Cloxacillin sodium for injection (Cloxacillini natrici ad injectionem)

**Description.** A white, crystalline powder.

**Category.** Antibacterial drug.

**Storage.** Cloxacillin sodium powder for injections should be protected from light.

**Labelling.** The designation on the container should state the quantity of Cloxacillin sodium in terms of the equivalent amount of cloxacillin. Expiry date.

**Additional information.** Strength in the current WHO Model list of essential medicines: the equivalent of 500 mg of cloxacillin in vials.

Cloxacillin sodium powder for injections is hygroscopic.

**Requirements**

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

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

The container of Cloxacillin sodium powder for injections contains not less than 90.0% and not more than 110.0% of the amount of C_{19}H_{17}ClN_{3}NaO_{5}S 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 cloxacillin sodium RS or with the **reference spectrum** of cloxacillin sodium.

  B. Carry out the test as described under 1.14.1 Thin-layer chromatography, using silanized silica gel R3 as the coating substance and a mixture of 30 volumes of acetone R and 70 volumes of a solution containing 154 g/l of ammonium acetate R, the pH of which has been adjusted to 5.0 with glacial acetic acid R, as the mobile phase. Apply separately to the plate 1 μl of each of the following three solutions. For solution (A) shake a quantity of the powder for injections equivalent to 0.25 g of Cloxacillin sodium with 50 mL of water, filter, and use the clear filtrate. For solution (B) dissolve 25 mg of cloxacillin sodium RS in 5 mL of water, and for solution (C) dissolve 25 mg of each of cloxacillin sodium RS, dicloxacillin sodium RS, and flucloxacillin sodium RS together in 5 mL of water. After removing the plate from the chromatographic chamber, allow it to dry in air and expose it to the vapour of iodine R until spots appear. Examine the chromatogram in daylight.

  The principal spot obtained with solution A corresponds in position, appearance, and intensity with that obtained with solution B. The test is valid only if the chromatogram obtained with solution C shows three distinctly separated spots.

  C. Place a quantity of the powder for injections equivalent to 2 mg of Cloxacillin sodium in a test-tube and add 2 mg of disodium chromotropate R and 2 mL of sulfuric acid (~1760 g/l) TS. Immerse the tube in a suitable bath at 150 °C for 3-4 minutes; a red-violet colour is produced.

  D. Ignite a quantity of the powder for injections equivalent to 20 mg of Cloxacillin sodium 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 solution containing a quantity of the powder for injections equivalent to 10 mg of Cloxacillin sodium per mL, and calculate with reference to the anhydrous substance; \([\alpha]_{D}^{20^\circ C} = +163^\circ \text{ to } +172^\circ \).

**Clarity and colour of solution.** A solution of the powder for injections equivalent to 0.2 g of Cloxacillin sodium in 10 mL of carbon-dioxide-free water R is clear and colourless. (Keep this solution for the "pH value").

**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 0.25 g of Cloxacillin sodium; the water content is not less than 35 mg/g and not more than 45 mg/g.

**pH value.** pH of the solution prepared above for the test of clarity and colour, 5.0-7.0.

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

Transfer a quantity of the powder for injections equivalent to about 0.1 g of Cloxacillin, accurately weighed, to a 500-mL flask and dilute to volume with water. Dilute 25 mL to 100 mL 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 343 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 the amount of \( \text{C}_{19}\text{H}_{17}\text{ClN}_{3}\text{NaO}_{5}\text{S} \) in the substance being examined by comparison with cloxacillin sodium RS. In an adequately calibrated spectrophotometer the absorbance of the reference solution should be 0.40 ± 0.02.

**Bacterial endotoxins.** Carry out the test as described under **3.4 Test for bacterial endotoxins;** contains not more than 0.40 IU of endotoxin RS per mg of cloxacillin.