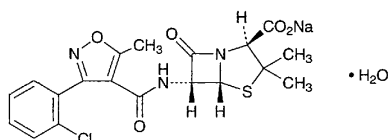


Cloxacillin Sodium

Methylchlorophenylisoxazolylpenicillin Sodium

クロキサシリンナトリウム



$C_{19}H_{17}ClN_3NaO_5S \cdot H_2O$: 475.88

Monosodium (2*S*,5*R*,6*R*)-6-[[3-(2-chlorophenyl)-5-methylisoxazole-4-carbonyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate monohydrate [7081-44-9]

Cloxacillin Sodium contains not less than 824 μ g (potency) per mg, calculated on the anhydrous basis. The potency of Cloxacillin Sodium is expressed as mass (potency) of cloxacillin ($C_{19}H_{18}ClN_3O_5S$: 435.88).

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

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

Identification (1) Determine the absorption spectrum of a solution of Cloxacillin Sodium in chloroform (1 in 20,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Cloxacillin Sodium Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

(2) Determine the infrared absorption spectrum of Cloxacillin 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 Cloxacillin Sodium Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) Cloxacillin Sodium responds to the Qualitative Test (1) for sodium salt.

pH Dissolve 1.0 g of Cloxacillin Sodium in 10 mL of water: the pH of the solution is between 4.5 and 8.0.

Purity Heavy metals—Proceed with 1.0 g of Cloxacillin Sodium according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

Water Not more than 6.0% (0.2 g, volumetric titration, direct titration).

Assay Perform the test according to the Cylinder-plate method as directed under the Microbial Assay for Antibiotics according to the following conditions.

(1) Test organism—*Bacillus subtilis* ATCC 6633

(2) Culture medium—Use the medium i in 1) Medium for test organism [5] under (1) Agar media for seed and base layer.

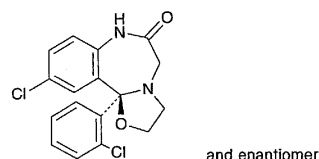
(3) Standard solution—Weigh accurately an amount of Cloxacillin Sodium Reference Standard equivalent to about 0.02 g (potency), and dissolve in 0.05 mol/L phosphate buffer solution, pH 7.0 to make exactly 100 mL. Take exactly a suitable amount of this solution, add 0.05 mol/L phosphate buffer solution, pH 7.0 to make solutions so that each mL contains 20 μ g (potency) and 5 μ g (potency), and use these solutions as the high concentration standard solution and the low concentration standard solution, respectively.

(4) Sample solution—Weigh accurately an amount of Cloxacillin Sodium equivalent to about 0.02 g (potency), and dissolve in 0.05 mol/L phosphate buffer solution, pH 7.0 to make exactly 100 mL. Take exactly a suitable amount of the solution, add 0.05 mol/L phosphate buffer solution, pH 7.0 to make solutions so that each mL contains 20 μ g (potency) and 5 μ g (potency), and use these solutions as the high concentration sample solution and the low concentration sample solution, respectively.

Containers and storage Containers—Tight containers.

Cloxazolam

クロキサゾラム



$C_{17}H_{14}Cl_2N_2O_2$: 349.21

(*RS*)-10-Chloro-11b-(2-chlorophenyl)-2,3,7,11b-tetrahydrooxazolo[3,2-*d*][1,4]benzodiazepin-6(5*H*)-one [24166-13-0]

Cloxazolam, when dried, contains not less than 99.0% of $C_{17}H_{14}Cl_2N_2O_2$.

Description Cloxazolam occurs as white crystals or crystalline powder.

It is odorless and tasteless.

It is freely soluble in acetic acid (100), sparingly soluble in dichloromethane, slightly soluble in ethanol (99.5) and in diethyl ether, very slightly soluble in ethanol (95), and practically insoluble in water.

It dissolves in dilute hydrochloric acid.

It is gradually colored by light.

Melting point: about 200°C (with decomposition).

Identification (1) Dissolve 0.01 g of Cloxazolam in 10 mL of ethanol (99.5) by heating, and add 1 drop of hydrochloric acid: the solution shows a light yellow color and a yellow-green fluorescence under ultraviolet light (main wavelength: 365 nm). Add 1 mL of sodium hydroxide TS to this solution: the color and fluorescence of this solution disappear immediately.

(2) Dissolve 0.01 g of Cloxazolam in 5 mL of dilute hydrochloric acid by heating in a water bath for 10 minutes. After cooling, 1 mL of this solution responds to the Qualitative Tests for primary aromatic amines.

(3) Place 2 g of Cloxazolam in a 200-mL flask, add 50 mL of ethanol (95) and 25 mL of sodium hydroxide TS, and boil under a reflux condenser for 4 hours. After cooling, neutralize with dilute hydrochloric acid, and extract with 30 mL of dichloromethane. Dehydrate with 3 g of anhydrous sodium sulfate, filter, and evaporate the dichloromethane of the filtrate. Dissolve the residue in 5 mL of methanol by heating on a water bath, and cool immediately in an ice bath. Collect the crystals, and dry the crystals in vacuum at 60°C for 1 hour: it melts between 87°C and 91°C.

(4) Determine the absorption spectrum of a solution of Cloxazolam in ethanol (99.5) (1 in 100,000) 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 wavelengths.

(5) Proceed with Cloxazolam as directed under the Flame Coloration Test (2), and perform the test: a green color appears.

Absorbance $E_{1\text{cm}}^{1\%}$ (244 nm): 390 – 410 (after drying, 1 mg, ethanol (99.5), 100 mL).

Purity (1) Chloride—To 1.0 g of Cloxazolam add 50 mL of water, allow to stand for 1 hour with occasional shaking, and filter. To 25 mL of this filtrate add 6 mL of dilute nitric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 0.20 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.014%).

(2) Heavy metals—Proceed with 1.0 g of Cloxazolam according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(3) Arsenic—Place 1.0 g of Cloxazolam in a Kjeldahl flask, add 5 mL of sulfuric acid and 5 mL of nitric acid, and heat gently. Repeat the addition of 2 to 3 mL of nitric acid at times, and continue heating until a colorless to light yellow solution is obtained. After cooling, add 15 mL of saturated ammonium oxalate solution, and heat the solution until dense white fumes are evolved, and evaporate to a volume of 2 to 3 mL. After cooling, dilute with water to 10 mL, and perform the test with this solution as the test solution using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.05 g of Cloxazolam in 10 mL of dichloromethane, and use this solution as the sample solution. Pipet 1 mL of this solution, add dichloromethane to make exactly 200 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Immediately after air-drying, develop the plate with a mixture of toluene and acetone (5:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution are not more intense than that from the standard solution.

Loss on drying Not more than 0.5% (1 g, 105°C, 3 hours).

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

Assay Weigh accurately about 0.5 g of Cloxazolam, previously dried, and dissolve in 50 mL of acetic acid (100). Titrate with 0.1 mol/L perchloric acid VS until the color of

the solution changes from purple through blue to blue-green (indicator: 2 drops of crystal violet TS). Perform a blank determination.

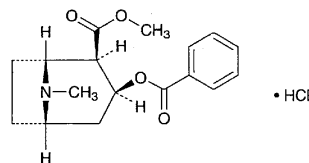
Each mL of 0.1 mol/L perchloric acid VS
= 34.922 mg of $\text{C}_{17}\text{H}_{14}\text{Cl}_2\text{N}_2\text{O}_2$

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Cocaine Hydrochloride

塩酸コカイン



$\text{C}_{17}\text{H}_{21}\text{NO}_4 \cdot \text{HCl}$: 339.81
(1*R*,2*R*,3*S*,5*S*)-2-Methoxycarbonyl-8-methyl-8-azabicyclo[3.2.1]oct-3-yl benzoate monohydrochloride [53-21-4]

Cocaine Hydrochloride, when dried, contains not less than 98.0% of $\text{C}_{17}\text{H}_{21}\text{NO}_4 \cdot \text{HCl}$.

Description Cocaine Hydrochloride occurs as colorless crystals or a white crystalline powder.

It is very soluble in water, freely soluble in ethanol (95) and in acetic acid (100), slightly soluble in acetic anhydride, and practically insoluble in diethyl ether.

Identification (1) Determine the absorption spectrum of a solution of Cocaine Hydrochloride in 0.01 mol/L hydrochloric acid TS (1 in 10,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 1: both spectra exhibit similar intensities of absorption at the same wavelengths. Separately, determine the absorption spectrum of a solution of Cocaine Hydrochloride in 0.01 mol/L hydrochloric acid TS (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 2: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Cocaine Hydrochloride, previously dried, 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) A solution of Cocaine Hydrochloride (1 in 50) responds to the Qualitative Tests (2) for chloride.

Optical rotation $[\alpha]_D^{20}$: -70 – -73° (after drying, 0.5 g, water, 20 mL, 100 mm).

Purity (1) Acid—Dissolve 0.5 g of Cocaine Hydrochloride in 10 mL of water, add 1 drop of methyl red TS, and neutralize with 0.01 mol/L sodium hydroxide VS: the consumed volume is not more than 1.0 mL.