Ampicillin sodium (Ampicillinum natricum)

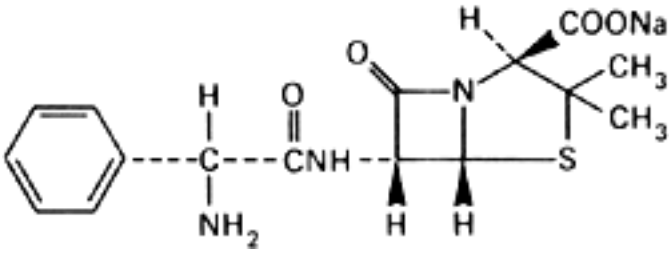
Ampicillin sodium (non-injectable)

Ampicillin sodium, sterile

Molecular formula. $C_{16}H_{18}N_3NaO_4S$

Relative molecular mass. 371.4

Graphic formula.



Chemical name. Sodium (2*S*,5*R*,6*R*)-6-[(*R*)-2-amino-2-phenylacetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate; sodium [2*S*-[2*α*,5*α*,6*β* (*S**)]]-6-[(aminophenylacetyl)amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate; CAS Reg. No. 69-52-3.

Description. A white or almost white powder; odourless.

Solubility. Soluble in about 2 parts of water; practically insoluble in ether R.

Category. Antibiotic.

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

Labelling. The designation sterile Ampicillin sodium indicates that the substance complies with the requirements for sterile Ampicillin sodium and may be used for parenteral administration or for other sterile applications.

Additional information. Ampicillin sodium is a crystalline or amorphous powder; it is very hygroscopic and is deliquescent in air with a relative humidity of 60% or more. Even in the absence of light, Ampicillin sodium is gradually degraded on exposure to a humid atmosphere, the decomposition being faster at higher temperatures.

Requirements

Definition. Ampicillin sodium contains not less than 85.0% and not more than 96.0% of $C_{16}H_{19}N_3O_4S$, calculated with reference to the anhydrous substance. Furthermore, the sum of the percentage of $C_{16}H_{19}N_3O_4S$ determined in the assay and the percentage of iodine-absorbing compounds, both calculated with reference to the anhydrous substance, is not less than 90.0%.

Identity tests

• Either tests A and C or tests B and C may be applied.

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 ampicillin sodium RS or with the *reference spectrum* of ampicillin sodium.

B. To 2 mg in a test-tube add 1 drop of water followed by 2 mL of sulfuric acid (~1760 g/l) TS and mix; the solution is colourless. Immerse the test-tube for 1 minute in a water-bath; the solution remains colourless. Place 2 mg in a second test-tube, add 1 drop of water and 2 mL of formaldehyde/sulfuric acid TS and mix; the solution is colourless. Immerse the test-tube for 1 minute in a water-bath; a dark yellow colour is produced.

C. When tested for sodium as described under 2.1 General identification tests yields the characteristic reactions. If reaction B is to be used, ignite a small quantity and dissolve the residue in acetic acid (~60 g/l) TS.

Specific optical rotation. Use a 5.0 mg/mL solution in acetate standard buffer TS and calculate with reference to the anhydrous substance; $[\alpha]_D^{20\,°C}$ = +260° to +290°.

Clarity of solution. A freshly prepared solution of 1.0 g in 10 mL of water is clear. A solution of 1.0 g in 10 mL of hydrochloric acid (1 mol/l) VS is also clear.

Water. Determine as described under 2.8 Determination of water by the Karl Fischer method, Method A, using about 0.5 g of the substance; the water content is not more than 20 mg/g.

pH value. pH of a 0.10 g/mL solution in carbon-dioxide-free water R, 8.0-10.0.

Iodine-absorbing compounds. Dissolve 0.25 g in sufficient water to produce 100 mL. To 10 mL of this solution add 0.5 mL of hydrochloric acid (1 mol/l) VS and 10 mL of iodine (0.01 mol/l) VS and titrate with sodium thiosulfate (0.02 mol/l) VS, using starch TS as indicator, added towards the end of the titration. Repeat the procedure without the substance being examined; the difference between the titrations represents the amount of iodine-absorbing compounds. Calculate as a percentage the amount of these compounds in the examined substance, taking into account that each mL of sodium thiosulfate (0.02 mol/l) VS is equivalent to 0.7392 mg of iodine-absorbing compounds expressed as $C_{16}H_{19}N_3O_4S$.

Assay. Dissolve about 0.12 g, accurately weighed, in sufficient water to produce 500 mL. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, add 10 mL of buffer borate, pH 9.0, TS, 1 mL of acetic anhydride/dioxan TS, allow to stand for 5 minutes at room temperature and dilute to volume with water.

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 325 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 as a percentage the amount of $C_{16}H_{19}N_3O_4S$ in the substance being tested by comparison with ampicillin RS similarly and concurrently examined. In an adequately calibrated spectrophotometer the absorbance of the reference solution should be 0.29 ± 0.02.

Additional Requirements for Ampicillin Sodium for sterile use

Bacterial endotoxins. Carry out the test as described under 3.4 Test for bacterial endotoxins; contains not more than 0.15 IU of endotoxin RS per mg of ampicillin.

Sterility. Complies with 3.2 Test for sterility.