Units in each mL of Vasopressin Injection

$$= \text{antilog}\, M \times \left(\begin{array}{l}\text{Units in each ml of the}\\ \text{high-dose standard solution}\end{array}\right) \times \frac{b}{a}$$

$$M = \frac{IY_a}{Y_b}$$

$$I = \log\frac{S_H}{S_L} = \log\frac{T_H}{T_L}$$

$$Y_a = -Y_1 + Y_2 + Y_3 - Y_4$$

$$Y_b = Y_1 + Y_2 + Y_3 + Y_4$$

a: Volume (mL) of Vasopressin Injection sampled.

b: Total volume (mL) of the high-dose sample solution prepared by diluting with isotonic sodium chloride solution.

Compute L (P = 0.95) by the following equation, and confirm L to be 0.15 or less. If L exceeds 0.15, repeat the test, improving the conditions of the assay or increasing the number of sets until L reaches 0.15 or less.

$$L = 2\sqrt{(C-1)(CM^2 + I^2)}$$

$$C = \frac{Y_b^2}{Y_b^2 - 4fs^2t^2}$$

f: Number of sets

$$s^2 = \frac{\Sigma y^2 - \frac{Y}{f} - \frac{Y'}{4} + \frac{Y_b^2}{4f}}{n}$$

Σy^2: The sum of the squares of y_1, y_2, y_3 and y_4.

$Y = Y_1^2 + Y_2^2 + Y_3^2 + Y_4^2$

Y': The sum of the squares of the sum of y_1, y_2, y_3 and y_4 in each set.

$n = 3(f - 1)$

t^2: Value shown in the table in the Assay under Insulin Injection against n for which s^2 is calculated.

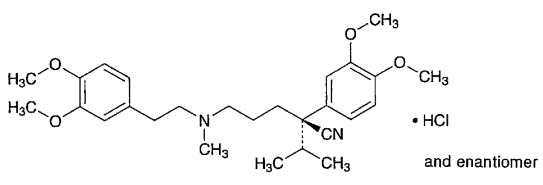
Containers and storage Containers—Hermetic containers. Storage—In a cold place, and avoid freezing.

Expiration date 36 months after preparation.

Verapamil Hydrochloride

Iproveratril Hydrochloride

塩酸ベラパミル



$C_{27}H_{38}N_2O_4.HCl$: 491.06

(*RS*)-5-[(3,4-Dimethoxyphenethyl)methylamino]-2-(3,4-dimethoxyphenyl)-2-(1-methylethyl)pentanenitrile monohydrochloride [*152-11-4*]

Verapamil Hydrochloride, when dried, contains not less than 98.5% of $C_{27}H_{38}N_2O_4.HCl$.

Description Verapamil Hydrochloride occurs as a white, crystalline powder. It is odorless.

It is freely soluble in methanol, in acetic acid (100) and in chloroform, soluble in ethanol (95) and in acetic anhydride, sparingly soluble in water, and practically insoluble in diethyl ether.

Identification (1) To 2 mL of a solution of Verapamil Hydrochloride (1 in 50) add 5 drops of Reinecke salt TS: a light red precipitate is produced.

(2) Determine the absorption spectrum of a solution of Verapamil Hydrochloride in 0.01 mol/L hydrochloric acid TS (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Determine the infrared absorption spectrum of Verapamil Hydrochloride, previously dried, as directed in the potassium chloride disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(4) A solution of Verapamil Hydrochloride (1 in 50) responds to the Qualitative Tests for chloride.

Melting point 141 - 145°C

pH Dissolve 1.0 g of Verapamil Hydrochloride in 20 mL of freshly boiled and cooled water by warming, and cool: the pH of this solution is between 4.5 and 6.5.

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Verapamil Hydrochloride in 20 mL of water by warming: the solution is clear and colorless.

(2) Heavy metals—Proceed with 1.0 g of Verapamil Hydrochloride according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(3) Arsenic—Prepare the test solution with 1.0 g of Verapamil Hydrochloride according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.50 g of Verapamil Hydrochloride in exactly 10 mL of chloroform, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add chloroform to make exactly 100 mL, and use this solution as the standard stock solution. Pipet 5 mL of the standard stock solution, add chloroform to make exactly 100 mL, and use this solution as the standard solution (1). Separately, pipet 5 mL of standard stock solution, add chloroform to make exactly 50 mL, and use this solution as the standard solution (2). Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL each of the sample solution, the standard solutions (1) and (2) on two plates of silica gel for thin-layer chromatography. With the one plate, develop the plate with a mixture of cyclohexane and diethylamine (17:3) to a distance of about 15 cm, air-dry the plate, heat at 110°C for 1 hour, and cool. Examine immediately after spraying evenly iron (III) chloride-iodine TS on the plate: the three spots, having more intense color in the spots other than the principal spot and the original point from the sample solution, are not more intense than the spot from the standard solution (2) in color. The remaining spots from the sample solution are not more intense than the spot from the standard solution (1) in color. With another plate, develop the plate with a mixture of toluene, methanol, acetone and acetic acid (100) (14:4:1:1), and perform the test in the same manner.

Loss on drying Not more than 1.0% (1 g, 105°C, 2 hours).

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

Assay Weigh accurately about 0.7 g of Verapamil Hydrochloride, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

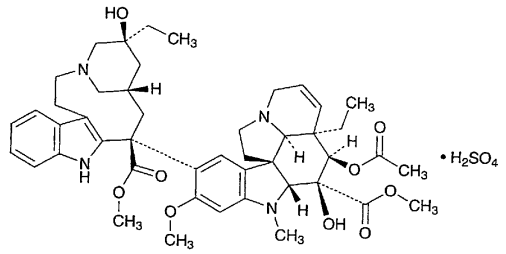
Each mL of 0.1 mol/L perchloric acid VS
= 49.11 mg of $C_{27}H_{38}N_2O_4.HCl$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Vinblastine Sulfate

硫酸ビンブラスチン



$C_{46}H_{58}N_4O_9.H_2SO_4$: 909.05

Methyl (3a*R*,4*R*,5*S*,5a*R*,10b*R*,13a*R*)-4-acetoxy-3a-ethyl-9-[(5*S*,7*S*,9*S*)-5-ethyl-5-hydroxy-9-methoxycarbonyl-1,4,5,6,7,8,9,10-octahydro-3,7-methano-3-azacycloundecino[5,4-*b*]indol-9-yl]-5-hydroxy-8-methoxy-6-methyl-3a,4,5,5a,6,11,12,13a-octahydro-1*H*-indolizino[8,1-*cd*]carbazole-5-carboxylate monosulfate [*143-67-9*]

Vinblastine Sulfate contains not less than 96.0% and not more than 102.0% of $C_{46}H_{58}N_4O_9.H_2SO_4$, calculated on the dried basis.

Description Vinblastine Sulfate occurs as a white to pale yellow powder.

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

It is hygroscopic.

Optical rotation $[\alpha]_D^{20}$: −28 – −35° (0.20 g, calculated on the dried basis, methanol, 10 mL, 100 mm).

Identification **(1)** Dissolve 5 mg of Vinblastine Sulfate in 2 mL of cerium (IV) tetraammonium sulfate-phosphoric acid TS: a red-purple color develops.

(2) Determine the absorption spectrum of a solution of Vinblastine Sulfate (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Vinblastine Sulfate Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Dissolve 0.02 g of Vinblastine Sulfate in 10 mL of sodium chloride TS, adjust its pH to between 9 and 10 with ammonia TS, and extract with two 5-mL portions of chloroform. Wash the combined chloroform extracts with a small quantity of sodium chloride TS, add a small quantity of anhydrous sodium sulfate, and allow to stand for several minutes. Filter through a pledget of absorbent cotton, evaporate the filtrate to dryness under reduced pressure, and dissolve the residue in a small quantity of chloroform. Determine the infrared absorption spectrum of the solution as directed in the solution method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(4) A solution of Vinblastine Sulfate (1 in 100) responds to the Qualitative Tests for sulfate.

pH Dissolve 0.015 g of Vinblastine Sulfate in 10 mL of water: the pH of this solution is between 3.5 and 5.0.

Purity **(1)** Clarity and color of solution—Dissolve 0.010 g of Vinblastine Sulfate in 10 mL of water: the solution is clear and colorless.

(2) Related substances—Dissolve 0.010 g of Vinblastine Sulfate in 10 mL of water, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add water to make exactly 25 mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area of these solutions by the automatic integration method: the total area of the peaks other than the principal peak of the sample solution is not larger than the peak area of vinblastine from the standard solution, and the area of any peak other than the principal peak of the sample solution is not larger than 1/2 of the peak area of vinblastine from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 262 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: Room temperature.

Mobile phase: To 7 mL of diethylamine add water to make 500 mL, and adjust with phosphoric acid to a pH of 7.5. To 380 mL of this solution add 620 mL of a mixture of methanol and acetonitrile (4:1).

Flow rate: Adjust the flow rate so that the retention time of vinblastine is about 20 minutes.

Selection of column: Dissolve 0.010 g each of Vinblastine Sulfate and vincristine sulfate in 250 mL of water. Proceed with 20 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of vincristine and vinblastine in this order with the resolution between these peaks being not less than 4.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of vinblastine from 20 μL of the standard solution is between 5 mm and 15 mm.

Time span of measurement: About 1.5 times as long as the retention time of vinblastine after the solvent peak.

Loss on drying Not more than 15.0% (0.05 g, in vacuum, 105°C, 2 hours).