

Chlorpromazine Hydrochloride Injection

塩酸クロルプロマジン注射液

Chlorpromazine Hydrochloride Injection is an aqueous solution for injection. It contains not less than 95% and not more than 105% of the labeled amount of chlorpromazine hydrochloride ($C_{17}H_{19}ClN_2S.HCl$: 355.33).

Method of preparation Prepare as directed under Injections, with Chlorpromazine Hydrochloride.

Description Chlorpromazine Hydrochloride Injection is a clear, colorless or pale yellow liquid.

pH: 4.0 – 6.5

Identification (1) Proceed with a volume of Chlorpromazine Hydrochloride Injection, equivalent to 5 mg of Chlorpromazine Hydrochloride according to the labeled amount, as directed in the Identification (1) under Chlorpromazine Hydrochloride.

(2) Proceed with a volume of Chlorpromazine Hydrochloride Injection, equivalent to 0.1 g of Chlorpromazine Hydrochloride according to the labeled amount, as directed in the Identification (2) under Chlorpromazine Hydrochloride.

Assay Transfer an exactly measured volume of Chlorpromazine Hydrochloride Injection, equivalent to about 0.15 g of chlorpromazine hydrochloride ($C_{17}H_{19}ClN_2S.HCl$) to a separator, add 30 mL of water and 10 mL of a solution of sodium hydroxide (1 in 5), and extract with two 30-mL portions and three 20-mL portions of diethyl ether. Wash the combined diethyl ether extracts with successive 10-mL portions of water until the last washing shows no red color upon the addition of phenolphthalein TS. Concentrate the diethyl ether extracts on a water bath to 20 mL, add 5 g of anhydrous sodium sulfate, allow to stand for 20 minutes, and filter through a pledget of absorbent cotton. Wash with diethyl ether, combine the washings with the filtrate, and evaporate the diethyl ether on a water bath. Dissolve the residue in 50 mL of acetone and 5 mL of acetic acid (100), and titrate with 0.05 mol/L perchloric acid VS until the color of the solution changes from red-purple to blue-purple (indicator: 3 drops of bromocresol green-methylrosaniline chloride TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.05 mol/L perchloric acid VS
= 17.767 mg of $C_{17}H_{19}ClN_2S.HCl$

Containers and storage Containers—Hermetic containers, and colored containers may be used.

Storage—Light-resistant.

Chlorpromazine Hydrochloride Tablets

塩酸クロルプロマジン錠

Chlorpromazine Hydrochloride Tablets contain not less than 93% and not more than 107% of the labeled amount of chlorpromazine hydrochloride ($C_{17}H_{19}ClN_2S.HCl$: 355.33).

Method of preparation Prepare as directed under Tablets, with Chlorpromazine Hydrochloride.

Identification (1) Shake a quantity of powdered Chlorpromazine Hydrochloride Tablets, equivalent to 0.2 g of Chlorpromazine Hydrochloride according to the labeled amount, with 40 mL of 0.1 mol/L hydrochloric acid TS, and filter. To 1 mL of the filtrate add 4 mL of water and 1 drop of iron (III) chloride TS: a red color develops.

(2) To 20 mL of the filtrate obtained in (1) add 10 mL of 2,4,6-trinitrophenol TS dropwise, and proceed as directed in the Identification (2) under Chlorpromazine Hydrochloride.

Dissolution test Perform the test with 1 tablet of Chlorpromazine Hydrochloride Tablet at 75 revolutions per minute according to Method 2 under the Dissolution Test, using 900 mL of diluted pH 6.8 phosphate buffer solution (1 in 2) as the test solution. Take 20 mL or more of the dissolved solution after 60 minutes from the start of the dissolution test, and filter through a membrane filter with pore size of not more than 0.8 μm . Discard the first 10 mL of the filtrate, pipet the subsequent V mL, add diluted pH 6.8 phosphate buffer solution (1 in 2) to make exactly V' mL so that each mL of the filtrate contains about 5.6 μg of chlorpromazine hydrochloride ($C_{17}H_{19}ClN_2S.HCl$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 0.09 g of chlorpromazine hydrochloride for assay, previously dried at 105°C for 2 hours, dissolve in diluted pH 6.8 phosphate buffer solution (1 in 2) to make exactly 200 mL. Pipet 5 mL of this solution, add diluted pH 6.8 phosphate buffer solution (1 in 2) to make exactly 100 mL, further pipet 5 mL of this solution, add diluted pH 6.8 phosphate buffer solution (1 in 2) to make exactly 20 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 254 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Chlorpromazine Hydrochloride Tablets in 60 minutes should be not less than 75%.

Dissolution rate (%) with respect to labeled amount of chlorpromazine hydrochloride ($C_{17}H_{19}ClN_2S.HCl$)

$$= W_S \times \frac{A_T}{A_S} \times \frac{V'}{V} \times \frac{1}{C} \times \frac{45}{8}$$

W_S : Amount (mg) of chlorpromazine hydrochloride for assay.

C : Labeled amount (mg) of chlorpromazine hydrochloride ($C_{17}H_{19}ClN_2S.HCl$) in 1 tablet.

Assay Weigh accurately, and powder not less than 20 Chlorpromazine Hydrochloride Tablets. Weigh accurately a portion of the powder, equivalent to about 0.15 g of chlorpromazine hydrochloride ($C_{17}H_{19}ClN_2S.HCl$), transfer to a

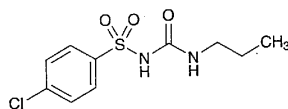
Soxhlet extractor, and extract with 100 mL of chloroform on a water bath for 3 hours. Distil the chloroform solution under reduced pressure on a water bath. Dissolve the residue in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.05 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.05 mol/L perchloric acid VS
= 17.767 mg of $C_{17}H_{19}ClN_2S \cdot HCl$

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

Chlorpropamide

クロルプロパミド



$C_{10}H_{13}ClN_2O_3S$: 276.74
4-Chloro-*N*-(propylcarbamoyl)benzenesulfonamide
[94-20-2]

Chlorpropamide, when dried, contains not less than 98.0% of $C_{10}H_{13}ClN_2O_3S$.

Description Chlorpropamide occurs as white, crystals or crystalline powder.

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

Identification (1) Dissolve 0.08 g of Chlorpropamide in 50 mL of methanol. To 1 mL of the solution add 0.01 mol/L hydrochloric acid TS to make 200 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.

(2) Determine the infrared absorption spectrum of Chlorpropamide, 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.

(3) Perform the test with Chlorpropamide as directed under the Flame Coloration Test (2): a green color appears.

Melting point 127–131°C

Purity (1) Acid—To 3.0 g Chlorpropamide add 150 mL of water, and warm at 70°C for 5 minutes. Allow to stand in ice water for 1 hour, and filter. To 25 mL of the filtrate add 2 drops of methyl red TS and 0.30 mL of 0.1 mol/L sodium hydroxide VS: a yellow color develops.

(2) Chloride—To 40 mL of the filtrate obtained in (1) add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.25 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.011%).

(3) Sulfate—To 40 mL of the filtrate obtained in (1) add 1 mL of dilute hydrochloric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.35 mL of 0.005 mol/L sulfuric acid VS (not more than 0.021%).

(4) Heavy metals—Proceed with 2.0 g of Chlorpropamide 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).

(5) Related substances—Dissolve 0.6 g of Chlorpropamide in acetone to make exactly 10 mL, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add acetone to make exactly 300 mL, and use this solution as the standard solution (1). Separately, dissolve 0.060 g of 4-chlorobenzene sulfonamide in acetone to make exactly 300 mL, and use this solution as the standard solution (2). Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μ L each of the sample solution, the standard solution (1) and (2) on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of cyclohexane, 3-methyl-1-butanol, methanol and ammonia solution (28) (15:10:5:1) to a distance of about 10 cm, and air-dry the plate. After drying the plate at 100°C for 1 hour, spray evenly sodium hypochlorite TS on the plate, and air-dry for 15 minutes. Then spray evenly potassium iodide-starch TS on the plate: the spot from the sample solution equivalent to the spot from the standard solution (2) is not more intense than the spot from the standard solution (2), and the spots other than the spot mentioned above and other than the principal spot from the sample solution is not more intense than the spot from the standard solution (1).

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

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

Assay Weigh accurately about 0.5 g of Chlorpropamide, previously dried, dissolve in 30 mL of neutralized ethanol, and add 20 mL of water. Titrate with 0.1 mol/L sodium hydroxide VS (indicator: 3 drops of phenolphthalein TS).

Each mL of 0.1 mol/L sodium hydroxide VS
= 27.674 mg of $C_{10}H_{13}ClN_2O_3S$

Containers and storage Containers—Well-closed containers.

Chlorpropamide Tablets

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Chlorpropamide Tablets contain not less than 95% and not more than 105% of the labeled amount of chlorpropamide ($C_{10}H_{13}ClN_2O_3S$: 276.74).

Method of preparation Prepare as directed under Tablets, with Chlorpropamide.

Identification Take a quantity of powdered Chlorpropamide Tablets, equivalent to 0.08 g of Chlorpropamide according to the labeled amount, add 50 mL of methanol, shake, and filter. To 1 mL of the filtrate add 0.01 mol/L hydrochloric acid TS to make 200 mL, and determine the ab-