Ampicillin sodium for injection (Ampicillini natrici ad injectionem)

Description. A white or almost white powder.

Category. Antibacterial drug.

Storage. Ampicillin sodium powder for injections should be protected from light and stored at a temperature not exceeding 25 °C. The reconstituted solution should be used immediately after preparation.

Labelling. The label should state the dose as the equivalent amount of anhydrous ampicillin. Expiry date.

Additional information. Strengths in the current WHO Model list of essential medicines: 500 mg, 1 g (as sodium salt) in vial. Strengths in the current WHO Model list of essential medicines for children: 500 mg, 1 g (as sodium salt) in vial.

Requirements

The powder for injections and the reconstituted solution for injections comply with the monograph for *Parenteral preparations*.

Definition. Ampicillin sodium powder for injections is a sterile powder of ampicillin sodium. The powder is sterilized by a suitable method (see *5.8 Methods of sterilization*).

The container of Ampicillin sodium powder for injections contains not less than 90.0% and not more than 110.0% of the amount of $C_{16}H_{19}N_3O_4S$ stated on the label.

Identity tests

-Either tests A and D or tests B, C and D 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. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R1 as the coating substance and a mixture of 65 volumes of acetone R, 10 volumes of water, 10 volumes of toluene R and 2.5 volumes of glacial acetic acid R as the mobile phase. Apply separately to the plate 2 µl of each of the following two solutions. For solution (A) shake a quantity of the powder for injections equivalent to 5 mg of Ampicillin sodium with 10 mL of a mixture of 4 volumes of acetone R and 1 volume of hydrochloric acid (0.1 mol/l) VS, filter and use the clear filtrate. For solution (B) dissolve 25 mg of ampicillin sodium RS in 5 mL of the same mixture of solvents. After removing the plate from the chromatographic chamber allow it to dry in air, spray lightly with triketohydrindene/ethanol TS, dry at 90 °C for 15 minutes and examine the chromatogram in daylight.

The principal spot obtained with solution A corresponds in position, appearance and intensity with that obtained with solution B.

C. To a quantity of the powder for injections equivalent to 2 mg of Ampicillin sodium 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 the same quantity of powder 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.

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

Specific optical rotation. Use a solution containing a quantity of the powder for injections equivalent to 5 mg of Ampicillin sodium per mL 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 the powder for injections equivalent to 1 g of Ampicillin sodium in 10 mL of water is clear. A similar solution 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 a quantity of the powder for injections equivalent to 0.5 g of Ampicillin sodium; the water content is not more than 20 mg/g.

pH value. pH of a solution containing a quantity of the powder for injections equivalent to 0.1 g of Ampicillin sodium per mL of carbon-dioxide-free water R, 8.0–10.0.

Assay

Mix the contents of 10 containers and carry out the assay as described.

Dissolve a quantity of the powder for injections equivalent to about 0.12 g of Ampicillin sodium, accurately weighed, in sufficient water to produce 500 mL. Transfer 10 mL of this solution to a 100 mL volumetric flask, add 10 mL of buffer borate, pH 9.0, TS and 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 mL aliquots of this solution into separate stoppered tubes. To one tube add 10 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 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 mL of water and 10 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 powder for injections by comparison with ampicillin RS. In an adequately calibrated spectrophotometer the absorbance of the *reference solution* should be 0.29 ± 0.02.

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.