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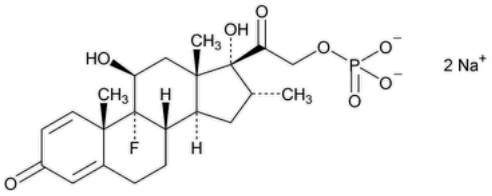
Dexamethasone Sodium Phosphate



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

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

9-Fluoro-11β,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione 21-(dihydrogen phosphate) disodium salt CAS RN®: 2392-39-4; UNII: AI9376Y64P.

DEFINITION

Dexamethasone Sodium Phosphate contains NLT 97.0% and NMT 102.0% of dexamethasone sodium phosphate ($C_{22}H_{28}FNa_2O_8P$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020) **:** If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the Reference Standard separately in a minimum of alcohol, evaporate on a water bath to dryness, and repeat the test on the residues.

• **B.** **Identification Tests—General, *Phosphate*⟨191⟩:** The residue from its ignition meets the requirements.

• **C.** **Identification Tests—General, *Sodium*⟨191⟩:** The residue from its ignition meets the requirements.

ASSAY

• **Procedure**

Mobile phase: Mix 520 mL of water with 2 mL of phosphoric acid. Bring the temperature to 20°, and adjust with sodium hydroxide to a pH of 2.6. Mix this solution with 36 mL of tetrahydrofuran and 364 mL of methanol.

System suitability stock solution: 0.02 mg/mL each of USP Dexamethasone Sodium Phosphate RS and USP Dexamethasone RS, prepared as follows. Dissolve 2 mg of each compound in 2 mL of tetrahydrofuran, and dilute with *Mobile phase* to 100 mL.

System suitability solution: 2 µg/mL each of USP Dexamethasone Sodium Phosphate RS and USP Dexamethasone RS in *Mobile phase* from the *System suitability stock solution*

Standard solution: 0.06 mg/mL of USP Dexamethasone Sodium Phosphate RS in *Mobile phase*

Sample solution: 0.06 mg/mL of Dexamethasone Sodium Phosphate in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 7-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: 3 times the retention time of the dexamethasone sodium phosphate peak

System suitability

[Note—The relative retention times of the dexamethasone sodium phosphate and dexamethasone peaks are 1.0 and 2.0, respectively.]

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

Suitability requirements

Resolution: NLT 6.0 between dexamethasone sodium phosphate and dexamethasone peaks, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dexamethasone sodium phosphate ($C_{22}H_{28}FNa_2O_8P$) in the portion of Dexamethasone 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 Dexamethasone Sodium Phosphate RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 97.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

• **Limit of Phosphate Ions**

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

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

Standard stock solution: 0.14 mg/mL of dried monobasic potassium phosphate in water. This solution contains the equivalent of 0.10 mg/mL of phosphate (PO_4) ion.

Standard solution: In a 25-mL volumetric flask, mix 5.0 mL of *Standard stock solution*, 10 mL of water, and 5 mL of 2 N sulfuric acid. 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. Prepare concomitantly with the *Sample solution*.

Sample solution: In a 25-mL volumetric flask, dissolve 50 mg of Dexamethasone Sodium Phosphate in a mixture of 10 mL of water and 5 mL of 2 N sulfuric acid, 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.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: Visible

Analytical wavelength: 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 Alcohol**

Internal standard solution: 0.4 mg/mL of acetonitrile, prepared as follows. Dilute 5.0 mL of USP Alcohol Determination–Acetonitrile RS with water to 200.0 mL.

Standard stock solution: 0.20 mg/mL of alcohol, prepared as follows. Dilute 25.0 mL of USP Alcohol Determination–Alcohol RS with water to 2000.0 mL.

Standard solution: 0.08 mg/mL of alcohol, prepared as follows. Dilute 10.0 mL of the *Standard stock solution* and 5.0 mL of the *Internal standard solution* with water to 25.0 mL.

Sample solution: 5.0 mg/mL of Dexamethasone Sodium Phosphate, prepared as follows. Transfer 125 mg of Dexamethasone Sodium Phosphate to a 25-mL volumetric flask, add 5.0 mL of the *Internal standard solution*, and dilute with water to volume.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 30-m capillary coated with 3-µm film of G43

Carrier gas: Hydrogen

Linear velocity: 36 cm/s

Split ratio: 2:1

Temperatures

Injection port: 210°

Detector: 280°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	—	50	5
50	50	200	4

Injection volume: 0.4 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between alcohol and acetonitrile

Relative standard deviation: NMT 3.0% for alcohol

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of alcohol in the portion of Dexamethasone Sodium Phosphate taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of the alcohol to the internal standard from the *Sample solution*

R_S = peak response ratio of the alcohol to the internal standard from the *Standard solution*

C_S = concentration of alcohol in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 1.5%

- **Organic Impurities**

Buffer: 7.0 g/L of ammonium acetate in water

Solution A: Mix 300 mL of *Buffer* and 350 mL of water, adjust with 5 M acetic acid to a pH of 3.8, and then add 350 mL of methanol.

Solution B: Adjust 300 mL of *Buffer* with 5 M acetic acid to a pH of 4.0, and then add 700 mL of methanol.

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	90	10
3.5	90	10
23.5	60	40
34.5	5	95
50	5	95

System suitability solution: 0.02 mg/mL each of USP Dexamethasone Sodium Phosphate RS and USP Betamethasone Sodium Phosphate RS in *Solution A*

Standard solution: 1 µg/mL of USP Dexamethasone Sodium Phosphate RS in *Solution A*

Sample solution: 1 mg/mL of Dexamethasone Sodium Phosphate in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 12.5-cm; 5-µm packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between dexamethasone sodium phosphate and betamethasone sodium phosphate peaks, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Dexamethasone 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 impurity from the *Sample solution*

r_S = peak response of dexamethasone phosphate from the *Standard solution*

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

C_U = concentration of Dexamethasone Sodium Phosphate in the *Sample solution* (µg/mL)

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*. Disregard any peak below 0.05%.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
16(17)a-Homodexamethasone sodium phosphate[a]	0.5	1.0	0.2
16(17)a-Homobetamethasone sodium phosphate[b]	0.6	1.0	0.2
16(17)a-17*R*-Homodexamethasone sodium phosphate[c]	0.8	1.0	0.2
13(17)a-Homodexamethasone sodium phosphate[d]	0.92	1.0	0.2
Betamethasone sodium phosphate	0.95	1.0	0.2
Dexamethasone sodium phosphate	1.00	—	—
Dexamethasone ethyl ester[e]	1.20	1.0	0.3
Dexamethasone	1.37	1.2	0.5
Fluoroandrostadiene carboxylic acid[f]	1.41	1.0	0.3
Dexamethasone sodium phosphate diester[g]	2.10	1.0	0.1
Any other individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] 9-Fluoro-11β,17,21-trihydroxy-16α-methyl-16(17)a-homopregna-1,4-diene-3,16a,20-trione 21-(dihydrogen phosphate) disodium salt.

[b] 9-Fluoro-11β,17,21-trihydroxy-16β-methyl-16(17)a-homopregna-1,4-diene-3,16a,20-trione 21-(dihydrogen phosphate) disodium salt.

[c] 9-Fluoro-11β,17a,21-trihydroxy-16β-methyl-16(17)a-homopregna-1,4-diene-3,16a,20-trione 21-(dihydrogen phosphate) disodium salt.

[d] 9-Fluoro-11β,17,21-trihydroxy-16α-methyl-13(17)a-homopregna-1,4-diene-3,13a,20-trione 21-(dihydrogen phosphate) disodium salt.

[e] Ethyl 11β,17α-dihydroxy-9-fluoro-16α-methylandrostane-1,4-diene-3-one-17-ylcarboxylate.

[f] 9-Fluoro-11β,17α-dihydroxy-16α-methylandrosta-1,4-diene-3-one-17β-carboxylic acid.

[g] Sodium bis[9-fluoro-11β,17-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione 21-yl]phosphate.

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation*⟨781S⟩
  Sample solution: 10 mg/mL in water
  Acceptance criteria: +74° to +82°, calculated on the anhydrous and solvent-free basis
- **pH** ⟨791⟩
  Sample solution: 10 mg/mL
  Acceptance criteria: 7.5–10.5
- **Water Determination,** *Method I*⟨921⟩
  Acceptance criteria: NMT 10.0%

ADDITIONAL REQUIREMENTS

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

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

Topic/Question	Contact	Expert Committee
DEXAMETHASONE SODIUM PHOSPHATE	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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