test for required detection. Pipet 1 mL of the solution for test for required detection, add the mobile phase A to make exactly 10 mL. Conform that the peak area of cefepime obtained from 5 μL of this solution is equivalent to 7 to 13% of that of cefepime obtained from 5 μL of the solution for test for required detection.

System performance: When the procedure is run with 5 μL of the solution for system suitability test under the above operating conditions, the number of theoretical steps of the peak of cefepime is not less than 6000 steps.

System repeatability: When the test is repeated 3 times with 5 μL of the solution for system suitability test under the above operating conditions, the relative standard deviation of the peak areas of cefepime is not more than 2.0%.

Water Not less than 3.0% and not more than 4.5% (Weigh accurately about 0.05 g, and add exactly 2 mL of methanol for water determination to dissolve. Use exactly 0.5 mL of this solution as the test solution; coulometric titration).

Residue on ignition Not more than 0.1% (1 g).

Bacterial endotoxins Less than 0.04 EU/mg (potency).

Assay Weigh accurately an amount of Cefepime Dihydrochloride and Cefepime Dihydrochloride Reference Standard, equivalent to about 0.06 g (potency), dissolve in the mobile phase to make exactly 500 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with exactly 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 peak areas, A_T and A_S, of cefepime of each solution.

Amount [μg (potency)] of cefepime ($C_{19}H_{24}N_6O_5S_2$)
= amount [mg (potency)] of Cefepime Dihydrochloride Reference Standard $\times \frac{A_T}{A_S} \times 1000$

Operating conditions—

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

Column: A stainless steel column 3.9 mm in inside diameter and 30 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10 μm in particle diameter).

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

Mobile phase: Adjust a solution of sodium 1-pentanesulfonate (261 in 100,000) to pH 3.0 with acetic acid (100), then adjust this solution to pH 4.0 with a solution of potassium hydroxide (13 in 20). To 950 mL of this solution add 50 mL of acetonitrile.

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

System suitability—

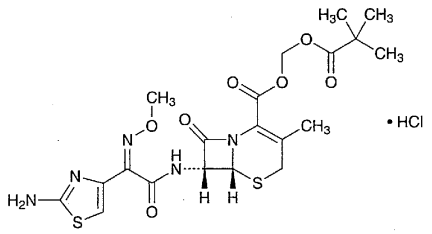
System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the number of theoretical steps of the peak of cefepime is not less than 1500 steps.

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 peak areas of cefepime is not more than 2.0%.

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

Cefetamet Pivoxil Hydrochloride

塩酸セフェタメト ピボキシル



$C_{20}H_{25}N_5O_7S_2.HCl$: 548.03

2,2-Dimethylpropanoyloxymethyl (6*R*,7*R*)-7-[(*Z*)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetylamino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate monohydrochloride [*111696-23-2*]

Cefetamet Pivoxil Hydrochloride contains not less than 653 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefetamet Pivoxil Hydrochloride is expressed as mass (potency) of cefetamet ($C_{14}H_{15}N_5O_5S_2$: 397.43).

Description Cefetamet Pivoxil Hydrochloride occurs as a white to light yellowish white crystalline powder.

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

Identification **(1)** Dissolve 0.01 g of Cefetamet Pivoxil Hydrochloride in 2 mL of diluted methanol (1 in 2), add 3 mL of hydroxylammonium chloride-ethanol TS, allow to stand for 5 minutes, then add 1 mL of acidic ammonium iron (III) sulfate TS, and shake: a red-brown color develops.

(2) Determine the absorption spectra of solutions of Cefetamet Pivoxil Hydrochloride and Cefetamet Pivoxil Hydrochloride Reference Standard in 0.1 mol/L hydrochloric acid TS (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare these spectra: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Determine the infrared absorption spectra of Cefetamet Pivoxil Hydrochloride and Cefetamet Pivoxil Hydrochloride Reference Standard as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare these spectra: both spectra exhibit similar intensities of absorption at the same wave numbers.

(4) Determine the spectrum of a solution of Cefetamet Pivoxil Hydrochloride in deuterated dimethylsulfoxide for nuclear magnetic resonance spectroscopy (1 in 20) as directed under the Nuclear Magnetic Resonance Spectroscopy (^1H), using tetramethylsilane for nuclear magnetic resonance spectroscopy as an internal reference compound: it exhibits single signals, A, B, C and D, at around δ 1.2 ppm, at around δ 2.0 ppm, at around δ 3.9 ppm and at around δ 6.9 ppm, respectively, and the ratio of integrated

intensity of each signal, A:B:C:D, is about 9:3:3:1.

(5) Dissolve 0.05 g of Cefetamet Pivoxil Hydrochloride in 2 mL of methanol, add 3 mL of dilute nitric acid and 1 mL of silver nitrate TS, and mix: a white precipitate is formed.

Absorbance $E^{1\%}_{1\,cm}$ (263 nm): 327 - 347 (0.02 g calculated on the anhydrous basis, 0.1 mol/L hydrochloric acid TS, 1000 mL).

Optical rotation $[\alpha]_D^{20}$: +76 - +84° (0.25 g calculated on the anhydrous basis, ethanol (95), 25 mL, 100 mm).

Purity **(1)** Heavy metals—Proceed with 1.0 g of Cefetamet 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 20 ppm).

(2) Arsenic—Being specified separately.

(3) Related substances—Being specified separately.

Water Not more than 1.0% (1 g, volumetric titration, direct titration).

Residue on ignition Being specified separately.

Assay Weigh accurately an amount of Cefetamet Pivoxil Hydrochloride and Cefetamet Pivoxil Hydrochloride Reference Standard, equivalent to about 0.019 g (potency), and dissolve in a mixture of water and acetonitrile (11:9) to make exactly 50 mL. Pipet 5 mL each of these solutions, add exactly 6 mL of the internal standard solution and a solution of tetra-*n*-heptylammonium bromide in a mixture of water, acetonitrile and methanol (137:90:23) (2 in 625) 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 calculate the ratios, Q_T and Q_S, of the peak area of cefetamet pivoxil to that of the internal standard of each solution.

$$\text{Amount [}\mu\text{g (potency)] of cefetamet } (C_{14}H_{15}N_5O_5S_2) = \text{amount [mg (potency)] of Cefetamet Pivoxil Hydrochloride Reference Standard} \times \frac{Q_T}{Q_S} \times 1000$$

Internal standard solution—Dissolve 1 g of diethyl phthalate in a solution of tetra-*n*-heptylammonium bromide in a mixture of water, acetonitrile and methanol (137:90:23) (2 in 625) to make 500 mL.

Operating conditions—

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

Column: A stainless steel column 6.0 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: Dissolve 5.796 g of anhydrous disodium hydrogenphosphate and 3.522 g of potassium dihydrogenphosphate in water to make exactly 1000 mL, and use as Solution A. Dissolve 20.256 g of citric acid monohydrate and 7.840 g of sodium hydroxide in water to make exactly 1000 mL, and use as Solution B. Dissolve 3.20 g of tetra-*n*-heptylammonium bromide in 360 mL of acetonitrile for liquid chromatography, and add 92 mL of methanol, 500 mL of water, 44 mL of the solution A and 4 mL of the solution B.

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

System suitability—

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

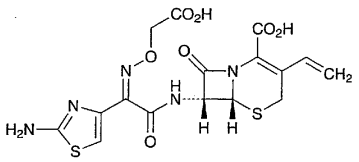
System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of cefetamet pivoxil to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Cefixime

セフィキシム



$C_{16}H_{15}N_5O_7S_2$: 453.45

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

[*79350-37-1*]

Cefixime contains not less than 930 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefixime is expressed as mass (potency) of cefixime ($C_{16}H_{15}N_5O_7S_2$: 453.46).

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

It is freely soluble in methanol and in dimethylsulfoxide, sparingly soluble in ethanol (99.5), and practically insoluble in water.

Identification **(1)** Determine the absorption spectrum of a solution of Cefixime in 0.1 mol/L phosphate buffer solution, pH 7.0 (1 in 62,500) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Cefixime Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

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

(3) Dissolve 0.05 g of Cefixime in 0.5 mL of a mixture of deuterated dimethylsulfoxide for nuclear magnetic resonance spectroscopy and heavy water for nuclear magnetic resonance spectroscopy (4:1). Determine the spectrum of