**Loss on drying** Not more than 0.20% (1 g, 105°C, 2 hours).

**Residue on ignition** Not more than 0.10% (1 g).

**Assay** Weigh accurately about 0.4 g of Prazepam, previously dried, dissolve in 60 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 32.481 mg of $C_{19}H_{17}ClN_2O$

**Containers and storage** Containers—Tight containers.

# Prazepam Tablets

プラゼパム錠

Prazepam Tablets contain not less than 93% and not more than 107% of the labeled amount of prazepam ($C_{19}H_{17}ClN_2O$: 324.80).

**Method of preparation** Prepare as directed under the Tablets, with Prazepam.

**Identification** (1) To a quantity of powdered Prazepam Tablets, equivalent to 0.05 g of Prazepam according to the labeled amount, add 25 mL of acetone, shake well, and filter. Take 5 mL of the filtrate, evaporate on a water bath to dryness, and dissolve the residue in 3 mL of sulfuric acid. With this solution, proceed as directed in the Identification (1) under Prazepam.

(2) To a quantity of powdered Prazepam Tablets, equivalent to 0.02 g of Prazepam according to the labeled amount, add 200 mL of a solution of sulfuric acid in ethanol (99.5) (3 in 1000), shake well, and filter. To 5 mL of the filtrate add a solution of sulfuric acid in ethanol (99.5) (3 in 1000) to make 50 mL, and determine the absorption spectrum as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 241 nm and 245 nm, between 283 nm and 287 nm and between 363 nm and 367 nm, and minima between 263 nm and 267 nm and between 334 nm and 338 nm.

**Dissolution test** Proceed with 1 tablet of Prazepam Tablets according to Method (1) in the Dissolution Test, and perform the test, using 900 mL of 0.1 mol/L hydrochloric acid TS as the test solution at 100 rotations per minute. 30 minutes after starting the test, separate 20 mL or more of the dissolved solution, and filter with a membrane filter with pore size not more than 0.8 $\mu$m. Discard the first 10 mL of the filtrate, measure exactly the subsequent $V$ mL of the filtrate, add 0.1 mol/L hydrochloric acid TS to make exactly $V'$ mL so that each mL of this solution might contain about 5 $\mu$g of prazepam ($C_{19}H_{17}ClN_2O$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 5 mg of prazepam for assay, previously dried at 105°C for 2 hours, add 200 mL of 0.1 mol/L hydrochloric acid TS and dissolve with shaking, or by ultrasonication if necessary, add 0.1 mol/L hydrochloric acid TS to make exactly 1000 mL and use this solution as the standard solution. Determine the absorbances, $A_T$ and $A_S$, of the sample solution and the standard solution at 240 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Prazepam Tablets during 30 minutes is not less than 80%: it meets the Dissolution Test.

Dissolution rate (%) of prazepam ($C_{19}H_{17}ClN_2O$) to the labeled amount
$$= W_S \times \frac{A_T}{A_S} \times \frac{V'}{V} \times \frac{90}{C}$$

$W_S$: Amount (mg) of prazepam for assay.
$C$: Labeled amount (mg) of prazepam ($C_{19}H_{17}ClN_2O$) in each tablet.

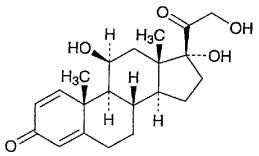
**Assay** Weigh accurately not less than 20 Prazepam Tablets, and powder. Weigh accurately a quantity of the powder, equivalent to about 0.05 g of prazepam ($C_{19}H_{17}ClN_2O$), add 30 mL of acetone, shake well, centrifuge, and separate the supernatant. Repeat the same procedure twice with 30 mL each of acetone, combine all the supernatants, and evaporate on a water bath to dryness. Dissolve the residue in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.02 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.02 mol/L perchloric acid VS
= 6.496 mg of $C_{19}H_{17}ClN_2O$

**Containers and storage** Containers—Tight containers.

# Prednisolone

プレドニゾロン




$C_{21}H_{28}O_5$: 360.44
11$\beta$,17,21-Trihydroxypregna-1,4-diene-3,20-dione
[*50-24-8*]

Prednisolone, when dried, contains not less than 97.0% and not more than 102.0% of $C_{21}H_{28}O_5$.

**Description** Prednisolone occurs as a white, crystalline powder.

It is soluble in methanol and in ethanol (95), slightly soluble in ethyl acetate and in chloroform, and very slightly soluble in water.

Melting point: about 235°C (with decomposition).

**Identification** (1) To 2 mg of Prednisolone 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) Determine the infrared absorption spectrum of Prednisolone, 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 Prednisolone Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers. If any difference appears between the spectra, dissolve Prednisolone and Prednisolone Reference Standard in ethyl acetate, respectively, then evaporate the ethyl acetate to dryness, and repeat the test on the residues.

**Optical rotation** $[\alpha]_D^{20}$: +113 – +119° (after drying, 0.2 g, ethanol (95), 20 mL, 100 mm).

**Purity** **(1)** Selenium—To 0.10 g of Prednisolone add 0.5 mL of a mixture of perchloric acid and sulfuric acid (1:1) and 2 mL of nitric acid, and heat on a water bath until no more brown gas evolves and the solution becomes to be a light yellow clear solution. After cooling, add 4 mL of nitric acid to this solution, then add water to make exactly 50 mL, and use this solution as the sample solution. Separately, pipet 3 mL of Standard Selenium Solution, add 0.5 mL of a mixture of perchloric acid and sulfuric acid (1:1) and 6 mL of nitric acid, then add water to make exactly 50 mL, and use this solution as the standard solution. Perform the test with the sample solution and the standard solution as directed under the Atomic Absorption Spectrophotometry according to the following conditions, and determine constant absorbances, $A_T$ and $A_S$, obtained on a recorder after rapid increasing of the absorption: $A_T$ is smaller than $A_S$ (not more than 30 ppm).

Perform the test by using a hydride generating system and a thermal absorption cell.

Lamp: An selenium hollow cathode lamp

Wavelength: 196.0 nm

Temperature of sample atomizer: When an electric furnace is used, about 1000°C.

Carrier gas: Nitrogen or Argon

**(2)** Other steroids—Dissolve 0.020 g of Prednisolone in exactly 2 mL of a mixture of methanol and chloroform (1:1), and use this solution as the sample solution. Separately, dissolve 0.020 g of hydrocortisone and 0.010 g of prednisolone acetate each in a mixture of methanol and chloroform (1:1) to make exactly 100 mL, and use these solutions as the standard solution (1) and the standard solution (2). Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μL each of the sample solution, the standard solutions (1) and (2) on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of acetone, toluene and diethylamine (55:45:2) to a distance of about 15 cm, and air-dry the plate (do not dip the filter paper in the developing vessel). Spray evenly alkaline blue tetrazolium TS on the plate: the spots from the sample solution corresponding to those from the standard solutions (1) and (2) are not more intense than the spots from the standard solutions (1) and (2), and no spots other than the principal spot, hydrocortisone and prednisolone acetate appear from the sample solution.

**Loss on drying** Not more than 1.0% (0.5 g, 105°C, 3 hours).

**Residue on ignition** Not more than 0.1% (0.5 g).

**Assay** Dissolve about 0.025 g each of Prednisolone and Prednisolone Reference Standard, previously dried and accurately weighed, in 50 mL of methanol, add exactly 25 mL of the internal standard solution to each, and add methanol to make 100 mL. To 1 mL each of these solutions add the mobile phase to make 10 mL, and use these solutions as the sample solution and the standard solution. Perform the test with 20 μL each of these solutions 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 to that of the internal standard.

$$\text{Amount (mg) of } C_{21}H_{28}O_5 = \text{amount (mg) of Prednisolne Reference Standard} \times \frac{Q_T}{Q_S}$$

*Internal standard solution*—A solution of methyl parahydroxybenzoate in methanol (1 in 2000).

*Operating conditions*—

Detector: An ultraviolet absorption photometer (wavelength: 247 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with fluorosilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: A mixture of water and methanol (13:7).

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

*System suitability*—

System performance: Dissolve 0.025 g of Prednisolone and 0.025 g of hydrocortisone in 100 mL of methanol. To 1 mL of this solution add the mobile phase to make 10 mL. When the procedure is run with 20 μL of this solution under the above operating conditions, hydrocortisone and prednisolone are eluted in this order with the resolution between these peaks being not less than 1.5.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of prednisolone to that of the internal standard is not more than 1.0%.

**Containers and storage** Containers—Tight containers.

# Prednisolone Tablets

プレドニゾロン錠

Prednisolone Tablets contain not less than 90% and not more than 110% of the labeled amount of prednisolone ($C_{21}H_{28}O_5$: 360.44).

**Method of preparation** Prepare as directed under Tablets, with Prednisolone.

**Identification** **(1)** Weigh a quantity of powdered Prednisolone Tablets, equivalent to 0.05 g of Prednisolone according to the labeled amount, add 10 mL of chloroform, shake for 15 minutes, and filter. Evaporate the filtrate on a water bath to dryness. Dry the residue at 105°C for 1 hour, and proceed as directed in the Identification (1) under Prednisolone.

**(2)** Determine the infrared absorption spectra of the residue obtained in (1) and Prednisolone Reference Stan-