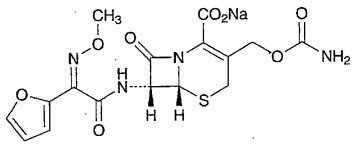
sparingly soluble in ethanol (95), slightly soluble in diethyl ether, and very slightly soluble in water.

Cefuroxime Sodium

セフロキシムナトリウム



$C_{16}H_{15}N_4NaO_8S$: 446.37
Monosodium (6*R*,7*R*)-3-carbamoyloxymethyl-7-[(*Z*)-2-furan-2-yl-2-methoxyiminoacetylamino]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate [*56238-63-2*]

Cefuroxime Sodium contains not less than 875 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefuroxime Sodium is expressed as mass (potency) of cefuroxime ($C_{16}H_{16}N_4O_8S$: 424.39).

Description Cefuroxime Sodium occurs as a white to light yellowish white, crystals or crystalline powder.

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

Identification **(1)** Determine the absorption spectrum of a solution of Cefuroxime Sodium (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Cefuroxime Sodium Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

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

(3) Determine the spectrum of a solution of Cefuroxime 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-trimethylsilylpropanesulfonate for nuclear magnetic resonance spectroscopy as an internal reference compound: it exhibits a single signal A at around δ 4.0 ppm, a quartet signal B at around δ 6.6 ppm, and double signals, C and D, at around δ 6.9 ppm and around δ 7.7 ppm, respectively. The ratio of integrated intensity of each signal, A:B:C:D, is about 3:1:1:1.

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

Optical rotation $[\alpha]_D^{20}$: +59 – +66° (0.5 g calculated on the anhydrous bases, water, 100 mL, 100 mm).

pH Dissolve 1.0 g of Cefuroxime Sodium in 10 mL of water: the pH of the solution is between 6.0 and 8.5.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Cefuroxime Sodium in 10 mL of water: the solution is clear, and its absorbance at 405 nm is not more than 0.25.

(2) Heavy metals—Proceed with 1.0 g of Cefuroxime Sodium according to Method 2, and perform the test. Prepare the control solution with 3.0 mL of Standard Lead Solution (not more than 30 ppm).

(3) Arsenic—Prepare the test solution with 1.0 g of Cefuroxime Sodium according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.025 g of Cefuroxime Sodium in 25 mL of water, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard 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 cefuroxime from the sample solution is not more than the peak area of cefuroxime from the standard solution, and the total of the peak areas other than cefuroxime from the sample solution is not more than 3 times of the peak area of cefuroxime from the standard solution.

Operating conditions—

Detector, column, column temperature, mobile phase, and flow rate: Proceed as directed in the operating conditions in the Assay.

Time span of measurement: About 4 times as long as the retention time of cefuroxime after the solvent peak.

System suitability—

Test for required detection: Pipet 1 mL of the standard solution, add water to make exactly 10 mL, and confirm that the peak area of cefuroxime obtained from 20 μL of this solution is equivalent to 7 to 13% of that of cefuroxime obtained from 20 μL of the standard solution.

System performance: Proceed as directed in the system suitability in the Assay.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of cefuroxime is not more than 2.0%.

Water Not more than 4.0% (0.4 g, volumetric titration, direct titration).

Assay Weigh accurately an amount of Cefuroxime Sodium and Cefuroxime Sodium Reference Standard, equivalent to about 0.025 g (potency), and dissolve each in water to make exactly 25 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 20 μL each of these solutions as directed under the Liquid Chromatography according to the following conditions, and calculate the peak area, A_T and A_S, of cefuroxime of each solution.

Amount [μg (potency)] of $C_{16}H_{16}N_4O_8S$
= amount [mg (potency)] of Cefuroxime Sodium Reference Standard $\times \frac{A_T}{A_S} \times 1000$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 273 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 125 mm 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 0.68 g of sodium acetate trihydrate in 900 mL of water, adjust to pH 3.4 with acetic acid (100), and add water to make 1000 mL. To 990 mL of this solution add 10 mL of acetonitrile.

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

System suitability—

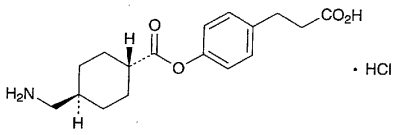
System performance: Allow the sample solution to stand at 60°C for 10 minutes. When the procedure is run with 20 μL of this solution soon after cooling under the above operating conditions, the resolution between the peak of cefuroxime and the peak corresponding to the retention time of about 0.7 to the peak of cefuroxime is being not less than 2.0.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of cefuroxime is not more than 1.0%.

Containers and storage Containers—Tight containers.

Cetraxate Hydrochloride

塩酸セトラキサート



$C_{17}H_{23}NO_4$.HCl: 341.83

trans-3-{4-[4-(Aminomethyl)cyclohexylcarbonyloxy]-phenyl}propanoic acid monohydrochloride [*27724-96-5*]

Cetraxate Hydrochloride, when dried, contains not less than 98.5% of $C_{17}H_{23}NO_4$.HCl.

Description Cetraxate Hydrochloride occurs as white crystals or crystalline powder.

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

Melting point: about 236°C (with decomposition).

Identification **(1)** Determine the absorption spectrum of a solution of Cetraxate Hydrochloride in methanol (1 in 2500) 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 wavelengths.

(2) Dissolve 0.5 g of Cetraxate Hydrochloride in 5 mL of a mixture of water and 2-propanol (1:1) by warming, cool to below 25°C. Filter, dry the formed crystals in vacuum for 4 hours, and further dry at 105°C for 1 hour. Determine the infrared absorption spectrum of the dried matter as directed in the potassium chloride 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) A solution of Cetraxate Hydrochloride (1 in 100) responds to the Qualitative Tests (2) for chloride.

Purity **(1)** Heavy metals—Proceed with 2.0 g of Cetraxate Hydrochloride 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) Arsenic—Prepare the test solution with 1.0 g of Cetraxate Hydrochloride according to Method 3, and perform the test with a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 5) using Apparatus B (not more than 2 ppm).

(3) *cis* Isomer—Dissolve 0.10 g of Cetraxate Hydrochloride in 10 mL of water, and use this solution as the sample solution. To exactly 5 mL of the sample solution add water to make exactly 100 mL. To exactly 2 mL of this solution add water to make exactly 50 mL, and use this solution as the standard solution. 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. Determine each peak area of both solutions by the automatic integration method: the area of the peak which has a retention time 1.3 to 1.6 times that of cetraxate from the sample solution is not larger than the peak area of cetraxate from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 220 nm).

Column: A stainless steel column about 6 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

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

Mobile phase: Adjust the pH of a mixture of water, methanol and 0.5 mol/L ammonium acetate TS (15:10:4) to 6.0 with acetic acid (31).

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

Selection of column: Dissolve 0.02 g of Cetraxate Hydrochloride and 0.01 g of phenol in 100 mL of water. To 2 mL of this solution add water to make 20 mL. Proceed with 10 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of cetraxate and phenol in this order with the resolution between these peaks being not less than 5.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of cetraxate obtained from 10 μL of the standard solution is not less than 20 mm.

(4) 3-(*p*-Hydroxyphenyl)propionic acid—To 0.10 g of Cetraxate Hydrochloride add exactly 2 mL of the internal standard solution and methanol to make 10 mL, and use this solution as the sample solution. Separately, dissolve 0.025 g of 3-(*p*-hydroxyphenyl)propionic acid in methanol to make exactly 100 mL. To exactly 2 mL of this solution add exactly 2 mL of the internal standard solution and methanol to make 10 mL, and use this solution as the standard solution. 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 3-(*p*-hydroxyphenyl)propionic acid to that of the internal standard: Q_T is not larger than Q_S.

Internal standard solution—A solution of caffeine in methanol (1 in 4000).