Internal standard solution—A solution of dimedon in 0.05 mol/L phosphate buffer solution, pH 7.0 (11 in 10,000).

Operating conditions—

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

Column: A stainless steel column 4.6 mm in inside diameter and 10 cm in length, packed with hexasilanized silica gel for liquid chromatography (5 μm in particle diameter).

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

Mobile phase: Dissolve 4.26 g of anhydrous disodium hydrogenphosphate and 2.72 g of potassium dihydrogenphosphate in 980 mL of water, and add 20 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of ceftazidime is about 4 minutes.

System suitability—

System performance: When the procedure is run with 5 μL of the standard solution under the above operating conditions, the internal standard and ceftazidime are eluted in this order with the resolution between these peaks being not less than 3.

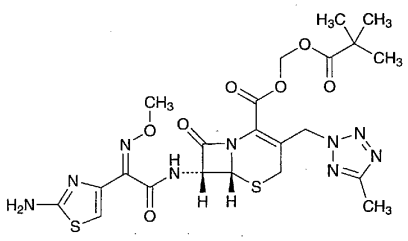
System repeatability: When the test is repeated 6 times with 5 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of ceftazidime to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Cefteram Pivoxil

セフテラムピボキシル



$C_{22}H_{27}N_9O_7S_2$: 593.64

2,2-Dimethylpropanoyloxymethyl (6*R*,7*R*)-7-[(*Z*)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetylamino]-3-(5-methyl-2*H*-tetrazol-2-ylmethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate [*82547-58-8*, Cefteram]

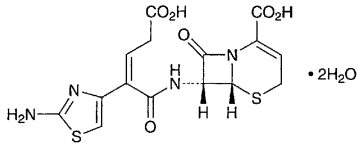
Cefteram Pivoxil conforms to the requirements of Cefteram Pivoxil in the Requirements for Antibiotic Products of Japan.

Description Cefteram Pivoxil occurs as a white to yellowish white powder. It has a bitter taste.

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

Ceftibuten

セフチブテン



$C_{15}H_{14}N_4O_6S_2.2H_2O$: 446.46

(6*R*,7*R*)-7-[(*Z*)-2-(2-Aminothiazol-4-yl)-4-carboxybut-2-enoylamino]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid dihydrate [*118081-34-8*]

Ceftibuten contains not less than 900 μg (potency) per mg, calculated on the anhydrous basis. The potency of Ceftibuten is expressed as mass (potency) of ceftibuten ($C_{15}H_{14}N_4O_6S_2$: 410.42).

Description Ceftibuten occurs as a white to pale yellowish white crystalline powder and has a slight, characteristic odor.

It is freely soluble in *N,N*-dimethylformamide and in dimethyl sulfoxide, and practically insoluble in water, in ethanol (95) and in diethyl ether.

Identification (1) Determine the absorption spectrum of a solution of Ceftibuten in 0.1 mol/L phosphate buffer solution for ceftibuten, pH 8.0 (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 261 nm and 265 nm.

(2) Determine the infrared absorption spectrum of Ceftibuten as directed in the paste method under the Infrared Spectrophotometry: it exhibits absorption at the wave numbers of about 3249 cm^{-1}, 1772 cm^{-1}, 1700 cm^{-1}, 1651 cm^{-1} and 1544 cm^{-1}.

(3) Determine the spectrum of a solution of Ceftibuten in deuterated dimethyl sulfoxide for nuclear magnetic resonance spectroscopy (1 in 30), using tetramethylsilane for nuclear magnetic resonance spectroscopy as an internal reference compound, as directed under the Nuclear Magnetic Resonance Spectroscopy (^1H): it exhibits double signals A and B, at around δ 3.2 ppm and at around δ 5.1 ppm, a quartet signal C, at around δ 5.8 ppm, and a single signal D, at around δ 6.3 ppm. The ratio of integrated intensity of each signal except the signal at around δ 3.2 ppm, B:C:D is about 1:1:1.

Absorbance $E^{1\%}_{1\,cm}$ (263 nm): 320 – 345 (0.02 g calculated on the anhydrous basis, 0.1 mol/L phosphate buffer solution for ceftibuten, pH 8.0, 1000 mL).

Optical rotation $[\alpha]^{20}_D$: +135 – +155° (0.3 g calculated on the anhydrous basis, 0.1 mol/L phosphate buffer solution for ceftibuten, pH 8.0, 50 mL, 100 mm).

Purity (1) Heavy metals—Proceed with 2.0 g of Ceftibuten 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—Being specified separately.

Water Not less than 8.0% and not more than 13.0% (0.2 g, volumetric titration, direct titration. Use a mixture of

pyridine for water determination and ethylene glycol for water determination (5:1) instead of methanol for water determination).

Residue on ignition Not more than 0.10% (1 g).

Assay Weigh accurately an amount of Ceftibuten and Ceftibuten Hydrochloride Reference Standard, equivalent to about 0.01 g (potency), dissolve each in 36 mL of 0.1 mol/L phosphate buffer solution for ceftibuten, pH 8.0, add exactly 4 mL each of the internal standard solution, shake, and use these solutions as the sample solution and the standard solution. Perform the test with 5 μL 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 ceftibuten to that of the internal standard. Keep the sample solution and the standard solution at 5°C or below and use within 2 hours.

Amount [μg (potency)] of ceftibuten ($C_{15}H_{14}N_4O_6S_2$)
= amount [mg (potency)] of Ceftibuten Hydrochloride Reference Standard $\times \frac{Q_T}{Q_S} \times 1000$

Internal standard solution—A solution of methyl *p*-hydroxybenzoate in acetonitrile (3 in 4000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 263 nm).

Column: A stainless steel column 4 mm in inside diameter and 20 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (7 μm in particle diameter).

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

Mobile phase: A mixture of 0.005 mol/L *n*-decyl trimethylammonium bromide TS and acetonitrile (4:1).

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

System suitability—

System performance: Dissolve 5 mg of Ceftibuten in 1 mol/L Hydrochloric acid TS to make 50 mL, and allow to stand for 4 hours at room temperature. To 10 mL of this solution add 0.1 mol/L phosphate buffer solution for ceftibuten, pH 8.0 to make 25 mL. When the procedure is run with 5 μL of this solution under the above operating conditions, trans-isomer and ceftibuten are eluted in this order with the resolution between these peaks being not less than 1.5.

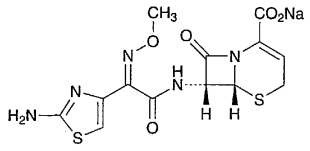
System repeatability: When the test is repeated 6 times with 5 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of ceftibuten to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Storage—Light-resistant, and not exceeding 5°C.

Ceftizoxime Sodium

セフチゾキシムナトリウム



$C_{13}H_{12}N_5NaO_5S_2$: 405.38

Monosodium (6*R*,7*R*)-7-[(*Z*)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetylamino]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate

[*68401-82-1*]

Ceftizoxime Sodium contains not less than 900 μg (potency) per mg, calculated on the anhydrous basis. The potency of Ceftizoxime Sodium is expressed as mass (potency) of ceftizoxime ($C_{13}H_{13}N_5O_5S_2$: 383.40).

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

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

Identification **(1)** Determine the absorption spectrum of a solution of Ceftizoxime Sodium (1 in 63,000) 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 Ceftizoxime Sodium 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 Ceftizoxime Sodium in heavy water for nuclear magnetic resonance spectroscopy (1 in 10) as directed under the Nuclear Magnetic Resonance Spectroscopy (^{1}H), using sodium 3-trimethylsilylpropionate-d_4 for nuclear magnetic resonance spectroscopy as an internal reference compound: it exhibits a single signal A at around δ 4.0 ppm, a multiple signal B around δ 6.3 ppm, and a single signal C at around δ 7.0 ppm. The ratio of integrated intensity of each signal, A:B:C, is about 3:1:1.

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

Optical rotation $[\alpha]_D^{20}$: +125 – +145° (0.25 g calculated on the anhydrous bases, water, 25 mL, 100 mm).

pH Dissolve 1.0 g of Ceftizoxime Sodium in 10 mL of water: the pH of the solution is between 6.0 and 8.0.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Ceftizoxime Sodium in 10 mL of water: the solution is clear, and colorless to light yellow.

(2) Heavy metals—Proceed with 2.0 g of Ceftizoxime Sodium 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—Prepare the test solution with 2.0 g of