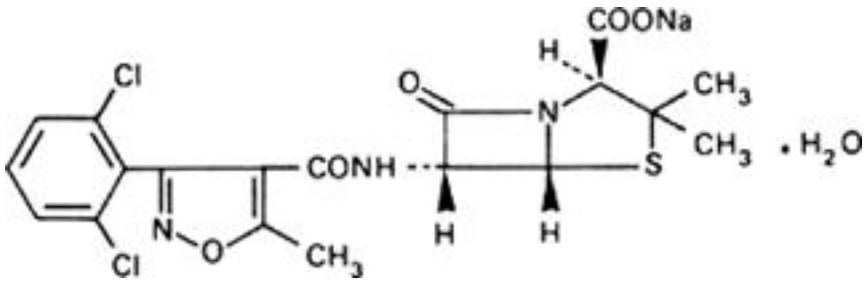
Dicloxacillin sodium (Dicloxacillinum natricum)

Molecular formula. $C_{19}H_{16}Cl_2N_3NaO_5S,H_2O$

Relative molecular mass. 510.3

Graphic formula.



Chemical name. Monosodium (2*S*,5*R*,6*R*)-6-[3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolecarboxamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate monohydrate; monosodium [2*S*-(2α,5α,6β)]-6-[[[3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolyl]carbonyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate monohydrate; monosodium [3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolyl]penicillin monohydrate; CAS Reg. No. 13412-64-1 (monohydrate).

Description. A white or almost white, crystalline powder.

Solubility. Freely soluble in water and methanol R; soluble in ethanol (~750 g/l) TS.

Category. Antibacterial drug.

Storage. Dicloxacillin sodium should be kept in a tightly closed container, protected from light.

Additional information. Even in the absence of light, Dicloxacillin sodium is gradually degraded on exposure to a humid atmosphere, the decomposition being faster at higher temperatures.

Requirements

Definition. Dicloxacillin sodium contains not less than 88.0% of total penicillins calculated as dicloxacillin free acid ($C_{19}H_{17}Cl_2N_3O_5S$) and with reference to the anhydrous substance.

Identity tests

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from dicloxacillin sodium RS or with the *reference spectrum* of dicloxacillin sodium.

B. To 10 mg of paraformaldehyde R dissolved in 1 mL of sulfuric acid (~1760 g/l) TS add about 1 mg of the test substance; a colourless solution is produced. Heat the solution in a water-bath for 2 minutes and cool; the solution remains colourless (distinction from cloxacillin sodium).

C. Ignite 20 mg and dissolve the residue in acetic acid (~60 g/l) TS. The solution yields reaction B described under 2.1 General identification tests as characteristic of sodium.

Specific optical rotation. Use a 10 mg/mL solution, and calculate with reference to the anhydrous substance; $[\alpha]_D^{20\,°C}$ = +128° to +143°.

Water. Determine as described under 2.8 Determination of water by the Karl Fischer method, Method A, using about 0.25 g of the substance; the water content is not less than 30 mg/g and not more than 50 mg/g.

pH value. pH of a 10 mg/mL solution, 4.5-7.5.

Chlorine. Carry out the combustion as described under 2.4 Oxygen flask method, but using 25 mg of the test substance and 10 mL of sodium hydroxide (0.1 mol/l) VS as the absorbing liquid. When the process is complete, transfer the resulting solution to a titration vessel, heat on a water-bath for 30 minutes, cool to room temperature, add 20 mL of nitric acid (~130 g/l) TS, and titrate with silver nitrate (0.01 mol/l) VS, determining the end-point potentiometrically using a silver/silver chloride electrode system. Repeat the operation without the substance being tested. Each mL of silver nitrate (0.01 mol/l) VS is equivalent to 0.3546 mg of Cl. Calculate the total content of chlorine in mg/g and subtract from it the content of free chlorides as determined below; the content of chlorine is between 130 mg/g and 142 mg/g.

Free chlorides. Dissolve about 0.12 g, accurately weighed, in 10 mL of sodium hydroxide (0.1 mol/l) VS, add 20 mL of water, and

heat on a water-bath for 30 minutes. Cool to room temperature, add 20 mL of nitric acid (~130 g/l) TS, and titrate with silver nitrate (0.01 mol/l) VS, determining the end-point potentiometrically using a silver/silver chloride electrode system. Repeat the operation without the substance being tested. Each mL of silver nitrate (0.01 mol/l) VS is equivalent to 0.3546 mg of Cl; the content of free chlorides is not more than 5 mg/g.

Assay. Dissolve about 50 mg, accurately weighed, in sufficient water to produce 1000 mL. Transfer two 2.0-mL aliquots of this solution into separate stoppered tubes. To one tube add 10.0 mL of imidazole/mercuric chloride TS, mix, stopper the tube and place in a water-bath at 60 °C for exactly 25 minutes. Cool the tube rapidly to 20 °C (solution A). To the second tube add 10.0 mL of water and mix (solution B).

Without delay measure the absorbance of a 1-cm layer at the maximum at about 343 nm against a solvent cell containing a mixture of 2.0 mL of water and 10.0 mL of imidazole/mercuric chloride TS for solution A and water for solution B.

From the difference between the absorbance of solution A and that of solution B, calculate the amount of $C_{19}H_{16}Cl_2N_3NaO_5S$ in the substance being tested by comparison with dicloxacillin sodium RS, similarly and concurrently examined.