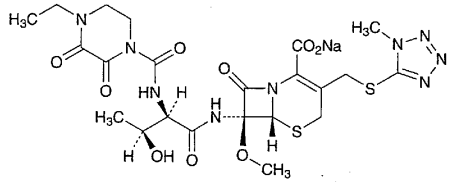
than 4.

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

Containers and storage Containers—Hermetic containers.
Storage—Light-resistant.

Cefbuperazone Sodium

セフブペラゾンナトリウム



$C_{22}H_{28}N_9NaO_9S_2$: 649.63
Monosodium (6*R*,7*S*)-7-{(2*R*,3*S*)-2-[(4-ethyl-2,3-dioxopiperazine-1-carbonyl)amino]-3-hydroxybutanoylamino}-7-methoxy-3-(1-methyl-1*H*-tetrazol-5-ylsulfanylmethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate
[*76648-01-6*]

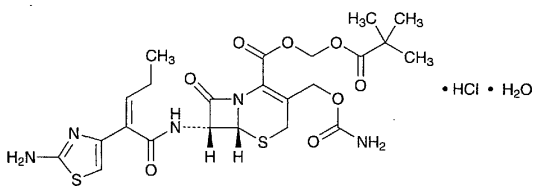
Cefbuperazone Sodium conforms to the requirements of Cefbuperazone Sodium in the Requirements for Antibiotic Products of Japan.

Description Cefbuperazone Sodium occurs as a white to light yellowish white powder.

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

Cefcapene Pivoxil Hydrochloride

塩酸セフカペン ピボキシル



$C_{23}H_{29}N_5O_8S_2.HCl.H_2O$: 622.11
2,2-Dimethylpropanoyloxymethyl (6*R*,7*R*)-7-[(*Z*)-2-(2-aminothiazol-4-yl)pent-2-enylamino]-3-carbamoyloxymethyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-caboxylate monohydrochloride monohydrate
[*147816-24-8*]

Cefcapene Pivoxil Hydrochloride contains not less than 722 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefcapene Pivoxil Hydrochloride is expressed as mass (potency) of cefcapene ($C_{17}H_{19}N_5O_6S_2$: 453.49).

Description Cefcapene Pivoxil Hydrochloride occurs as a white to pale yellowish white, crystalline powder or mass. It has slightly a characteristic odor.

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

Identification (1) Determine the infrared absorption spectra of Cefcapene Pivoxil Hydrochloride and Cefcapene Pivoxil Hydrochloride Reference Standard as directed in the paste method under the Infrared Spectrophotometry, and compare these spectra: both spectra exhibit similar intensities of absorption at the same wave numbers.

(2) Determine the spectrum of a solution of Cefcapene Pivoxil Hydrochloride in deuterated methanol for nuclear magnetic resonance spectroscopy (1 in 50) as directed under the Nuclear Magnetic Resonance Spectroscopy (^{1}H), using tetramethylsilane for nuclear magnetic resonance spectroscopy as an internal reference compound: it exhibits a triplet signal A at around δ 6.3 ppm, and a single signal B at around δ 6.7 ppm, and the ratio of integrated intensity of each signal, A:B, is about 1:1.

(3) Dissolve 0.01 g of Cefcapene Pivoxil Hydrochloride in 2 mL of a mixture of water and methanol (1:1), and add 1 drop of silver nitrate TS: a white precipitate is formed.

Absorbance $E^{1\%}_{1\,cm}$ (265 nm): 255 – 285 (0.03 g calculated on the anhydrous basis, a mixture of acetate buffer solution, pH 5.5 and methanol (1:1), 2000 mL).

Optical rotation $[\alpha]^{20}_D$: +51 – +54° (0.1 g calculated on the anhydrous basis, methanol, 10 mL, 100 mm).

Purity (1) Heavy metals—Proceed with 2.0 g of Cefcapene Pivoxil Hydrochloride 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) Related substance I—Dissolve an amount of Cefcapene Pivoxil Hydrochloride, equivalent to about 0.01 g (potency), in 2 mL of methanol, add a mixture of water and methanol (1:1) to make 50 mL, and use this solution as the sample solution. Perform the test with 30 μL of the sample solution as directed under the Liquid Chromatography according to the following conditions. If necessary, correct the change of the base-line by performing in the same manner as the test with 30 μL of a mixture of water and methanol (1:1). Determine each peak area by the automatic integration method: the total area of the peaks other than cefcapene pivoxil and other than the solvent is not more than 1.5% of the total area of the peaks other than the solvent.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 265 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 μm in particle diameter).

Column temperature: A constant temperature of about 20°C.

Mobile phase A: Dissolve 5.99 g of potassium dihydrogenphosphate in water to make 1100 mL. To this solution add a solution prepared by dissolving 1.89 g of tetra-*n*-pentylam-

monium bromide in methanol to make 1000 mL.

Mobile phase B: A mixture of methanol and water (22:3).

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

Time after injection of the sample (min)	Mobile phase A (%)	Mobile phase B (%)
0 - 20	98	2
20 - 40	98→50	2→50
40 - 50	50	50

Flow rate: 0.8 mL per minute.

Time span of measurement: About 2.5 times as long as the retention time of cefcapene pivoxil.

System suitability—

Test for required detection: To exactly 1 mL of the sample solution add a mixture of water and methanol (1:1) to make exactly 100 mL, and use this solution as the solution for system suitability test. Pipet 1 mL of the solution for system suitability test, and add a mixture of water and methanol (1:1) to make exactly 10 mL. Conform that the peak area of cefcapene pivoxil obtained from 30 μL of this solution is equivalent to 7 to 13% of that of cefcapene pivoxil obtained from 30 μL of the solution for system suitability test.

System performance: Dissolve 0.01 g of Cefcapene Pivoxil Hydrochloride and 0.01 g of propyl parahydroxybenzoate in 25 mL of methanol, and add water to make 50 mL. To 5 mL of this solution add a mixture of water and methanol (1:1) to make 50 mL. When the procedure is run with 30 μL of this solution under the above operating conditions, cefcapene pivoxil and propyl parahydroxybenzoate are eluted in this order with the resolution between these peaks being not less than 7.

System repeatability: When the test is repeated 3 times with 30 μL of the solution for system suitability test under the above operating conditions, the relative standard deviation of the peak areas of cefcapene pivoxil is not more than 4.0%.

(3) Related substance II—Dissolve an amount of Cefcapene Pivoxil Hydrochloride, equivalent to about 2 mg (potency), in *N,N*-dimethylformamide for liquid chromatography to make 20 mL, and use this solution as the sample solution. Perform the test with 20 μL of the sample solution as directed under the Liquid Chromatography according to the following conditions, and determine each peak area by the automatic integration method: the total area of the peaks which appear earlier than cefcapene pivoxil is not more than 1.7% of the total area of the peaks other than the solvent.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 280 nm).

Column: A stainless steel column 7.8 mm in inside diameter and 30 cm in length, packed with styrene-divinylbenzene copolymer for liquid chromatography.

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

Mobile phase: A solution of lithium bromide in *N,N*-dimethylformamide for liquid chromatography (13 in 5000).

Flow rate: Adjust the flow rate so that the retention time of cefcapene pivoxil is about 22 minutes.

Time span of measurement: About 1.8 times as long as the retention time of cefcapene pivoxil.

System suitability—

Test for required detection: To exactly 1 mL of the sample solution add *N,N*-dimethylformamide for liquid chromatography to make exactly 100 mL, and use this solution as the solution for system suitability test. Pipet 3 mL of the solution for system suitability test, and add *N,N*-dimethylformamide for liquid chromatography to make exactly 10 mL. Conform that the peak area of cefcapene pivoxil obtained from 20 μL of this solution is equivalent to 20 to 40% of that of cefcapene pivoxil obtained from 20 μL of the solution for system suitability test.

System performance: When the procedure is run with 20 μL of the sample solution under the above operating conditions, the number of theoretical steps of the peak of cefcapene pivoxil is not less than 12,000 steps.

System repeatability: When the test is repeated 6 times with 20 μL of the solution for system suitability test under the above operating conditions, the relative standard deviation of the peak areas of cefcapene pivoxil is not more than 4.0%.

Water Not less than 2.8% and not more than 3.7% (0.5 g, volumetric titration, back titration).

Assay Weigh accurately an amount of Cefcapene Pivoxil Hydrochloride and Cefcapene Pivoxil Hydrochloride Reference Standard, equivalent to about 0.04 g (potency), and dissolve each in methanol to make exactly 100 mL. Pipet 10 mL each of these solutions, add exactly 10 mL of the internal standard solution and a mixture of water and methanol (1:1) to them to make 50 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and determine the ratios, Q_T and Q_S, of the peak area of cefcapene pivoxil to that of the internal standard of these solutions.

$$\text{Amount [}\mu\text{g (potency)] of cefcapene } (C_{17}H_{19}N_5O_6S_2) = \text{amount [mg (potency)] of Cefcapene Pivoxil Hydrochloride Reference Standard} \times \frac{Q_T}{Q_S} \times 1000$$

Internal standard solution—A solution of *p*-benzylphenol in a mixture of water and methanol (1:1) (7 in 4000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 265 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 μm in particle diameter).

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

Mobile phase: Dissolve 1.56 g of sodium dihydrogenphosphate dihydrate and 1.22 g of sodium 1-decanesulfonate in water to make 1000 mL. To 700 mL of this solution add 300 mL of acetonitrile and 100 mL of methanol.

Flow rate: Adjust the flow rate so that the retention time of cefcapene pivoxil is about 16 minutes.

System suitability—

System performance: Dissolve 0.2 g of Cefcapene Pivoxil Hydrochloride in 10 mL of methanol, and warm in a water bath at 60°C for 20 minutes. After cooling, pipet 1 mL of this solution, and add exactly 10 mL of the internal standard solution and a mixture of water and methanol (1:1) to make 50 mL. When the procedure is run with 10 μL of this solution under the above operating conditions, cefcapene pivoxil, *trans*-cefcapene pivoxil and the internal standard are eluted in this order, the ratios of the retention time of *trans*-cefcapene pivoxil and the internal standard to that of cefcapene pivoxil are about 1.8 and 2.0, respectively, and the resolution between the peaks of *trans*-cefcapene pivoxil and the internal standard is not less than 1.5.

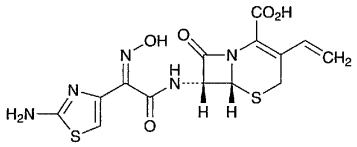
System repeatability: When the test is repeated 5 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of peak area of cefcapene pivoxil to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Storage—Light-resistant, at a temperature not exceeding 5°C.

Cefdinir

セフジニル



$C_{14}H_{13}N_5O_5S_2$: 395.41

(6*R*,7*R*)-7-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-hydroxyiminoacetylamino]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid

[*91832-40-5*]

Cefdinir contains not less than 900 μg (potency) per mg. The potency of Cefdinir is expressed as mass (potency) of cefdinir ($C_{14}H_{13}N_5O_5S_2$).

Description Cefdinir occurs as a white to light yellow crystalline powder.

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

It dissolves in 0.1 mol/L phosphate buffer solution, pH 7.0.

Identification **(1)** Determine the absorption spectra of solutions of Cefdinir and Cefdinir Reference Standard in 0.1 mol/L phosphate buffer solution, pH 7.0 (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare these spectra: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectra of Cefdinir and Cefdinir Reference Standard as directed in the paste method under the Infrared Spectrophotometry, and compare these spectra: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) Determine the spectrum of a solution of Cefdinir in a mixture of deuterated dimethyl sulfoxide and heavy water for nuclear magnetic resonance spectroscopy (4:1) (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 multiple signals, A and B, at around δ 5.0 - 6.1 ppm and B at around δ 6.4 - 7.5 ppm. The ratio of integrated intensity of each signal, A:B is about 2:1.

Absorbance $E^{1\%}_{1\,cm}$ (287 nm): 570 - 610 (0.05 g, 0.1 mol/L phosphate buffer solution, pH 7.0, 5000 mL).

Optical rotation $[\alpha]^{20}_D$: −58 - −66° (0.25 g, 0.1 mol/L phosphate buffer solution, pH 7.0, 25 mL, 100 mm).

Purity **(1)** Heavy metals—Proceed with 2.0 g of Cefdinir according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(2) Related substances—Dissolve about 0.1 g of Cefdinir in 10 mL of 0.1 mol/L phosphate buffer solution, pH 7.0. Pipet 3 mL of this solution, add tetramethylammonium hydroxide TS, pH 5.5 to make exactly 20 mL, and use this solution as the sample solution. Perform the test with 10 μL of the sample solution as directed under the Liquid Chromatography according to the following conditions, determine the areas of each peak by the automatic integration method, and calculate the amounts of their peaks by the area percentage method: the amount of E-isomer having the relative retention time 1.5 to cefdinir is not more than 0.8%, and the amount of total peak areas other than cefdinir is not more than 3.0%.

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 μm in particle diameter).

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

Mobile phase A: To 1000 mL of tetramethylammonium hydroxide TS, pH 5.5, add 0.4 mL of 0.1 mol/L disodium dihydrogen ethylenediamine tetraacetate TS.

Mobile phase B: To 500 mL of tetramethylammonium hydroxide TS, pH 5.5 add 300 mL of acetonitrile for liquid chromatography and 200 mL of methanol, and add 0.4 mL of 0.1 mol/L disodium dihydrogen ethylenediamine tetraacetate TS.

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 the sample (min)	Mobile phase A (%)	Mobile phase B (%)
0 - 2	95	5
2 - 22	95→75	5→25
22 - 32	75→50	25→50
32 - 37	50	50
37 - 38	50→95	50→5
38 - 58	95	5