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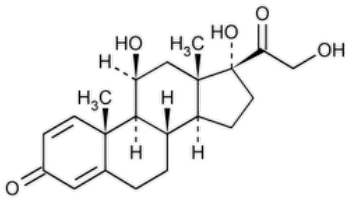
Prednisolone



$C_{21}H_{28}O_5$ (anhydrous) 360.44

Pregna-1,4-diene-3,20-dione, 11,17,21-trihydroxy-, (11β)-.

11β,17,21-Trihydroxypregna-1,4-diene-3,20-dione (anhydrous) CAS RN®: 50-24-8; UNII: 9PHQ9Y1OLM.

Sesquihydrate 387.48 CAS RN®: 52438-85-4; UNII: 4937O9X01I.

» Prednisolone is anhydrous or contains one and one-half molecules of water of hydration. It contains not less than 97.0 percent and not more than 102.0 percent of $C_{21}H_{28}O_5$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

Labeling—Label it to indicate whether it is anhydrous or hydrous.

USP Reference standards ⟨11⟩—

USP Prednisolone RS

Identification—

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

B: *Spectroscopic Identification Tests ⟨197⟩, Ultraviolet-Visible Spectroscopy: 197U*

Solution: 10 µg per mL.

Medium: methanol.

Absorptivities at 242 nm, calculated on the dried basis, do not differ by more than 2.5%. If a difference appears, dissolve portions of both the test specimen and the Reference Standard in ethyl acetate, evaporate the solutions to dryness, and repeat the test on the residues.

Specific rotation ⟨781S⟩**:** between +97° and +103°.

Test solution: 10 mg per mL, in dioxane.

Loss on drying ⟨731⟩—Dry it in vacuum at 105° for 3 hours: anhydrous Prednisolone loses not more than 1.0%, and hydrous Prednisolone not more than 7.0%, of its weight.

Residue on ignition ⟨281⟩**:** negligible, from 100 mg.

Change to read:

▲**Selenium** ⟨291⟩, *Procedures, Procedure 1*▲ (CN 1-Jun-2023) **:** 0.003%, a 200-mg test specimen being used.

Chromatographic purity—

Solution A—Prepare a filtered and degassed mixture of water and acetonitrile (77:23).

Solution B—Prepare a filtered and degassed mixture of water and acetonitrile (60:40).

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system*. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluent: a mixture of water and acetonitrile (1:1).

Standard solution—Dissolve an accurately weighed quantity of USP Prednisolone RS in *Diluent*, and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 0.01 mg per mL.

System suitability solution—Dissolve an accurately weighed quantity of USP Prednisolone RS and hydrocortisone in *Diluent* to obtain a solution having a known concentration of about 1 mg per mL and 0.06 mg per mL, respectively.

Test solution—Transfer about 25 mg of Prednisolone, accurately weighed, to a 25-mL volumetric flask, dissolve in and dilute with *Diluent* to volume, and mix.

Chromatographic system (see Chromatography ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 30-cm column that contains 5-µm packing L1. The flow rate is about 1.5 mL per minute. The column temperature is maintained at 40°. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0	100	0	equilibration
0–25	100	0	isocratic
25–45	100→0	0→100	linear gradient
45–60	0	100	isocratic
60–61	0→100	100→0	linear gradient
61–100	100	0	re-equilibration

Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the relative retention times for prednisolone and hydrocortisone are about 1.0 and 1.06, respectively; and the height of the smallest peak is not less than 2 times the height of the valley between the prednisolone and hydrocortisone peaks. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 5.0% for the prednisolone peak.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of each impurity in the portion of Prednisolone taken by the formula:

$$2500(C/W)(r_i/r_S)$$

in which C is the concentration, in mg per mL, of USP Prednisolone RS in the *Standard solution; W* is the weight, in mg, of prednisolone used to prepare the *Test solution;* r_i is the peak response for each impurity in the *Test solution;* and r_S is the peak response obtained from the *Standard solution:* no impurity greater than 1.0% and only one peak greater than 0.5% is found; and not more than 2.0% of total impurities is found.

Assay—

Mobile phase—Prepare a solution containing a mixture of butyl chloride, water-saturated butyl chloride, tetrahydrofuran, methanol, and glacial acetic acid (95:95:14:7:6). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Prepare a solution of betamethasone in tetrahydrofuran containing 5 mg per mL. Dilute this solution with water-saturated chloroform, and mix to obtain a solution having a final concentration of 0.5 mg per mL.

Standard preparation—Transfer about 10 mg of USP Prednisolone RS, accurately weighed, to a 100-mL volumetric flask, and dissolve in 5.0 mL of methanol. Add 20.0 mL of *Internal standard solution*, and mix. Dilute with water-saturated chloroform to 100.0 mL, and mix.

Assay preparation—Transfer about 10 mg of Prednisolone, accurately weighed, to a 100-mL volumetric flask, and dissolve in 5.0 mL of methanol. Add 20.0 mL of *Internal standard solution*, and mix. Dilute with water-saturated chloroform to 100.0 mL, and mix.

Chromatographic system (see Chromatography ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4-mm × 30-cm column that contains packing L3. The flow rate is about 1 mL per minute. Chromatograph four replicate injections of the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.7 for betamethasone and 1.0 for prednisolone; the resolution, *R,* between prednisolone and betamethasone is not less than 3.5; and the relative standard deviation for replicate injections is not more than 2.0%.

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 quantity, in mg, of $C_{21}H_{28}O_5$ in the portion of Prednisolone taken by the formula:

$$0.1C(R_U/R_S)$$

in which C is the concentration, in µg per mL, of USP Prednisolone RS in the *Standard preparation;* and R_U and R_S are the peak response ratios of prednisolone to the internal standard 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
PREDNISOLONE	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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