

water to make exactly 50 mL. To 2 mL of this solution, exactly measured, add acetic acid-sodium acetate buffer solution, pH 5.0, to make exactly 50 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 361 nm as directed under the Ultraviolet-visible Spectrophotometry.

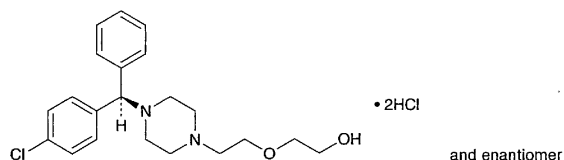
Amount (mg) of $C_{62}H_{89}CoN_{13}O_{15}P \cdot C_2H_4O_2$
 = amount (mg) of Cyanocobalamin Reference Standard, calculated on the dried basis

$$\times \frac{A_T}{A_S} \times 1.0377$$

Containers and storage Containers—Tight containers.
 Storage—Light-resistant, and in a cold place.

Hydroxyzine Hydrochloride

塩酸ヒドロキシジン



$C_{21}H_{27}ClN_2O_2 \cdot 2HCl$: 447.83
 2-(2-{4-[(*RS*)-(4-Chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)ethanol dihydrochloride [2192-20-3]

Hydroxyzine Hydrochloride, when dried, contains not less than 98.5% of $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$.

Description Hydroxyzine Hydrochloride occurs as a white, crystalline powder. It is odorless, and has a bitter taste.

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

Melting point: about 200°C (with decomposition).

Identification (1) To 5 mL of a solution of Hydroxyzine Hydrochloride (1 in 100) add 2 to 3 drops of ammonium thiocyanate-cobaltous nitrate TS: a blue precipitate is formed.

(2) Determine the absorption spectrum of a solution of Hydroxyzine Hydrochloride in methanol (1 in 100,000) 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) A solution of Hydroxyzine Hydrochloride (1 in 10) responds to the Qualitative Tests for chloride.

pH Dissolve 1.0 g of Hydroxyzine Hydrochloride in 20 mL of water: the pH of this solution is between 1.3 and 2.5.

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Hydroxyzine Hydrochloride in 10 mL of water: the solution is clear and colorless.

(2) Heavy metals—Proceed with 1.0 g of Hydroxyzine 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) Related substances—Dissolve 0.20 g of Hydroxyzine Hydrochloride in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add methanol to make exactly 200 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μ L 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 ethyl acetate, ethanol (95) and ammonia solution (28) (150:95:1) to a distance of about 10 cm, and air-dry the plate. Allow the plate to stand in iodine vapor: 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 3.0% (1 g, 105°C, 2 hours).

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

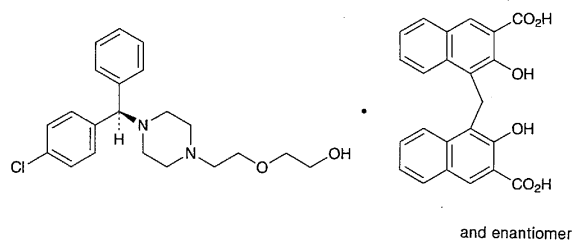
Assay Weigh accurately about 0.1 g of Hydroxyzine Hydrochloride, previously dried, dissolve in 60 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
 = 22.392 mg of $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$

Containers and storage Containers—Tight containers.

Hydroxyzine Pamoate

パモ酸ヒドロキシジン



$C_{21}H_{27}ClN_2O_2 \cdot C_{23}H_{16}O_6$: 763.27
 2-(2-{4-[(*RS*)-(4-Chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)ethanol mono[4,4'-methylenebis(3-hydroxy-2-naphthoate)] (1/1) [10246-75-0]

Hydroxyzine Pamoate contains not less than 98.0% of $C_{21}H_{27}ClN_2O_2 \cdot C_{23}H_{16}O_6$, calculated on the anhydrous basis.

Description Hydroxyzine Pamoate occurs as a light yellow, crystalline powder. It is odorless, and has a slightly bitter taste.

It is freely soluble in *N,N*-dimethylformamide, slightly soluble in acetone, and practically insoluble in water, in methanol, in ethanol (95) and in diethyl ether.

Identification (1) To 0.1 g of Hydroxyzine Pamoate add 25 mL of sodium hydroxide TS, and shake well. Extract

with 20 mL of chloroform, and use the chloroform layer as the sample solution. Use the water layer for test (4). To 5 mL of the sample solution add 2 mL of ammonium thiocyanate-cobaltous nitrate TS, shake well, and allow to stand: a blue color is produced in the chloroform layer.

(2) Evaporate 2 mL of the sample solution obtained in (1) on a water bath to dryness, and dissolve the residue in 0.1 mol/L hydrochloric acid TS to make 500 mL. Determine the absorption spectrum of the solution 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) Perform the test with Hydroxyzine Pamoate as directed under the Flame Coloration Test (2): a green color appears.

(4) To 1 mL of the water layer obtained in (1), add 2 mL of 1 mol/L hydrochloric acid TS: a yellow precipitate is produced. Collect the precipitate, dissolve the precipitate in 5 mL of methanol, and add 1 drop of iron (III) chloride TS: a green color is produced.

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Hydroxyzine Pamoate in 10 mL of *N,N*-dimethylformamide: the solution is clear, and shows a slightly greenish, light yellow-brown color.

(2) Chloride—To 0.3 g of Hydroxyzine Pamoate add 6 mL of dilute nitric acid and 10 mL of water, shake for 5 minutes, and filter. Wash the residue with two 10-mL portions of water, combine the washings with the filtrate, and add water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.80 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.095%).

(3) Heavy metals—Proceed with 1.0 g of Hydroxyzine Pamoate 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).

(4) Arsenic—Prepare the test solution with 2.0 g of Hydroxyzine Pamoate according to Method 3, and perform the test using Apparatus B (not more than 1 ppm).

(5) Related substances—Dissolve 0.40 g of Hydroxyzine Pamoate in 10 mL of a mixture of sodium hydroxide TS and acetone (1:1), and use the solution as the sample solution. Pipet 1 mL of this solution, add a mixture of sodium hydroxide TS and acetone (1:1) to make exactly 20 mL. Pipet 5 mL of this solution, add a mixture of sodium hydroxide TS and acetone (1:1) to make exactly 50 mL, and use the solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μ L 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 ethyl acetate, ethanol (95) and ammonia TS (150:95:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly hydrogen hexachloroplatinate (IV)-potassium iodide TS on the plate: the spots other than the spots from hydroxyzine and pamoic acid obtained from the sample solution are not more intense than the spot from the standard solution.

Water Not more than 3.0% (1 g, direct titration).

Residue on ignition Not more than 0.5% (1 g).

Assay Weigh accurately about 0.6 g of Hydroxyzine Pamo-

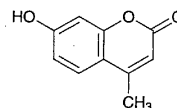
ate, add 25 mL of sodium hydroxide TS, shake well, and extract with six 25-mL portions of chloroform. Filter each extract through 5 g of anhydrous sodium sulfate on a pledget of absorbent cotton. Combine the chloroform extracts, and evaporate the combined chloroform extracts on a water bath to about 30 mL. Add 30 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple through blue to blue-green (indicator: 2 drops of crystal violet TS). Perform a blank determination.

Each mL of 0.1 mol/L perchloric acid VS
= 38.165 mg of $C_{21}H_{27}ClN_2O_2 \cdot C_{23}H_{16}O_6$

Containers and storage Containers—Tight containers.

Hymecromone

ヒメクロモン



$C_{10}H_8O_3$: 176.17

7-Hydroxy-4-methylchromen-2-one [90-33-5]

Hymecromone, when dried, contains not less than 98.0% of $C_{10}H_8O_3$.

Description Hymecromone occurs as white crystals or crystalline powder. It is odorless and tasteless.

It is freely soluble in *N,N*-dimethylformamide, sparingly soluble in ethanol (95), in ethanol (99.5) and in acetone, slightly soluble in diethyl ether, and practically insoluble in water.

Identification (1) Dissolve 2 mg of Hymecromone in 5 mL of ammonia-ammonium chloride buffer solution, pH 11.0: the solution shows an intense blue-purple fluorescence.

(2) Dissolve 0.025 g of Hymecromone in 5 mL of diluted ethanol (95) (1 in 2), and add 1 drop of iron (III) chloride TS: initially a blackish brown color develops, and when allowed to stand the color changes to yellow-brown.

(3) Determine the absorption spectrum of a solution of Hymecromone in ethanol (99.5) (1 in 250,000) 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.

(4) Determine the infrared absorption spectrum of Hymecromone, previously dried, as directed in the potassium bromide 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.

Melting point 187 – 191°C

Purity (1) Chloride—Dissolve 0.8 g of Hymecromone in 40 mL of a mixture of acetone and water (2:1), and add 6 mL of dilute nitric acid and a mixture of acetone and water