Cefotiam Hydrochloride contains not less than 790 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefotiam Hydrochloride is expressed as mass (potency) of cefotiam ($C_{18}H_{23}N_9O_4S_3$: 525.63).

Description Cefotiam Hydrochloride occurs as white to light yellow, crystals or crystalline powder.

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

Identification **(1)** Determine the absorption spectrum of a solution of Cefotiam Hydrochloride (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Cefotiam Hydrochloride Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

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

(3) Determine the spectrum of a solution of Cefotiam Hydrochloride in heavy water for nuclear magnetic resonance spectroscopy (1 in 10) as directed under the Nuclear Magnetic Resonance Spectroscopy (^1H), using sodium 3-trimethylsilylpropanesulfonate for nuclear magnetic resonance spectroscopy as an internal reference compound: it exhibits single signals at around δ 3.1 ppm and at around δ 6.7 ppm, respectively. The ratio of integrated intensity of each signal is about 6:1.

(4) Dissolve 0.1 g of Cefotiam Hydrochloride in 5 mL of dilute nitric acid, and immediately add 1 mL of silver nitrate TS: a white precipitate is formed.

Optical rotation $[\alpha]_D^{20}$: +60 – +72° (1 g calculated on the anhydrous bases, water, 100 mL, 100 mm).

pH Dissolve 1.0 g of Cefotiam Hydrochloride in 10 mL of water: the pH of the solution is between 1.2 and 1.7.

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

(2) Heavy metals—To 1.0 g of Cefotiam Hydrochloride add 1 mL of sulfuric acid, and heat gently to carbonize. After cooling, add 10 mL of a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 10), fire the ethanol to burn, then heat gradually to incinerate. If a carbonized residue still retains, moisten the residue with a little amount of sulfuric acid, and ignite again to incinerate. After cooling, add 2 mL of hydrochloric acid to the residue, heat on a water bath to dissolve, then heat to dryness. Add 10 mL of water, and heat to dissolve. After cooling, add ammonia TS dropwise to adjust to pH 3 – 4, if necessary, filter, wash the residue on the filter with 10 mL of water, transfer the filtrate and washings into a Nessler tube, add water to make 50 mL, and use this solution as the test solution. Prepare the control solution with 2.0 mL of Standard Lead Solution in the same manner as for preparation of the test solution (not more than 20 ppm).

(3) Arsenic—Incinerate 1.0 g of Cefotiam Hydrochloride according to Method 4. After cooling, add 10 mL of dilute hydrochloric acid to the residue, heat to dissolve on the water bath, and use this solution as the test solution. Perform the test using Apparatus B (not more than 2 ppm).

Water Not more than 7.0% (0.25 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).

Assay Weigh accurately an amount of Cefotiam Hydrochloride and Cefotiam Hydrochloride Reference Standard, equivalent to about 0.1 g (potency), and dissolve each in the mobile phase to make exactly 100 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 calculate the peak areas, A_T and A_S, of cefotiam of these solutions.

Amount [μg (potency)] of cefotiam ($C_{18}H_{23}N_9O_4S_3$)
= amount [mg (potency)] of Cefotiam Hydrochloride 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 4.0 mm in inside diameter and 125 mm 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: To 800 mL of 0.05 mol/L disodium hydrogenphosphate TS add 0.05 mol/L potassium dihydrogenphosphate TS to adjust the pH to 7.7. To 440 mL of this solution add 60 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of cefotiam is about 14 minutes.

System suitability—

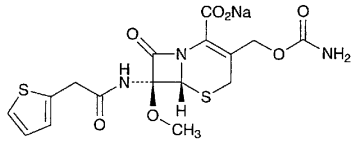
System performance: Dissolve 0.04 g of orcine in 10 mL of the standard solution. When the procedure is run with 10 μL of the standard solution under the above operating conditions, orcine and cefotiam are eluted in this order with the resolution between these peaks being not less than 5.

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 peak areas of cefotiam is not more than 1.0%.

Containers and storage Containers—Hermetic containers.

Cefoxitin Sodium

セフォキシチンナトリウム



$C_{16}H_{16}N_3NaO_7S_2$: 449.43
Monosodium (6*R*,7*R*)-3-carbamoyloxymethyl-7-methoxy-8-oxo-7-[(thiophen-2-ylacetyl)amino]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate [*33564-30-6*]

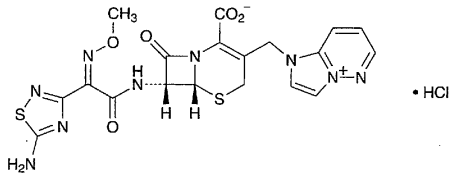
Cefoxitin Sodium conforms to the requirements of Cefoxitin Sodium in the Requirements for Antibiotic Products of Japan.

Description Cefoxitin Sodium occurs as white to light yellowish white granules or powder. It has a faint, characteristic odor.

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

Cefozopran Hydrochloride

塩酸セフォゾプラン



$C_{19}H_{17}N_9O_5S_2$.HCl: 551.99
(6*R*,7*R*)-7-[(*Z*)-2-(5-Amino-1,2,4-thiadiazol-3-yl)-2-methoxyiminoacetylamino]-3-(1*H*-imidazo[1,2-*b*]pyridazin-4-ium-1-ylmethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate monohydrochloride
[*113359-04-9*, Cefozopran]

Cefozopran Hydrochloride contains not less than 841 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefozopran Hydrochloride is expressed as mass (potency) of cefozopran ($C_{19}H_{17}N_9O_5S_2$: 515.53).

Description Cefozopran Hydrochloride occurs as a white to pale yellow, crystals or crystalline powder.

It is freely soluble in dimethylsulfoxide and in formamide, slightly soluble in water, in methanol and in ethanol (95), and practically insoluble in acetonitrile.

Identification (1) Dissolve 0.02 g of Cefozopran Hydrochloride in 10 mL of water, add 1 mL of a solution of hydroxylammonium chloride (1 in 10) and 2 mL of sodium hydroxide TS, allow to stand for 5 minutes, then add 3 mL of 1 mol/L hydrochloric acid TS and 3 drops of iron (III) chloride TS, and mix: a red-purple color develops.

(2) Determine the absorption spectra of solutions of Cefozopran Hydrochloride and Cefozopran Hydrochloride Reference Standard in a mixture of sodium chloride TS and methanol (3:2) (1 in 100,000) 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 spectrum of a solution of Cefozopran Hydrochloride in deuterated dimethylsulfoxide for nuclear magnetic resonance spectroscopy (1 in 20) 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 single signal A at around δ 3.9 ppm, a double signal B at around δ 5.2 ppm, and a quartet signal C at around δ 8.0 ppm, and the ratio of integrated intensity of each signal, A:B:C, is about 3:1:1.

(4) Dissolve 0.01 g of Cefozopran Hydrochloride in 1 mL of water and 2 mL of acetic acid (100), add 2 drops of silver nitrate TS, and mix: a white turbidity is formed.

Absorbance $E^{1\%}_{1\,cm}$ (238 nm): 455 – 485 (0.05 g calculated on the anhydrous basis, a mixture of sodium chloride TS and methanol (3:2), 5000 mL).

Optical rotation $[\alpha]^{20}_D$: −73 – −78° (0.1 g calculated on the anhydrous basis, a mixture of sodium chloride TS and methanol (3:2), 10 mL, 100 mm).

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

(2) Heavy metals—Proceed with 2.0 g of Cefozopran 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).

(3) Arsenic—Being specified separately.

(4) Related substances—Being specified separately.

Water Not more than 2.5% (0.5 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).

Residue on ignition Being specified separately.

Bacterial endotoxins Less than 0.05 EU/mg (potency).

Assay Weigh accurately an amount of Cefozopran Hydrochloride and Cefozopran Hydrochloride Reference Standard, equivalent to about 0.05 g (potency), and dissolve each in the mobile phase to make exactly 50 mL. Pipet 10 mL each of these solutions, add exactly 10 mL of the internal standard solution and the mobile phase to make 25 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 cefozopran to that of the internal standard of these solutions.

Amount [μg (potency)] of cefozopran ($C_{19}H_{17}N_9O_5S_2$)
= amount [mg (potency)] of Cefozopran Hydrochloride Reference Standard $\times \frac{Q_T}{Q_S} \times 1000$

Internal standard solution—A solution of 2,4-dihydroxybenzoic acid in the mobile phase (1 in 1250).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 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 25°C.