

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 Cefprozime and Cefprozime Hydrochloride Reference Standard, equivalent to about 0.01 g (potency), dissolve each in 36 mL of 0.1 mol/L phosphate buffer solution for cefprozime, 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  $\mu$ L 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 cefprozime 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 [ $\mu$ g (potency)] of cefprozime ( $C_{15}H_{14}N_4O_6S_2$ )  
 = amount [mg (potency)] of Cefprozime 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  $\mu$ m 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 cefprozime is about 10 minutes.

**System suitability**—

**System performance:** Dissolve 5 mg of Cefprozime 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 cefprozime, pH 8.0 to make 25 mL. When the procedure is run with 5  $\mu$ L of this solution under the above operating conditions, trans-isomer and cefprozime are eluted in this order with the resolution between these peaks being not less than 1.5.

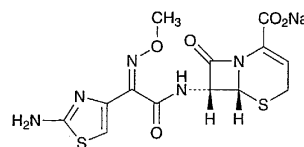
**System repeatability:** When the test is repeated 6 times with 5  $\mu$ L of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of cefprozime to that of the internal standard is not more than 1.0%.

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

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

## Cefprozime 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-methoxyiminoacetyl-amino]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate  
 [68401-82-1]

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

**Description** Cefprozime 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 Cefprozime 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 Cefprozime 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 Cefprozime Sodium in heavy water for nuclear magnetic resonance spectroscopy (1 in 10) as directed under the Nuclear Magnetic Resonance Spectroscopy ( $^1H$ ), using sodium 3-trimethylsilylpropionate- $d_4$  for nuclear magnetic resonance spectroscopy as an internal reference compound: it exhibits a single signal A at around  $\delta$  4.0 ppm, a multiple signal B around  $\delta$  6.3 ppm, and a single signal C at around  $\delta$  7.0 ppm. The ratio of integrated intensity of each signal, A:B:C, is about 3:1:1.

(4) Cefprozime 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 Cefprozime 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 Cefprozime Sodium in 10 mL of water: the solution is clear, and colorless to light yellow.

(2) Heavy metals—Proceed with 2.0 g of Cefprozime 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

Ceftizoxime Sodium according to Method 3, and perform the test using Apparatus B (not more than 1 ppm).

(4) Related substances—Dissolve 0.11 g of Ceftizoxime Sodium in 100 mL of 0.1 mol/L phosphate buffer solution, pH 7.0, and use this solution as the sample solution. Perform the test with 5  $\mu$ L of the sample solution as directed under the Liquid Chromatography according to the following conditions, and calculate the areas of each peak by the automatic integration method: each peak area other than ceftizoxime is not more than 0.5% of the peak area of ceftizoxime, and the total of peak areas other than ceftizoxime is not more than 1.0% of that of ceftizoxime.

**Operating conditions—**

Detector, column, and column temperature: Proceed as directed in the operating conditions in the Assay.

Mobile phase: Dissolve 2.31 g of disodium hydrogenphosphate 12-water and 1.42 g of citric acid monohydrate in 1000 mL of water, adjust to pH 3.6 with diluted phosphoric acid (1 in 10) or dilute sodium hydroxide TS. To 200 mL of this solution add 10 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of ceftizoxime is about 12 minutes.

Time span of measurement: About 5 times as long as the retention time of ceftizoxime after the solvent peak.

**System suitability—**

Test for required detection: Pipet 1 mL of the sample solution, add 0.1 mol/L phosphate buffer solution, pH 7.0 to make exactly 100 mL, and use this solution as the solution for test for required detection. Pipet 1 mL of the solution, add 0.1 mol/L phosphate buffer solution, pH 7.0 to make exactly 10 mL, and confirm that the peak area of ceftizoxime obtained from 5  $\mu$ L of this solution is equivalent to 7 to 13% of that of ceftizoxime obtained from 5  $\mu$ L of the solution for test for required detection.

System performance: Dissolve about 0.01 g of Ceftizoxime Reference Standard in 100 mL of 0.1 mol/L phosphate buffer solution, pH 7.0, and use this solution as the solution for system suitability test. When the procedure is run with 5  $\mu$ L of this solution under the above operating conditions, the number of theoretical steps and the symmetry coefficient of the peak of ceftizoxime are not less than 4000 steps and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 5  $\mu$ L of the solution for system suitability test under the above operating conditions, the relative standard deviation of the peak areas of ceftizoxime is not more than 2.0%.

**Water** Not more than 8.5% (0.4 g, volumetric titration, direct titration).

**Assay** Weigh accurately an amount of Ceftizoxime Sodium and Ceftizoxime Reference Standard, equivalent to about 0.1 g (potency), and dissolve each in 0.1 mol/L phosphate buffer solution, pH 7.0 to make exactly 20 mL. Pipet 2 mL each of these solutions, add exactly 10 mL of the internal standard solution, then add 0.1 mol/L phosphate buffer solution, pH 7.0 to make 20 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 5  $\mu$ L each of these solutions 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 ceftizoxime to that of the internal standard of each solution.

Amount [ $\mu$ g (potency)] of  $C_{13}H_{13}N_5O_5S_2$

= amount [mg (potency)] of Ceftizoxime

$$\text{Reference Standard} \times \frac{Q_T}{Q_S} \times 1000$$

**Internal standard solution—**A solution of 3-hydroxybenzoic acid in 0.1 mol/L phosphate buffer solution, pH 7.0 (3 in 500).

**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 (10  $\mu$ m in particle diameter).

Column temperature: A constant temperature of about 35°C.

Mobile phase: Dissolve 2.31 g of disodium hydrogenphosphate 12-water and 1.42 g of citric acid monohydrate in 1000 mL of water, and adjust to pH 3.6 with diluted phosphoric acid (1 in 10) or dilute sodium hydroxide TS. To 450 mL of this solution add 50 mL of acetonitrile.

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

**System suitability—**

System performance: When the procedure is run with 5  $\mu$ L of the standard solution under the above operating conditions, ceftizoxime and the internal standard are eluted in this order with the resolution between these peaks being not less than 7.0 and the symmetry coefficient of each peak is not more than 2.

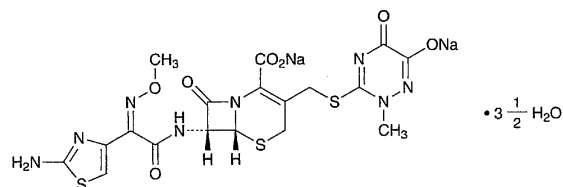
System repeatability: When the test is repeated 6 times with 5  $\mu$ L of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of ceftizoxime to that of the internal standard is not more than 1.0%.

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

Storage—Light-resistant.

## Ceftriaxone Sodium

セフトリアキソンナトリウム



$C_{18}H_{16}N_8Na_2O_7S_3 \cdot 3\frac{1}{2}H_2O$ : 661.60

Disodium (6R,7R)-7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetylamino]-3-(6-hydroxy-2-methyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-ylsulfanylmethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate hemiheptahydrate [104376-79-6]

Ceftriaxone Sodium contains not less than 834  $\mu$ g (potency) per mg, calculated on the anhydrous basis. The potency of Ceftriaxone Sodium is expressed as mass (potency) of ceftriaxone ( $C_{18}H_{18}N_8O_7S_3$ : 554.58).