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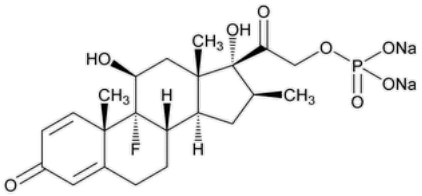
Betamethasone Sodium Phosphate



$C_{22}H_{28}FNa_2O_8P$ 516.40

Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-(phosphonooxy)-, disodium salt, (11β,16β)-;

9-Fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 21-(disodium phosphate) CAS RN®: 151-73-5; UNII: 7BK02SCL3W.

DEFINITION

Betamethasone Sodium Phosphate contains NLT 97.0% and NMT 103.0% of betamethasone sodium phosphate ($C_{22}H_{28}FNa_2O_8P$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**▲ (CN 1-May-2020)
- **B.** **Thin-Layer Chromatographic Identification Test ⟨201⟩**

Standard solution: 1 mg/mL of USP Betamethasone Sodium Phosphate RS in methanol

Sample solution: 1 mg/mL of Betamethasone Sodium Phosphate in methanol

Chromatographic system

Application volume: 10 µL

Developing solvent system: 500 mL of butyl alcohol and 200 mL of dilute hydrochloric acid (1 in 12). Place in a separatory funnel, and mix. Use the organic layer as the developing solvent.

Spray reagent: Sulfuric acid, methanol, and nitric acid (10:10:1)

Analysis

Samples: *Standard solution* and *Sample solution*

Proceed as directed in the chapter, except to spray the plate with *Spray reagent*, and heat at 105° for 10 min.

Acceptance criteria: Meets the requirements

- **C.** **Identification Tests—General, *Sodium* ⟨191⟩** and ***Phosphate* ⟨191⟩**

Analysis: Ignite it at 800° (see *Residue on Ignition* ⟨281⟩).

Acceptance criteria: The residue meets the requirements for sodium and phosphate.

ASSAY

- **Procedure**

Mobile phase: Methanol and 0.07 M anhydrous monobasic potassium phosphate (3:2)

Diluent: Methanol and water (3:2)

Standard solution: 0.17 mg/mL of USP Betamethasone Sodium Phosphate RS in *Diluent*

Sample solution: 0.17 mg/mL of Betamethasone Sodium Phosphate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of betamethasone sodium phosphate ($C_{22}H_{28}FNa_2O_8P$) in the portion of Betamethasone Sodium Phosphate taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 97.0%–103.0% on the anhydrous basis

IMPURITIES

• **Limit of Phosphate Ions**

Standard phosphate solution and **Phosphate reagent A:** Prepare as directed in *Phosphate in Reagents* (see *Reagents, Indicators, and Solutions—General Tests for Reagents*).

Phosphate reagent B: Dissolve 350 mg of *p*-methylaminophenol sulfate in 50 mL of water. Add 20 g of sodium metabisulfite, mix to dissolve, and dilute with water to 100 mL.

Standard solution: Dilute 5.0 mL of *Standard phosphate solution* in a mixture of 10 mL of water and 5 mL of 2 N sulfuric acid contained in a 25-mL volumetric flask, by warming if necessary. Add 1 mL each of *Phosphate reagent A* and *Phosphate reagent B*, dilute with water to 25.0 mL, mix, and allow to stand at room temperature for 30 min.

Sample solution: Dissolve 50 mg of Betamethasone Sodium Phosphate in a mixture of 10 mL of water and 5 mL of 2 N sulfuric acid contained in a 25-mL volumetric flask, by warming if necessary. Add 1 mL each of *Phosphate reagent A* and *Phosphate reagent B*, dilute with water to 25.0 mL, mix, and allow to stand at room temperature for 30 min.

Instrumental conditions

Mode: Vis

Analytical wavelength: Maximum absorbance at about 730 nm

Cell: 1 cm

Blank: Water

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: The absorbance of the *Sample solution* is NMT that of the *Standard solution*. The limit is 1.0% of phosphate (PO_4).

• **Limit of Free Betamethasone**

Sample stock solution: 1.0 mg/mL of Betamethasone Sodium Phosphate in water, prepared as follows. Dissolve 25.0 mg of Betamethasone Sodium Phosphate in water to make 25.0 mL.

Sample solution: Transfer 5.0 mL of the *Sample stock solution* to a separator, and extract with three 25-mL portions of chloroform. Filter each extract through a chloroform-saturated cotton pledget, combining the filtrates in a conical flask. Evaporate the chloroform on a steam bath to dryness with the aid of a current of air, and dissolve the residue in methanol to make 25.0 mL.

Blank solution: Transfer 5.0 mL of water to a separator. Proceed as directed in *Sample solution*, beginning with “extract with three 25-mL portions of chloroform”.

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at about 239 nm

Cell: 1 cm

Blank: *Blank solution*

Analysis

Sample: *Sample solution*

Calculate the quantity, in mg, of free betamethasone in the portion of Betamethasone Sodium Phosphate taken:

$$\text{Result} = A \times 3.125$$

A = absorbance of the *Sample solution*

Acceptance criteria: NMT 0.25 mg (1.0%)

SPECIFIC TESTS

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

Sample solution: 10 mg/mL

Acceptance criteria: +99° to +105°

- **Water Determination, *Method I*⟨921⟩:** NMT 10.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.
- **USP Reference Standards ⟨11⟩**
  USP Betamethasone Sodium Phosphate RS

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

Topic/Question	Contact	Expert Committee
BETAMETHASONE SODIUM PHOSPHATE	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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