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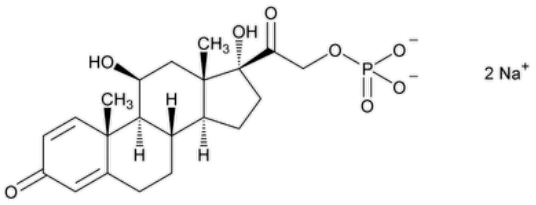
# Prednisolone Sodium Phosphate




$C_{21}H_{27}Na_2O_8P$ 484.39

Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-(phosphonooxy)-, disodium salt, (11β)-;

11β,17,21-Trihydroxypregna-1,4-diene-3,20-dione 21-(disodium phosphate) CAS RN®: 125-02-0; UNII: IV021NXA9J.

## DEFINITION

Prednisolone Sodium Phosphate contains NLT 96.0% and NMT 102.0% of prednisolone sodium phosphate ($C_{21}H_{27}Na_2O_8P$), calculated on the anhydrous basis.

## IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

• **B. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Sodium*** and **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Phosphate***

**Sample:** The residue from the ignition of 20 mg of Prednisolone Sodium Phosphate

**Acceptance criteria:** Meets the requirements

## ASSAY

***Change to read:***

• **Procedure**

**Buffer solution:** Transfer 6.6 g of hexylamine and 5.32 g of monobasic ammonium phosphate into an appropriate flask. After 10 min, add 1850 g of water and dissolve the contents while stirring. Adjust with phosphoric acid to a pH of 6.40 ± 0.05.

**Mobile phase:** To the entire quantity of *Buffer solution* prepared above add 390 g of acetonitrile, mix by stirring, and then sonicate for NMT 2 min.

**System suitability solution:** 0.01 mg/mL each of USP Prednisolone RS and USP Prednisolone Sodium Phosphate RS in *Mobile phase*

**Standard solution:** 0.3 mg/mL of USP Prednisolone RS in *Mobile phase*

**Sample solution:** 0.42 mg/mL of Prednisolone Sodium Phosphate in *Mobile phase*

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 254 nm

**Column:** 4.6-mm × 7.5-cm; 3.5-µm packing L1

**Temperatures**

**▲Autosampler:▲** (USP 1-Aug-2022) 6°

**Column:** 35°

**Flow rate:** 1.5 mL/min

**Injection volume:** 20 µL

**Run time:** ▲NLT 1.6 times the retention time of prednisolone sodium phosphate▲ (USP 1-Aug-2022)

**System suitability**

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

[NOTE—The relative retention times for prednisolone and prednisolone sodium phosphate are about 0.52 and 1, respectively.]

**Suitability requirements**

**Resolution:** NLT 12 between prednisolone and prednisolone sodium phosphate, *System suitability solution*

**Relative standard deviation:** NMT 1.0%, *Standard solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of prednisolone sodium phosphate ($C_{21}H_{27}Na_2O_8P$) in the portion of Prednisolone Sodium Phosphate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

$r_U$ = peak response of prednisolone sodium phosphate from the *Sample solution*

$r_S$ = peak response of prednisolone from the *Standard solution*

$C_S$ = concentration of USP Prednisolone RS in the *Standard solution* (mg/mL)

$C_U$ = concentration of Prednisolone Sodium Phosphate in the *Sample solution* (mg/mL)

$M_{r1}$ = molecular weight of prednisolone sodium phosphate, 484.39

$M_{r2}$ = molecular weight of prednisolone, 360.45

**Acceptance criteria:** 96.0%–102.0% on the anhydrous basis

## IMPURITIES

***Delete the following:***

▲• **SELENIUM** ⟨291⟩

**Sample:** 200 mg of Prednisolone Sodium Phosphate

**Acceptance criteria:** 0.003%▲ (USP 1-Aug-2022)

***Change to read:***

• **PHOSPHATE IONS**

**Solution A:** 50 mg/mL of ammonium molybdate in 1 N sulfuric acid

**Solution B:** 3.5 mg/mL of *p*-methylaminophenol sulfate and 200 mg/mL of sodium bisulfite in water prepared as follows. Dissolve 350 mg of *p*-methylaminophenol sulfate in 50 mL of water, add 20 g of sodium bisulfite, mix and dissolve, then dilute with water to 100 mL.

**Sample solution:** Dissolve 50 mg of Prednisolone Sodium Phosphate in a mixture of 10 mL of water and 5 mL of ▲2 N sulfuric acid TS▲ (USP 1-Aug-2022) contained in a 25-mL volumetric flask, by warming, if necessary. Add 1 mL each of *Solution A* and *Solution B*, dilute with water to volume, and allow to stand at room temperature for 30 min.

**Standard stock solution:** 0.10 mg/mL of phosphate ($PO_4$) prepared as follows. Dissolve 143.3 mg of dried monobasic potassium phosphate ($KH_2PO_4$) in water to make 1000.0 mL.

**Standard solution:** Concomitantly prepare as directed for the *Sample solution*, using 5.0 mL of *Standard stock solution* instead of the 50 mg of Prednisolone Sodium Phosphate.

**Instrumental conditions**

**Mode:** Vis

**Analytical wavelength:** 730 nm

**Cell:** 1 cm

**Blank:** Water

**Analysis:**

Concomitantly determine the absorbances of the *Sample solution* and the *Standard solution*.

**Acceptance criteria:** The absorbance of the *Sample solution* is NMT that of the *Standard solution*; NMT 1.0%

***Change to read:***

• **ORGANIC IMPURITIES**

**Buffer solution, Mobile phase,** and **System suitability solution:** Prepare as directed in the *Assay*.

**Standard solution:** 0.001 mg/mL of USP Prednisolone Sodium Phosphate RS in *Mobile phase*

**Sample solution:** 1 mg/mL of Prednisolone Sodium Phosphate in *Mobile phase*

**Chromatographic system:** Proceed as directed in the *Assay*, except for the *Run time*.

**Run time:** NLT 4 times the retention time of prednisolone sodium phosphate

**System suitability**

**Samples:** *System suitability solution* ▲and *Standard solution*▲ (USP 1-Aug-2022)

[NOTE—See *Table 1* for the relative retention times.]

**Suitability requirements**

**Resolution:** NLT 12 between prednisolone and prednisolone sodium phosphate, *System suitability solution*

▲**Relative standard deviation:** NMT 5.0%, *Standard solution*▲ (USP 1-Aug-2022)

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Prednisolone Sodium Phosphate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

$r_U$ = peak response of each individual impurity from the *Sample solution*

$r_S$ = peak response of prednisolone sodium phosphate from the *Standard solution*

$C_S$ = concentration of USP Prednisolone Sodium Phosphate RS in the *Standard solution* (mg/mL)

$C_U$ = concentration of Prednisolone Sodium Phosphate in the *Sample solution* (mg/mL)

$F$ = relative response factor (see *Table 1*)

**Acceptance criteria:** See *Table 1*.

**Table 1**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Impurity A[a] | 0.18 | 1 | 0.2 |
| Impurity B[b] | 0.29 | 1 | 1.0 |
| D-Homo A derivative[c] | 0.40 | 1 | 1.0 |
| Prednisolone (free)[d] | 0.54 | 1.3 | 1.0 |
| D-Homo B derivative[e] | 0.72 | 1 | 1.0 |
| Prednisone sodium phosphate | 0.77 | 1.0 | 0.5 |
| Impurity C[f] | 0.85 | 1 | 0.3 |
| Impurity D[g] | 0.94 | 1 | 0.2 |
| Prednisolone sodium phosphate | 1.00 | — | — |
| Impurity E[h] | 2.72 | 1 | 0.5 |
| Impurity F[i] | 3.50 | 1 | 0.2 |
| Any individual unspecified impurity | — | 1 | 0.1 |
| Total impurities | — | — | 3.0 |

[a] 11β,17,20-Trihydroxy-21-nor-13(17)a-homopregnane-1,4-diene-3,13a-dione 20-phosphate.

[b] 11β,17α-Dihydroxyandrosta-1,4-diene-3-one 17β-carboxylic acid.

[c] 11β,17β,20-Trihydroxy-21-nor-14(15)a-homopregnane-1,4-diene-3,16-dione 20-phosphate.

[d] 11β,17,21-Trihydroxypregna-1,4-diene-3,20-dione.

[e] 11β,17α,20-Trihydroxy-21-nor-14(15)a-homopregnane-1,4-diene-3,16-dione 20-phosphate.

[f] 21-Oxo-11β,17,21-trihydroxypregna-1,4-diene-3,20-dione.

[g] 11β-Hydroxyandrosta-1,4-diene-3,17-dione.

[h] 16β-Phosphoryloxyacetyl-11β,16α-dihydroxyandrosta-1,4-diene-3-one 11-phosphate.

[i] 21-Oxo-20-phosphoryloxy-11β-hydroxypregna-1,4,17-triene-3-one.

## SPECIFIC TESTS

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

**Sample solution:** 10 mg/mL of Prednisolone Sodium Phosphate in a mixture of pH 7.0 phosphate buffer and carbon dioxide-free water (90:10)

**Acceptance criteria:** +95° to +102°

• **pH** ⟨791⟩

**Sample solution:** 10 mg/mL of Prednisolone Sodium Phosphate in water

**Acceptance criteria:** 7.5–10.5

• **Water Determination** ⟨921⟩, *Method I*: NMT 6.5%

## ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **USP Reference Standards** ⟨11⟩

USP Prednisolone RS

USP Prednisolone Sodium Phosphate RS

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| PREDNISOLONE SODIUM PHOSPHATE | Documentary Standards Support | SM52020 Small Molecules 5 |
| REFERENCE STANDARD SUPPORT | RS Technical Services<br>RSTECH@usp.org | SM52020 Small Molecules 5 |

**Chromatographic Database Information:** Chromatographic Database

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