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Penicillin G Sodium for Injection

DEFINITION

Penicillin G Sodium for Injection is sterile Penicillin G Sodium or a sterile mixture of Penicillin G Sodium and NLT 4.0% and NMT 5.0% of Sodium Citrate, of which NMT 0.15% may be replaced by Citric Acid. It contains NLT 90.0% and NMT 120.0% of the labeled amount of penicillin G. In addition, where it contains Sodium Citrate, it has a potency of NLT 1420 and NMT 1667 Penicillin G Units/mg.

IDENTIFICATION

• **A. Thin-Layer Chromatography**

Solution A: Acetone, 0.1 M citric acid, and 0.1 M sodium citrate (2:1:1)

Standard solution: Prepare a solution containing the equivalent of 12,000 Penicillin G Units/mL from USP Penicillin G Potassium RS in *Solution A*.

Sample solution: Nominally 12,000 Penicillin G Units/mL from Penicillin G Sodium for Injection in *Solution A*

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 20 µL

Developing solvent system: Toluene, dioxane, and glacial acetic acid (90:25:4)

Spray reagent 1: Starch TS

Spray reagent 2: Iodine TS diluted 1 in 10 with water

Analysis

Samples: *Standard solution* and *Sample solution*

Place the plate in a suitable chromatographic chamber. Develop the chromatogram using the *Developing solvent system* until the solvent front has moved three-fourths of the length of the plate. Remove the plate from the chamber, mark the solvent front, and allow to air-dry. Spray the plate with *Spray reagent 1* followed by *Spray reagent 2*. Penicillin G appears as a white spot on a purple background.

Acceptance criteria: The R_F value of the penicillin G spot from the *Sample solution* corresponds to that from the *Standard solution*.

ASSAY

• **Procedure**

Solution A: 0.01 M monobasic potassium phosphate

Mobile phase: Methanol and *Solution A* (40:60)

System suitability solution: 0.1 mg/mL each of USP Penicillin G Potassium RS and 2-phenylacetamide in water

Standard solution: 0.1 mg/mL of USP Penicillin G Potassium RS in water. Shake as needed to dissolve. This solution contains about 160 Penicillin G Units/mL.

Sample solution 1 (where it is represented as being in a single-dose container)**:** Constitute Penicillin G Sodium for Injection as directed in the labeling. Withdraw all of the withdrawable contents, using a hypodermic needle and syringe, and dilute with water to obtain a solution containing nominally 160 Penicillin G Units/mL.

Sample solution 2 (where the label states the quantity of penicillin G in a given volume of constituted solution)**:** Constitute Penicillin G Sodium for Injection as directed in the labeling. Dilute a suitable aliquot of the constituted solution with water to obtain a solution containing nominally 160 Penicillin G Units/mL.

Sample solution 3 (where it contains sodium citrate)**:** Transfer about 50 mg of the Penicillin G Sodium for Injection to a 500-mL volumetric flask, add about 400 mL of water, and shake to dissolve. Dilute with water to volume, and mix.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 10-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for 2-phenylacetamide and penicillin G are about 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between 2-phenylacetamide and penicillin G, *System suitability solution*

Column efficiency: NLT 1000 theoretical plates, *Standard solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution 1*, *Sample solution 2*, or *Sample solution 3*

Perform the *Assay* on 10 containers where it is represented as being in a single-dose container and, if necessary, on 10 containers where the label states the quantity of penicillin G in a given volume of constituted solution. Use the individual results to determine the *Uniformity of Dosage Units* and the average of the results as the *Assay* value.

Calculate the percentage of the labeled amount of penicillin G in the container or in the portion of constituted solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times 100$$

r_U = peak response from *Sample solution 1* or *Sample solution 2*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Penicillin G Potassium RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of *Sample solution 1* or *Sample solution 2* (Penicillin G Units/mL)

P = potency of penicillin G in USP Penicillin G Potassium RS (Penicillin G Units/mg)

Calculate the potency, in Penicillin G Units/mg, in the portion of Penicillin G Sodium for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P$$

r_U = peak response from *Sample solution 3*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Penicillin G Potassium RS in the *Standard solution* (mg/mL)

C_U = concentration of Penicillin G Sodium for Injection in *Sample solution 3* (mg/mL)

P = potency of penicillin G in USP Penicillin G Potassium RS (Penicillin G Units/mg)

Acceptance criteria: 90.0%–120.0% of the labeled amount of penicillin G. Where Penicillin G Sodium for Injection contains sodium citrate, it has a potency of NLT 1420 and NMT 1667 Penicillin G Units/mg.

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements. Perform the *Assay* on 10 containers where it is represented as being in a single-dose container and, if necessary, on 10 containers where the label states the quantity of penicillin G in a given volume of constituted solution. Use the individual results to determine the *Uniformity of Dosage Units* and the average of the results as the *Assay* value.

SPECIFIC TESTS

• **Injections and Implanted Drug Products ⟨1⟩, *Specific Tests, Completeness and clarity of solutions*:** At the time of use, it meets the requirements.

• **Crystallinity ⟨695⟩:** Meets the requirements

• **Sterility Tests ⟨71⟩:** It meets the requirements when tested as directed in *Test for Sterility of the Product to Be Examined, Membrane Filtration*.

• **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 0.01 USP Endotoxin Units/100 Penicillin G Units.

• **pH ⟨791⟩**

Sample solution: A solution containing 60 mg/mL

Acceptance criteria: 5.0–7.5. Where it is labeled as containing sodium citrate, the pH is between 6.0 and 7.5.

• **Loss on Drying ⟨731⟩**

Sample: 100 mg of Penicillin G Sodium for Injection

Analysis: Dry the *Sample* in a capillary-stoppered bottle under vacuum at a pressure NMT 5 mm of mercury at 60° for 3 h.

Acceptance criteria: NMT 1.5%

- **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections
- **Labeling ⟨7⟩, *Labels and Labeling for Injectable Products*:** Meets the requirements

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for constitution*.
- **USP Reference Standards ⟨11⟩**
  USP Penicillin G Potassium RS

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

Topic/Question	Contact	Expert Committee
PENICILLIN G SODIUM FOR INJECTION	Ying Han Associate Science & Standards Liaison	BIO42020 Biologics Monographs 4 - Antibiotics
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	BIO42020 Biologics Monographs 4 - Antibiotics

Chromatographic Database Information: Chromatographic Database

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