System suitability—

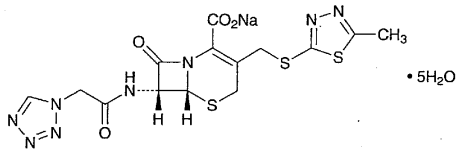
System performance: When the procedure is run with 5 μL of the standard solution under the above operating conditions, cefazolin and the internal standard are eluted in this order with the resolution between these peaks being not less than 4.

System repeatability: When the test is repeated 6 times with 5 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of cefazolin to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Cefazolin Sodium Hydrate

セファゾリンナトリウム水和物



$C_{14}H_{13}N_8NaO_4S_3.5H_2O$: 566.57

Monosodium (6*R*,7*R*)-3-(5-methyl-1,3,4-thiadiazol-2-ylsulfanylmethyl)-8-oxo-7-[2-(1*H*-tetrazol-1-yl)acetylamino]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate pentahydrate [*115850-11-8*]

Cefazolin Sodium Hydrate contains not less than 890 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefazolin Sodium Hydrate is expressed as mass (potency) of cefazolin ($C_{14}H_{14}N_8O_4S_3$: 454.51).

Description Cefazolin Sodium Hydrate occurs as white to pale yellowish white crystals.

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

Identification (1) Determine the absorption spectrum of a solution of Cefazolin Sodium Hydrate (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 270 nm and 274 nm.

(2) Determine the infrared absorption spectrum of Cefazolin Sodium Hydrate as directed in the potassium bromide disk method under the Infrared Spectrophotometry: it exhibits absorption at the wave numbers of about 1761 cm^{-1}, 1667 cm^{-1}, 1599 cm^{-1}, 1540 cm^{-1} and 1389 cm^{-1}.

(3) Determine the spectrum of a solution of Cefazolin Sodium Hydrate in heavy water for nuclear magnetic resonance spectroscopy (1 in 10), using sodium 3-trimethylsilylpropionate-d_4 for nuclear magnetic resonance spectroscopy as an internal reference compound, as directed under the Nuclear Magnetic Resonance Spectroscopy (^1H): it exhibits single signals, A and B, at around δ 2.7 ppm and at around δ 9.3 ppm. The ratio of integrated intensity of each signal, A:B, is about 3:1.

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

Absorbance $E^{1\%}_{1\,cm}$ (272 nm): 272 - 292 (0.08 g calculated on the anhydrous basis, water, 5000 mL).

Optical rotation $[\alpha]^{20}_D$: −20 - −25° (2.5 g calculated on the anhydrous basis, water, 25 mL, 100 mm).

pH Dissolve 1.0 g of Cefazolin Sodium Hydrate in 10 mL of water: the pH of the solution is between 4.8 and 6.3.

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

(2) Heavy metals—Proceed with 2.0 g of Cefazolin Sodium Hydrate 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).

(3) Arsenic—Being specified separately.

(4) Related substances—Being specified separately.

(5) Residual solvents—Being specified separately.

Water Not less than 13.7% and not more than 16.0% (0.1 g, volumetric titration, direct titration. Use a mixture of formamide for water determination and methanol for water determination (2:1) instead of methanol for water determination).

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

Assay Weigh accurately an amount of Cefazolin Sodium Hydrate and Cefazolin Reference Standard, equivalent to about 0.1 g (potency), dissolve in the internal standard solution to make exactly 100 mL, and use these solutions as the sample solution and the standard solution. Perform the test with 5 μL 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 cefazolin to that of the internal standard.

$$\text{Amount [}\mu\text{g (potency)] of cefazolin } (C_{14}H_{14}N_8O_4S_3) = \text{amount [mg (potency)] of Cefazolin Reference Standard} \times \frac{Q_T}{Q_S} \times 1000$$

Internal standard solution—A solution of *p*-acetoanisidide in 0.1 mol/L phosphate buffer solution, pH 7.0 (11 in 20,000).

Operating conditions—

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

Column: A stainless steel column 4 mm in inside diameter and 15 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 2.27 g of disodium hydrogenphosphate 12-water and 0.47 g of citric acid monohydrate in water to make 935 mL. To this solution, add 65 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of cefazolin is about 8 minutes.

System suitability—

System performance: When the procedure is run with 5 μL of the standard solution under the above operating conditions, cefazolin and the internal standard are eluted in this order with the resolution between these peaks being not less

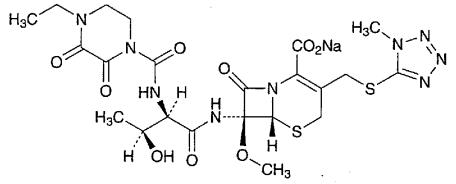
than 4.

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*]

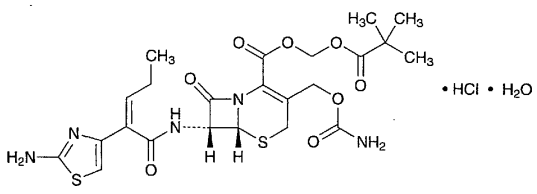
Cefbuperazone Sodium conforms to the requirements of Cefbuperazone Sodium in the Requirements for Antibiotic Products of Japan.

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-