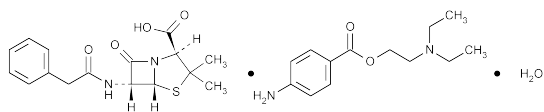


Penicillin G Procaine



$C_{16}H_{18}N_2O_4S \cdot C_{13}H_{20}N_2O_2 \cdot H_2O$ 588.72

4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 3,3-dimethyl-7-oxo-6-[(phenylacetyl)amino]-, 2*S*-(2*α*,5*α*,6*β*)-, compd. with 2-(diethylamino)ethyl 4-aminobenzoate (1:1) monohydrate.
(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 2-(diethylamino)ethyl *p*-aminobenzoate (1:1) monohydrate [6130-64-9].

Anhydrous 570.71 [54-35-3].

» Penicillin G Procaine has a potency of not less than 900 Penicillin G Units and not more than 1050 Penicillin G Units per mg.

Packaging and storage—Preserve in Containers for Sterile Solids as described under *Injections* (1).

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 Endotoxin RS

USP Penicillin G Potassium RS

USP Procaine Hydrochloride RS

Identification—Prepare a solution of it containing about 12,000 Penicillin G Units per mL in a solvent mixture consisting of acetone, 0.1 M citric acid, and 0.1 M sodium citrate (2:1:1). Prepare a Standard solution of USP Penicillin G Potassium RS containing about 12,000 Penicillin G Units per mL in the same solvent mixture (*Standard solution A*). Prepare a Standard solution of USP Procaine Hydrochloride RS containing about 5 mg per mL in the same solvent system (*Standard solution B*). Apply separately 20 μ L of each solution to a thin-layer chromatographic plate (see *Chromatography* (621)) coated with a 0.25-mm layer of chromatographic silica gel mixture. Place the plate in a suitable chromatographic chamber, and develop the chromatogram in a solvent system consisting of a mixture of toluene, dioxane, and glacial acetic acid (90:25:4) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, mark the solvent front, and allow to air-dry. Examine the plate under short- and long-wavelength UV light, noting the positions of the spots. Spray the plate with starch TS followed by dilute iodine TS (1 in 10). Penicillin G appears as a white spot on a purple background: the R_f value of the penicillin G spot obtained from the test solution corresponds to that obtained from *Standard solution A*. Spray the location of the spots visualized with UV light with a 1 in 20 solution of *p*-dimethylaminobenzaldehyde in methanol. Procaine appears as a bright yellow spot: the R_f value of the procaine spot obtained from the test solution corresponds to that obtained from *Standard solution B*.

Crystallinity (695): meets the requirements.

Bacterial endotoxins (85)—Where the label states that Penicillin G Procaine 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 (71)—Where the label states that Penicillin G Procaine is sterile it meets the requirements when tested as directed for *Membrane Filtration under Test for Sterility of the Product to be Examined*, except to use *Fluid A* to which has been added sufficient sterile penicillinase to inactivate the penicillin G and to swirl the vessel until solution is complete before filtering.

pH (791): between 5.0 and 7.5, in a (saturated) solution containing about 300 mg per mL.

Water, Method I (921): between 2.8% and 4.2%.

Content of Penicillin G and procaine—

Mobile phase—Dissolve 14 g of monobasic potassium phosphate and 6.5 g of tetrabutylammonium hydroxide solution (4 in 10) in about 700 mL of water, adjust with 1 N potassium hydroxide to a pH of 7.0, dilute with water to 1000 mL, and mix. Mix 500 mL of this solution, 250 mL of acetonitrile, and 250 mL of water. Adjust with 1 N potassium hydroxide or dilute phosphoric acid (1 in 10) to a pH of 7.5 ± 0.05 , filter through a membrane filter of 5 μ m or finer porosity, and degas. Make adjustments if necessary (see *System Suitability under Chromatography* (621)).

Standard preparation—Using accurately weighed quantities of USP Penicillin G Potassium RS and USP Procaine Hydrochloride RS, prepare a solution in *Mobile phase* having known concentrations of about 0.8 mg per mL and 0.54 mg per mL, respectively.

Test preparation—Transfer about 70 mg of Penicillin G Procaine, accurately weighed, to a 50-mL volumetric flask, add about 30 mL of *Mobile phase*, sonicate to dissolve, dilute with *Mobile phase* to volume, and mix.

Resolution solution—Prepare a solution of penicillin V potassium in *Mobile phase* containing 2.4 mg per mL. Mix 1 volume of this solution and 3 volumes of *Standard preparation*.

Chromatographic system (see *Chromatography* (621))—The liquid chromatograph is equipped with a 235-nm detector and a 4-mm \times 30-cm column that contains 10- μ m packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the relative standard deviation for replicate injections is not more than 3.0%. Chromatograph about 10 μ L of the *Resolution solution*, and record the peak responses as directed for *Procedure*: the resolution, R , between penicillin G and penicillin V is not less than 2.0.

Procedure—Separately inject equal volumes (about 10 μ L) of the *Standard preparation* and the *Test preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are 1.0 for procaine and about 2.2 for penicillin G. Calculate the percentage of penicillin G ($C_{16}H_{18}N_2O_4S$) in the specimen under test by the formula:

$$50C(G_s / W_U)(r_U / r_s)$$

in which C is the concentration, in mg per mL, of USP Penicillin G Potassium RS in the *Standard preparation*, G_s is the designated penicillin G content, in percentage, of USP Penicillin G Potassium RS, W_U is the amount, in mg, of Penicillin G Procaine taken, and r_U and r_s are the responses of the penicillin G peaks obtained from the *Test preparation* and the *Standard preparation*, respectively: between 51.0% and 59.6% of $C_{16}H_{18}N_2O_4S$ is found. Calculate the percentage of procaine ($C_{13}H_{20}N_2O_2$) in the specimen under test by the formula:

$$(236.32 / 272.78)(5000C / W_U)(r_U / r_s)$$

in which 236.32 and 272.78 are the molecular weights of procaine and procaine hydrochloride, respectively, C is the concentration, in mg per mL, of USP Procaine Hydrochloride RS in the *Standard preparation*, W_U is the amount, in mg, of Penicillin G Procaine taken, and r_U and r_s are the responses of the procaine peaks obtained from the *Test preparation* and the *Standard preparation*, respectively: between 37.5% and 43.0% is found.

Assay—

Standard preparation—Using USP Penicillin G Potassium RS, prepare as directed for *Standard preparation under Iodometric Assay—Antibiotics* (425).

Assay preparation—Prepare as directed for *Assay Preparation under Iodometric Assay—Antibiotics* (425), except to dissolve about 100 mg of Penicillin G Procaine, accurately weighed, in

2.0 mL of methanol, and to dilute quantitatively with *Buffer No. 1* to obtain a solution containing about 2000 Penicillin G Units per mL.

Procedure—Proceed as directed for *Procedure* under *Iodometric Assay—Antibiotics* (425). Calculate the potency, in Penicillin G Units per mg, of the Penicillin G Procaine taken by the formula:

$$F(B - I) / (2D)$$

in which *D* is the concentration, in mg per mL, of the *Assay preparation*, on the basis of the weight of Penicillin G Procaine taken and the extent of dilution, and the other terms are as defined therein.

Penicillin G Procaine Intramammary Infusion

» Penicillin G Procaine Intramammary Infusion is a suspension of Penicillin G Procaine in a suitable vegetable oil vehicle. It may contain one or more buffers, dispersants, preservatives, and thickening agents. It contains not less than 90.0 percent and not more than 115.0 percent of the labeled amount of penicillin G.

Packaging and storage—Preserve in well-closed disposable syringes.

Labeling—Label it to indicate that it is for veterinary use only.

USP Reference standards (11)—

USP Penicillin G Potassium RS

USP Penicillin G Procaine RS

Identification—Transfer a portion of it, equivalent to about 100,000 Penicillin G Units, to a test tube, add 25 mL of methanol, and shake. Allow to separate, and use the methanol layer as the test solution. Prepare a Standard solution of USP Penicillin G Procaine RS in methanol containing about 4.5 mg per mL. Apply separately 10 µL of each solution to a thin-layer chromatographic plate (see *Chromatography* (621)) coated with a 0.25-mm layer of chromatographic silica gel mixture. Allow the spots to dry, and develop the chromatogram in a solvent system consisting of a mixture of butanol, isopropyl alcohol, acetone, and water (4:4:2:2) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Expose the plate to iodine vapors in a closed chamber for about 15 minutes, and locate the spots: the *R_f* values and colors of the two principal spots obtained from the test solution correspond to those obtained from the Standard solution.

Water, Method I (921): not more than 1.4%, 20 mL of a mixture of toluene and methanol (7:3) being used in place of methanol in the titration vessel.

Assay—Proceed as directed under *Antibiotics—Microbial Assays* (81), expelling the contents of 1 syringe of Intramammary Infusion into a high-speed glass blender jar containing 499.0 mL of *Buffer No. 1* and 1.0 mL of polysorbate 80, and blending for 3 to 5 minutes. Allow to stand for about 10 minutes, and dilute an accurately measured volume of the aqueous phase quantitatively and stepwise with *Buffer No. 1* to obtain a *Test Dilution* having a concentration assumed to be equal to the median dose level of the Standard.

Penicillin G Procaine Injectable Suspension

» Penicillin G Procaine Injectable Suspension is a sterile suspension of Penicillin G, Procaine or, where labeled for veterinary use only of sterile penicillin G procaine, in Water for Injection and contains one or more suitable buffers dispersants, or suspending agents, and a suitable preservative. It may contain procaine hydrochloride in a concentration not exceeding 2.0 percent, and may contain one or more suitable stabilizers. It contains not less than 90.0 percent and not more than 115.0 percent of the labeled amount of penicillin G, the labeled amount being not less than 300,000 Penicillin G Units per mL or per container.

Packaging and storage—Preserve in single-dose or multiple-dose containers, preferably of Type I or Type III glass, in a refrigerator.

Labeling—Where it is intended for veterinary use only, the label so states.

USP Reference standards (11)—

USP Endotoxin RS

USP Penicillin G Potassium RS

USP Procaine Hydrochloride RS

Identification—It responds to the *Identification* test under *Penicillin G Procaine*.

Crystallinity (695) (where it is prepared from penicillin G procaine and is labeled for veterinary use only): meets the requirements, the dried residue prepared as directed in the test for *Penicillin G and procaine contents* being used.

Bacterial endotoxins (85)—It contains not more than 0.01 USP Endotoxin Unit per 100 Penicillin G Units.

Sterility (71)—It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined*, except to use a portion of specimen from each container equivalent to 300,000 Penicillin G Units, instead of the minimum volume specified in the *Table 2, Minimum Quantity to be Used for Each Medium*, and to use *Fluid A* to which has been added sufficient sterile penicillinase to inactivate the penicillin G and to swirl the vessel until solution is complete before filtering. If the Injectable Suspension contains lecithin, use *Fluid D*. If it contains carboxymethylcellulose sodium, add sufficient sterile carboxymethylcellulase to *Fluid A* or *Fluid D* to dissolve the carboxymethylcellulose sodium before filtering. If it does not dissolve completely, proceed as directed for *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 an amount of sterile penicillinase sufficient to inactivate the penicillin G in each vessel.

pH (791): between 5.0 and 7.5.

Penicillin G and procaine contents (where it is prepared from penicillin G procaine and is labeled for veterinary use only)—Dilute a portion of it, equivalent to about 300,000 Penicillin G Units, with water to obtain a volume of 10 mL, centrifuge, and remove and discard the supernatant. Resuspend the sediment in 10 mL of water, centrifuge, and remove and discard the supernatant. Dry the sediment in a vacuum desiccator containing silica gel for 18 hours at a temperature not exceeding 25°. The dried material meets the requirements of the test for *Penicillin G and procaine contents* under *Penicillin G Procaine*. [NOTE—Reserve a portion of the dried material for the test for *Crystallinity*.]

Other requirements—It meets the requirements under *Injections* (1).