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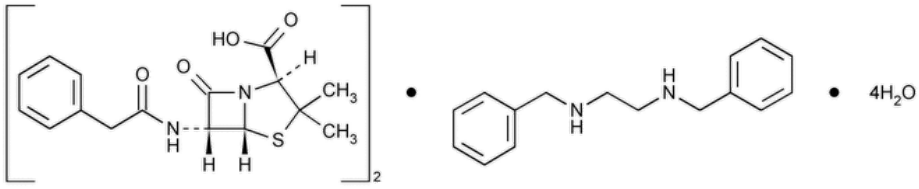
Penicillin G Benzathine



$(C_{16}H_{18}N_2O_4S)_2 \cdot C_{16}H_{20}N_2 \cdot 4H_2O$ 981.18

4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 3,3-dimethyl-7-oxo-6-[(phenylacetyl)amino-], 2[*S*-(2α,5α,6β)]-, compd. with *N*,*N*'-bis(phenylmethyl)-1,2-ethanediamine (2:1), tetrahydrate.

(2*S*,5*R*,6*R*)-3,3-Dimethyl-7-oxo-6-(2-phenylacetamido)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid compound with *N*,*N*'-dibenzylethylenediamine (2:1), tetrahydrate CAS RN®: 41372-02-5; UNII: RIT82F58GK.

Anhydrous 909.15 CAS RN®: 1538-09-6; UNII: SSZ1S4I0US.

» Penicillin G Benzathine has a potency of not less than 1090 Penicillin G Units and not more than 1272 Penicillin G Units per mg.

Packaging and storage—Preserve in tight containers.

Labeling—Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

USP Reference standards ⟨11⟩—

USP Penicillin G Benzathine RS
USP Penicillin G Potassium RS

Change to read:

Identification, ▲*Spectroscopic Identification Tests* ⟨197⟩*, Ultraviolet-Visible Spectroscopy: 197U*▲ (CN 1-May-2020) —

Solution: 500 µg per mL.

Medium: methanol.

Absorptivity at 263 nm is between 85.0% and 110.0% of that of USP Penicillin G Benzathine RS.

Crystallinity ⟨695⟩: meets the requirements.

Bacterial Endotoxins Test ⟨85⟩ —Where the label states that Penicillin G Benzathine is sterile or that it must be subjected to further processing during the preparation of injectable dosage forms it contains not more than 0.01 USP Endotoxin Unit per 100 Penicillin G Units.

Sterility Tests ⟨71⟩ —Where the label states that Penicillin G Benzathine is sterile it meets the requirements when tested as directed in the section *Direct Inoculation of the Culture Medium* under *Test for Sterility of the Product to be Examined*, except to use Fluid Thioglycollate Medium and Soybean–Casein Digest Medium containing polysorbate 80 solution (1 in 200) and an amount of sterile penicillinase sufficient to inactivate the penicillin G in each tube, and to shake the vessels once daily.

pH ⟨791⟩: between 4.0 and 6.5, in a solution prepared by dissolving 50 mg in 50 mL of dehydrated alcohol, adding 50 mL of water, and mixing.

Water Determination, *Method I* ⟨921⟩: between 5.0% and 8.0%.

Benzathine content—To about 1 g of Pencillin G Benzathine, accurately weighed, add 30 mL of a saturated solution of sodium chloride and 10 mL of 5 N sodium hydroxide, and extract with four 50-mL portions of ether. Wash the combined ether extracts with three 10-mL portions of water. Extract the combined water washings with 25 mL of ether, and add the ether extract to the water-washed combined ether extracts. Evaporate this combined ether solution to a volume of about 5 mL, add 2 mL of dehydrated alcohol, and evaporate to dryness. Dissolve the residue in 50 mL of glacial acetic acid, add 1 mL of *p*-naphtholbenzein TS, and titrate with 0.1 N perchloric acid VS to a green endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 12.02 mg of benzathine ($C_{16}H_{20}N_2$): between 24.0% and 27.0% of benzathine in Penicillin G Benzathine, calculated on the anhydrous basis, is found.

Assay—

0.05 M phosphate buffer, pH 6.0—Dissolve 6.8 g of monobasic potassium phosphate in 900 mL of water, adjust with 1 N sodium hydroxide to a pH of 6.0, dilute with water to 1000 mL, and mix.

Mobile phase—Prepare a mixture of *0.05 M phosphate buffer, pH 6.0* and acetonitrile (4:1), pass through a membrane filter having a 5-µm or finer porosity, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Transfer about 40 mg of USP Penicillin G Potassium RS, accurately weighed, to a 50-mL volumetric flask, add 10 mL of acetonitrile and 5 mL of methanol, and swirl to dissolve. Without delay, dilute with *0.05 M phosphate buffer, pH 6.0* to volume, and mix.

System suitability preparation—Prepare a solution of penicillin V potassium in *Mobile phase* containing about 1 mg per mL. Mix equal volumes of this solution and the *Standard preparation*.

Assay preparation—Transfer about 53 mg of Penicillin G Benzathine, accurately weighed, to a 50-mL volumetric flask, add 10 mL of acetonitrile and 5 mL of methanol, and swirl to dissolve. Without delay, dilute with *0.05 M phosphate buffer, pH 6.0* to volume, and mix.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 225-nm detector and a 4-mm × 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation* and the *System suitability preparation*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.7 for penicillin G and 1.0 for penicillin V; the resolution, *R,* between penicillin G and penicillin V is not less than 2.0; the column efficiency determined from the analyte peak is not less than 600 theoretical plates; and the relative standard deviation for replicate injections of the *Standard preparation* is not more than 1.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the potency, in Penicillin G Units per mg, of the Penicillin G Benzathine taken by the formula:

$$50(CP/W)(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Penicillin G Potassium RS in the *Standard preparation; P* is the stated potency, in Penicillin G Units per mg, of USP Penicillin G Potassium RS; *W* is the quantity, in mg, of Penicillin G Benzathine taken to prepare the *Assay preparation;* and r_U and r_S are the penicillin G peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
PENICILLIN G BENZATHINE	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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