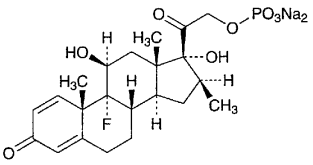
of 0.5 mL of 0.01 mol/L sodium hydroxide TS and 20 mL of water as the absorbing liquid.

Containers and storage Containers—Tight containers. Storage—Light-resistant.

Betamethasone Sodium Phosphate

リン酸ベタメタゾンナトリウム



$C_{22}H_{28}FNa_2O_8P$: 516.40
Disodium 9-fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 21-phosphate
[*151-73-5*]

Betamethasone Sodium Phosphate contains not less than 97.0% and not more than 103.0% of $C_{22}H_{28}FNa_2O_8P$, calculated on the anhydrous basis.

Description Betamethasone Sodium Phosphate occurs as white to pale yellowish white, crystalline powder or masses. It is odorless.

It is freely soluble in water, sparingly soluble in methanol, slightly soluble in ethanol (95), and practically insoluble in diethyl ether.

It is hygroscopic.

Melting point: about 213°C (with decomposition).

Identification **(1)** Dissolve 2 mg of Betamethasone Sodium Phosphate in 2 mL of sulfuric acid: a brown color develops, and gradually changes to blackish brown.

(2) Prepare the test solution with 0.01 g of Betamethasone Sodium Phosphate as directed under the Oxygen Flask Combustion Method, using a mixture of 0.5 mL of 0.01 mol/L sodium hydroxide TS and 20 mL of water as an absorbing liquid: the test solution responds to the Qualitative Tests (2) for fluoride.

(3) Take 0.04 g of Betamethasone Sodium Phosphate in a platinum crucible, and carbonize by heating. After cooling, add 5 drops of nitric acid, and incinerate by heating. To the residue add 10 mL of diluted nitric acid (1 in 50), and boil for several minutes. After cooling, neutralize the solution with ammonia TS, filter if necessary, and use this solution as the sample solution. The sample solution responds to the Qualitative Tests for sodium salt and for phosphate.

(4) Determine the infrared absorption spectrum of Betamethasone Sodium Phosphate, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of previously dried Betamethasone Sodium Phosphate Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

Optical rotation $[\alpha]_D^{20}$: +99 – +105° (0.1 g, calculated on the anhydrous basis, water, 10 mL, 100 mm).

pH Dissolve 0.10 g of Betamethasone Sodium Phosphate in 20 mL of water: the pH of this solution is between 7.5 and 9.0.

Purity **(1)** Clarity and color of solution—Dissolve 0.25 g of Betamethasone Sodium Phosphate in 10 mL of water: the solution is clear and colorless.

(2) Free phosphoric acid—Weigh accurately about 0.02 g of Betamethasone Sodium Phosphate, dissolve in 20 mL of water, and use this solution as the sample solution. Separately, pipet 4 mL of Standard Phosphoric Acid Solution, add 20 mL of water, and use this solution as the standard solution. To each of the sample solution and the standard solution add exactly 7 mL of dilute sulfuric acid, exactly 2 mL of hexaammonium heptamolybdate-sulfuric acid TS and exactly 2 mL of *p*-methylaminophenol sulfate TS, shake well, and allow to stand at 20 ± 1°C for 15 minutes. To each add water to make exactly 50 mL, and allow to stand at 20 ± 1°C for 15 minutes. Perform the test with these solutions as directed under the Ultraviolet-visible Spectrophotometry, using a solution prepared with 20 mL of water in the same manner as the blank. Determine the absorbances, A_T and A_S, of each solution from the sample solution and the standard solution at 730 nm: the amount of free phosphoric acid is not more than 0.5%.

$$\text{Amount (\%) of free phosphoric acid } (H_3PO_4) = \frac{A_T}{A_S} \times \frac{1}{W} \times 10.32$$

W: Amount (mg) of Betamethasone Sodium Phosphate, calculated on the anhydrous basis.

(3) Betamethasone—Dissolve 0.020 g of Betamethasone Sodium Phosphate in exactly 2 mL of methanol, and use this solution as the sample solution. Separately, dissolve 0.020 g of Betamethasone Reference Standard in exactly 10 mL of methanol. Pipet 1 mL of this solution, add methanol to make exactly 20 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μL each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a freshly prepared mixture of 1-butanol, water and acetic anhydride (3:1:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spot from the sample solution corresponding to the spot from the standard solution is not more intense than the spot from the standard solution.

Water Not more than 10.0% (0.2 g, back titration).

Assay Weigh accurately about 0.02 g each of Betamethasone Sodium Phosphate and Betamethasone Sodium Phosphate Reference Standard (determine its water content before using in the same manner as Betamethasone Sodium Phosphate), and dissolve each in methanol to make exactly 20 mL. Pipet 5 mL each of these solutions, add exactly 5 mL of the internal standard solution, then add methanol to make 50 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of betamethasone phosphate to that of the internal standard, respectively.

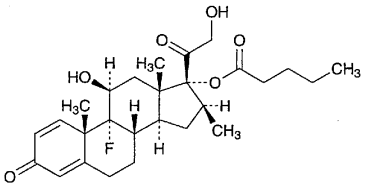
Amount (mg) of $C_{22}H_{28}FNa_2O_8P$
= amount (mg) of Betamethasone Sodium Phosphate Reference Standard, calculated on the anhydrous basis
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of butyl parahydroxybenzoate in methanol (1 in 5000).
Operating conditions—
Detector: An ultraviolet absorption photometer (wavelength: 254 nm).
Column: A stainless steel column about 4 mm in inside diameter and about 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (7 μm in particle diameter).
Column temperature: A constant temperature of about 25°C.
Mobile phase: Dissolve 1.6 g of tetra-*n*-butylammonium bromide, 3.2 g of disodium hydrogenphosphate 12-water and 6.9 g of potassium dihydrogenphosphate in 1000 mL of water, and add 1500 mL of methanol.
Flow rate: Adjust the flow rate so that the retention time of betamethasone phosphate is about 5 minutes.
Selection of column: Proceed with 10 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of betamethasone phosphate and the internal standard in this order with the resolution between these peaks being not less than 10.

Containers and storage Containers—Tight containers.

Betamethasone Valerate

吉草酸ベタメタゾン



$C_{27}H_{37}FO_6$: 476.58
9-Fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17-valerate [*2152-44-5*]

Betamethasone Valerate, when dried, contains not less than 97.0% and not more than 103.0% of $C_{27}H_{37}FO_6$.

Description Betamethasone Valerate occurs as a white, crystalline powder. It is odorless.
It is freely soluble in chloroform, soluble in ethanol (95), sparingly soluble in methanol, slightly soluble in diethyl ether, and practically insoluble in water.
Melting point: about 190°C (with decomposition).

Identification **(1)** Proceed with 0.01 g of Betamethasone Valerate as directed under the Oxygen Flask Combustion Method, using a mixture of 0.5 mL of 0.01 mol/L sodium hydroxide TS and 20 mL of water as the absorbing liquid, and prepare the test solution: the test solution so obtained responds to the Qualitative Tests for fluoride.
(2) Determine the infrared absorption spectrum of Betamethasone Valerate, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of dried Betamethasone Valerate Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

Optical rotation $[\alpha]_D^{20}$: +77 – +83° (after drying, 0.10 g, methanol, 20 mL, 100 mm).

Purity Other steroids—Conduct this procedure without exposure to daylight. Dissolve 0.02 g of Betamethasone Valerate in 5 mL of a mixture of chloroform and methanol (9:1), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a mixture of chloroform and methanol (9:1) to make exactly 50 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μL each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of chloroform and methanol (9:1) to a distance of about 12 cm, and air-dry the plate. Spray evenly alkaline blue tetrazolium TS on the plate: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Loss on drying Not more than 0.5% (1 g, 105°C, 3 hours).

Residue on ignition Not more than 0.2% (0.5 g, platinum crucible).

Assay Dissolve about 0.01 g each of Betamethasone Valerate and Betamethasone Valerate Reference Standard, previously dried and accurately weighed, in methanol to make exactly 100 mL. Pipet 10 mL each of these solutions, add 10 mL each of the internal standard solution, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following operating conditions, and calculate the ratios, Q_T and Q_S, of the peak area of betamethasone valerate to that of the internal standard, respectively.

Amount (mg) of $C_{27}H_{37}FO_6$
= amount (mg) of Betamethasone Valerate Reference Standard
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of isoamyl benzoate in methanol (1 in 1000).
Operating conditions—
Detector: An ultraviolet absorption photometer (wavelength: 254 nm).
Column: A stainless steel column about 4 mm in inside diameter and 20 to 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (7 μm in particle diameter).
Column temperature: A constant temperature of about 25°C.
Mobile phase: A mixture of methanol and water (7:3).
Flow rate: Adjust the flow rate so that the retention time of betamethasone valerate is about 10 minutes.