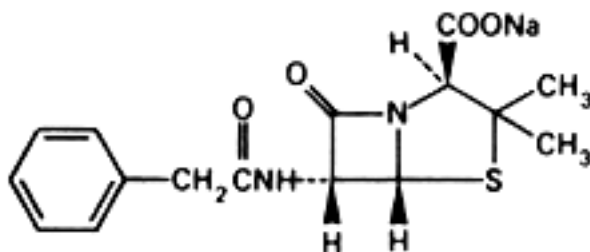


**Benzylpenicillin sodium (Benzylpenicillinum natricum)****Benzylpenicillin sodium (non-injectable)****Benzylpenicillin sodium, sterile****Molecular formula.**  $C_{16}H_{17}N_2NaO_4S$ **Relative molecular mass.** 356.4**Graphic formula.****Chemical name.**

Sodium (2*S*,5*R*,6*R*)-3,3-dimethyl-7-oxo-6-(2-phenylacetamido)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate; sodium [2*S*-(2*α*,5*α*,6*β*)]-3,3-dimethyl-7-oxo-6-[(phenylacetyl)amino]-4-thia-1-azabicyclo[3.2.0]-heptane-2-carboxylate; CAS Reg. No. 69-57-8.

**Description.** A white or almost white, crystalline powder; odourless or with a faint characteristic odour.**Solubility.** Soluble in about 0.5 part of water; practically insoluble in ether R.**Category.** Antibiotic.**Storage.** Benzylpenicillin sodium should be kept in a tightly closed container, protected from light, and stored at a temperature not exceeding 25°C.**Labelling.** The designation sterile Benzylpenicillin sodium indicates that the substance complies with the additional requirements for sterile Benzylpenicillin sodium and may be used for parenteral administration or for other sterile applications.**Additional information.** Benzylpenicillin sodium is hygroscopic; it is readily decomposed by acid, alkalis and oxidizing agents. Even in the absence of light, Benzylpenicillin sodium is gradually degraded on exposure to a humid atmosphere, the decomposition being faster at higher temperatures.**Requirements****Definition.** Benzylpenicillin sodium contains not less than 96.0% and not more than 102.0% of  $C_{16}H_{17}N_2NaO_4S$ , calculated with reference to the dried substance.**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 benzylpenicillin sodium RS or with the *reference spectrum* of benzylpenicillin 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 brownish yellow. Immerse the test-tube for 1 minute in a water-bath; a reddish brown colour is produced.

C. When tested for sodium as described under [2.1 General identification tests](#) yields the characteristic reaction. 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 20 mg/mL solution;  $[\alpha]_D^{20} = +280^\circ$  to  $+310^\circ$ .

**Clarity and colour of solution.** A solution of 0.20 g in 10 mL of water is clear and colourless.**Loss on drying.** Dry to constant weight at 105°C; it loses not more than 10 mg/g.**pH value.** pH of a 20 mg/mL solution in carbon-dioxide-free water R, 5.0-7.5.

**Light-absorbing impurities.** Using a freshly prepared 1.8 mg/mL solution in water, measure the absorbances of a 1-cm layer at 280 nm and at 325 nm; the absorbance at each of these wavelengths does not exceed 0.10.

**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 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 the amount of  $C_{16}H_{17}N_2NaO_4S$  in the substance being tested by comparison with benzylpenicillin sodium RS similarly and concurrently examined. In an adequately calibrated spectrophotometer the absorbance of the reference solution should be  $0.62 \pm 0.03$ .

#### **Additional Requirements for Benzylpenicillin Sodium for sterile use**

**Bacterial endotoxins.** Carry out the test as described under [3.4 Test for bacterial endotoxins](#); contains not more than 0.01 IU of endotoxin RS per mg of benzylpenicillin.

**Sterility.** Complies with [3.2 Test for sterility](#).