

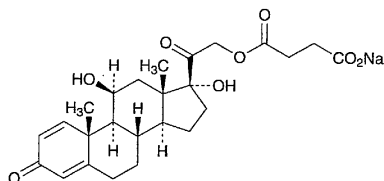
previously dried, and dissolve each in methanol to make exactly 100 mL. Pipet 5 mL each of these solutions, add methanol to make exactly 50 mL, and use these solutions as the sample solution and the standard solution. Determine the absorbances, A_T and A_S , of the sample solution and the standard solution at 242 nm as directed under the Ultraviolet-visible Spectrophotometry.

$$\begin{aligned} & \text{Amount (mg) of } C_{25}H_{32}O_8 \\ &= \text{amount (mg) of Prednisolone Succinate Reference Standard} \\ & \times \frac{A_T}{A_S} \end{aligned}$$

Containers and storage Containers—Tight containers.

Prednisolone Sodium Succinate for Injection

注射用コハク酸プレドニゾロンナトリウム



$C_{25}H_{31}NaO_8$: 482.50
Monosodium 11 β ,17,21-trihydroxypregna-1,4-diene-3,20-dione 21-succinate [1715-33-9]

Prednisolone Sodium Succinate for Injection is a preparation for injection which is dissolved before used. It contains not less than 72.4% and not more than 83.2% of prednisolone sodium succinate ($C_{25}H_{31}NaO_8$: 482.50), and the equivalent of not less than 90% and not more than 110% of the labeled amount of prednisolone ($C_{21}H_{28}O_5$: 360.44).

The amount should be stated as the amount of prednisolone ($C_{21}H_{28}O_5$).

Method of preparation Prepare as directed under Injections, with Prednisolone Succinate and Dried Sodium Carbonate or Sodium Hydroxide.

It contains a suitable buffer agent.

Description Prednisolone Sodium Succinate for Injection occurs as a white powder or porous, friable mass.

It is freely soluble in water.

It is hygroscopic.

Identification (1) To 2 mg of Prednisolone Sodium Succinate for Injection add 2 mL of sulfuric acid, and allow to stand for 2 to 3 minutes: a deep red color, without fluorescence, develops. To this solution add 10 mL of water cautiously: the color disappears and a gray, flocculent precipitate is formed.

(2) Dissolve 0.01 g of Prednisolone Sodium Succinate for Injection in 1 mL of methanol, add 1 mL of Fehling's TS, and heat: an orange to red precipitate is formed.

(3) Dissolve 0.1 g of Prednisolone Sodium Succinate for

Injection in 2 mL of sodium hydroxide TS, allow to stand for 10 minutes, and filter. Add 1 mL of dilute hydrochloric acid to the filtrate, shake, and filter if necessary. Adjust the solution with diluted ammonia TS (1 in 10) to a pH of about 6, and add 2 to 3 drops of iron (III) chloride TS: a brown precipitate is formed.

(4) Prednisolone Sodium Succinate for Injection responds to the Qualitative Tests (1) for sodium salt.

pH Dissolve 1.0 g of Prednisolone Sodium Succinate for Injection in 40 mL of water: the pH of the solution is between 6.5 and 7.2.

Purity Clarity and color of solution—Dissolve 0.25 g of Prednisolone Sodium Succinate for Injection in 10 mL of water: the solution is clear and colorless.

Loss on drying Not more than 2.0% (0.15 g, in vacuum, phosphorus (V) oxide, 60°C, 3 hours).

Assay Take a quantity of sealed containers of Prednisolone Sodium Succinate for Injection, equivalent to about 0.10 g of prednisolone ($C_{21}H_{28}O_5$), and dissolve the contents in a suitable amount of diluted methanol (1 in 2), and transfer to a 100-mL volumetric flask. Wash each container with diluted methanol (1 in 2), collect the washings in the volumetric flask, and add diluted methanol (1 in 2) to make volume. Pipet 4 mL of this solution, add diluted methanol (1 in 2) to make exactly 50 mL. Pipet 5 mL of this solution, add exactly 5 mL of the internal standard solution, mix, and use this solution as the sample solution. Separately, weigh accurately about 0.025 g of Prednisolone Succinate Reference Standard, previously dried in a desiccator for 6 hours (in vacuum, phosphorus (V) oxide, 60°C), dissolve in methanol to make exactly 25 mL. Pipet 5 mL of this solution, add diluted methanol (1 in 2) to make exactly 50 mL. Pipet 5 mL of this solution, add exactly 5 mL of the internal standard solution, mix, and use this solution as the standard solution. Perform the test with 10 μ L 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 prednisolone succinate to that of the internal standard.

$$\begin{aligned} & \text{Amount (mg) of prednisolone sodium succinate} \\ & (C_{25}H_{31}NaO_8) \\ &= \text{amount (mg) of Prednisolone Succinate} \\ & \text{Reference Standard} \\ & \times \frac{Q_T}{Q_S} \times 5 \times 1.0477 \end{aligned}$$

$$\begin{aligned} & \text{Amount (mg) of prednisolone } (C_{21}H_{28}O_5) \\ &= \text{amount (mg) of prednisolone sodium succinate} \\ & (C_{25}H_{31}NaO_8) \times 0.7470 \end{aligned}$$

Internal standard solution—A solution of propyl parahydroxybenzoate in diluted methanol (1 in 2) (1 in 25,000).

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 (5 μ m in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: Dissolve 0.32 g of tetra *n*-butylammonium bromide, 3.22 g of disodium hydrogenphosphate 12-water and 6.94 g of potassium dihydrogenphosphate in 1000 mL of water. To 840 mL of this solution add 1160 mL of methanol.

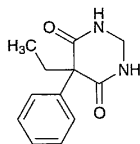
Flow rate: Adjust the flow rate so that the retention time of prednisolone succinate is about 15 minutes.

Selection of column: Proceed with 10 μ L of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of prednisolone succinate and the internal standard in this order with the resolution between these peaks being not less than 6.

Containers and storage Containers—Hermetic containers.

Primidone

プリミドン



$C_{12}H_{14}N_2O_2$: 218.25
5-Ethyl-2-phenyl-1,2,4-dihydro-1,4-diazepine-3,6-dione
[125-33-7]

Primidone, when dried, contains not less than 98.5% of $C_{12}H_{14}N_2O_2$.

Description Primidone occurs as a white, crystalline powder or granules. It is odorless and has a slightly bitter taste.

It is soluble in *N,N*-dimethylformamide, sparingly soluble in pyridine, slightly soluble in ethanol (95), very slightly soluble in water, and practically insoluble in diethyl ether.

Identification (1) Heat 0.5 g of Primidone with 5 mL of diluted sulfuric acid (1 in 2): the odor of formaldehyde is perceptible.

(2) Mix 0.2 g of Primidone with 0.2 g of anhydrous sodium carbonate, and heat: the gas evolved changes moistened red litmus paper to blue.

Melting point 279 – 284°C

Purity (1) Clarity and color of solution—Dissolve 0.10 g of Primidone in 10 mL of *N,N*-dimethylformamide: the solution is clear and colorless.

(2) Heavy metals—Proceed with 2.0 g of Primidone according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(3) 2-Ethyl-2-phenylmalonediamide—Dissolve 0.10 g of Primidone in 2 mL of pyridine, add exactly 2 mL of the internal standard solution, then add 1 mL of bis-trimethyl silyl acetamide, shake well, and heat at 100°C for 5 minutes. Cool, add pyridine to make 10 mL, and use this solution as the sample solution. Separately, dissolve 0.050 g of 2-ethyl-2-phenylmalonediamide in pyridine to make exactly 100 mL. Pipet 2 mL of this solution, add exactly 2 mL of the internal standard solution, proceed in the same manner as

Primidone, and use this solution as the standard solution. Perform the test with 2 μ L of the sample solution and the standard solution as directed under the Gas Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S , of the peak area of 2-ethyl-2-phenylmalonediamide to that of the internal standard: Q_T is not more than Q_S .

Internal standard solution—A solution of stearylalcohol in pyridine (1 in 2000).

Operating conditions—

Detector: A hydrogen flame-ionization detector.

Column: A glass column about 3 mm in inside diameter and about 1.5 m in length, packed with siliceous earth for gas chromatography (125 to 150 μ m in particle diameter) coated with 50% phenyl-methyl silicon polymer for gas chromatography at the ratio of 3%.

Column temperature: A constant temperature of about 195°C.

Carrier gas: Nitrogen

Flow rate: Adjust the flow rate so that the retention time of stearylalcohol is 8 to 9 minutes.

Selection of column: Proceed with 2 μ L of the standard solution under the above operating condition, and calculate the resolution. Use a column giving elution of 2-ethyl-2-phenylmalonediamide and the internal standard in this order with the resolution between these peaks being not less than 3.

Loss on drying Not more than 0.5% (1 g, 105°C, 2 hours).

Residue on ignition Not more than 0.20% (1 g).

Assay Weigh accurately about 0.02 g each of Primidone and Primidone Reference Standard, previously dried, dissolve each in 20 mL of ethanol (95) by warming, and after cooling, add ethanol (95) to make exactly 25 mL, and use these solutions as the sample solution and the standard solution, respectively. Determine the absorbance, A_1 , of the sample solution and the standard solution at the wavelength of maximum absorption at about 257 nm, and the absorbances, A_2 and A_3 , at the wavelength of minimum absorption at about 254 nm and at about 261 nm, as directed under the Ultraviolet-visible Spectrophotometry, using ethanol (95) as the blank.

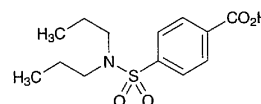
$$\begin{aligned} & \text{Amount (mg) of } C_{12}H_{14}N_2O_2 \\ &= \text{amount (mg) of Primidone Reference Standard} \\ & \times \frac{(2A_1 - A_2 - A_3)_T}{(2A_1 - A_2 - A_3)_S} \end{aligned}$$

where, $(2A_1 - A_2 - A_3)_T$ is the value from the sample solution, and $(2A_1 - A_2 - A_3)_S$ is from the standard solution.

Containers and storage Containers—Tight containers.

Probenecid

プロベネシド



$C_{13}H_{19}NO_4S$: 285.36