

lute nitric acid, add water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 0.70 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.041%).

(3) Sulfate—Dissolve 0.5 g of Lidocaine in 5 mL of dilute hydrochloric acid, add water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 1.0 mL of 0.005 mol/L sulfuric acid VS, 5 mL of dilute hydrochloric acid and water to make 50 mL (not more than 0.096%).

(4) Heavy metals—Carbonize 2.0 g of Lidocaine by gentle ignition. After cooling, add 10 mL of a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 10), and fire the ethanol to burn. After cooling, add 1 mL of sulfuric acid, proceed according to Method 4, 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 0.10 g of Lidocaine in 2 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add methanol to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the thin-layer Chromatography. Spot 10  $\mu$ L each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of ethyl acetate, 2-butanone, water and formic acid (5:3:1:1) to a distance of about 10 cm, air-dry the plate, and dry more at 80°C for 30 minutes. After cooling, examine under ultraviolet light (main wavelength: 254 nm): 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 0.5% (1 g, in vacuum, silica gel, 24 hours).

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

**Assay** Dissolve about 0.5 g of Lidocaine, previously dried and accurately weighed, in 20 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (indicator: 1 drop of crystal violet TS) until the color of the solution changes from purple to blue-green through blue. Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS  
= 23.434 mg of  $C_{14}H_{22}N_2O$

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

## Lidocaine Injection

### Lidocaine Hydrochloride Injection

リドカイン注射液

Lidocaine Injection is an aqueous injection. It contains not less than 95% and not more than 105% of the labeled amount of lidocaine hydrochloride ( $C_{14}H_{22}N_2O.HCl$ : 270.80).

**Method of preparation** Prepare as directed under Injections, with Lidocaine and an equivalent amount of Hydrochloric Acid.

No preservative is added in the case of intravenous injections.

**Description** Lidocaine Injection is a colorless, clear liquid. pH: 5.0 – 7.0

**Identification** To a volume of Lidocaine Injection, equivalent to 0.02 g of Lidocaine Hydrochloride ( $C_{14}H_{22}N_2O.HCl$ ) according to the labeled amount, add 1 mL of sodium hydroxide TS, and extract with 20 mL of hexane. To 10 mL of the hexane extract add 20 mL of 1 mol/L hydrochloric acid TS, and shake vigorously. Determine the absorption spectrum of the water layer as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 261 nm and 265 nm.

**Pyrogen** Perform the test with Lidocaine Injection stored in a container in a volume exceeding 10 mL and intended to intravenous injection: it meets the requirements of the Pyrogen Test.

**Assay** To an exactly measured volume of Lidocaine Injection, equivalent to about 0.1 g of lidocaine hydrochloride ( $C_{14}H_{22}N_2O.HCl$ ), add exactly 10 mL of the internal standard solution and 0.001 mol/L hydrochloric acid TS to make 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.085 g of lidocaine for assay, previously dried in a desiccator (in vacuum, silica gel) for 24 hours, dissolve in 0.5 mL of 1 mol/L hydrochloric acid TS and a suitable volume of 0.001 mol/L hydrochloric acid TS, and add exactly 10 mL of the internal standard solution, then add 0.001 mol/L hydrochloric acid TS to make 50 mL, and use this solution as the standard solution. Perform the test with 5  $\mu$ L each 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 lidocaine to that of the internal standard.

$$\begin{aligned} & \text{Amount (mg) of lidocaine hydrochloride} \\ & \text{( $C_{14}H_{22}N_2O.HCl$ )} \\ & = \text{amount (mg) of lidocaine for assay} \\ & \quad \times \frac{Q_T}{Q_S} \times 1.1556 \end{aligned}$$

**Internal standard solution**—A solution of benzophenone in methanol (1 in 4000).

**Operating conditions**—

**Detector:** An ultraviolet absorption photometer (wavelength: 254 nm).

**Column:** A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10  $\mu$ m in particle diameter).

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

**Mobile phase:** Dissolve 2.88 g of sodium lauryl sulfate in 1000 mL of a mixture of 0.02 mol/L phosphate buffer solution, pH 3.0 and acetonitrile (11:9).

**Flow rate:** Adjust the flow rate so that the retention time of lidocaine is about 6 minutes.

**System suitability**—

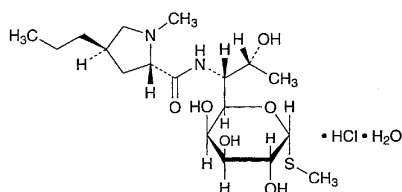
**System performance:** When proceed with 5  $\mu$ L of the standard solution under the above operating conditions, lidocaine and the internal standard are eluted in this order with the resolution between these peaks being not less than 6.

System repeatability: When the test is repeated 6 times with 5  $\mu\text{L}$  of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of lidocaine to that of the internal standard is not more than 1.0%.

**Containers and storage** Containers—Hermetic containers.

## Lincomycin Hydrochloride

塩酸リンコマイシン



$\text{C}_{18}\text{H}_{34}\text{N}_2\text{O}_6\text{S}\cdot\text{HCl}\cdot\text{H}_2\text{O}$ : 461.01

Methyl 6,8-dideoxy-6-[(2*S*,4*R*)-1-methyl-4-propylpyrrolidine-2-carboxamido]-1-thio-*D*-erythro- $\alpha$ -*D*-galacto-octopyranoside monohydrochloride monohydrate [7179-49-9]

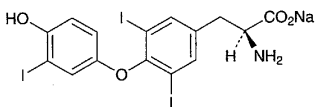
Lincomycin Hydrochloride conforms to the requirements of Lincomycin Hydrochloride in the Requirements for Antibiotic Products of Japan.

**Description** Lincomycin Hydrochloride occurs as white crystals or crystalline powder. It has a bitter taste.

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

## Liothyronine Sodium

リオチロニンナトリウム



$\text{C}_{15}\text{H}_{11}\text{I}_3\text{NNaO}_4$ : 672.96

Monosodium *O*-(4-hydroxy-3-iodophenyl)-3,5-diiodo-*L*-tyrosinate [55-06-1]

Liothyronine Sodium contains not less than 95.0% of  $\text{C}_{15}\text{H}_{11}\text{I}_3\text{NNaO}_4$ , calculated on the dried basis.

**Description** Liothyronine Sodium occurs as a white to light brown powder. It is odorless.

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

It dissolves in sodium hydroxide TS and in ammonia TS.

**Identification** (1) To 5 mL of a solution of Liothyronine Sodium in ethanol (95) (1 in 1000) add 1 mL of ninhydrin TS, and warm in a water bath for 5 minutes: a purple color develops.

(2) Heat 0.02 g of Liothyronine Sodium with a few drops of sulfuric acid over a flame: a purple gas is evolved.

(3) Determine the absorption spectrum of a solution of Liothyronine Sodium in ethanol (95) (1 in 10,000) 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) Ignite 0.02 g of Liothyronine Sodium until thoroughly charred. After cooling, add 5 mL of water to the residue, shake, and filter: the filtrate responds to the Qualitative Tests (1) for sodium salt.

**Optical rotation**  $[\alpha]_D^{20}$ : +18 - +22° (0.2 g, calculated on the dried basis, a mixture of ethanol (95) and 1 mol/L hydrochloric acid TS (4:1), 10 mL, 100 mm).

**Purity** (1) Soluble halide—To 0.010 g of Liothyronine Sodium add 10 mL of water and 1 drop of dilute nitric acid, shake for 5 minutes, and filter. Add water to the filtrate to make 10 mL, and mix with 3 drops of silver nitrate TS: the solution shows no more turbidity than the following control solution.

Control solution: To 0.35 mL of 0.01 mol/L hydrochloric acid VS add 1 drop of dilute nitric acid and water to make 10 mL, and add 3 drops of silver nitrate TS.

(2) Iodine and iodide—Dissolve 0.10 g of Liothyronine Sodium in 10 mL of dilute sodium hydroxide TS and 15 mL of water, add 5 mL of dilute sulfuric acid, and allow to stand for 10 minutes with occasional shaking. Filter the mixture into a Nessler tube, add 10 mL of chloroform and 3 drops of a solution of potassium iodate (1 in 100) to the filtrate, mix for 30 seconds, and allow to stand: the chloroform layer has no more color than the following control solution.

Control solution: Weigh exactly 0.111 g of potassium iodide, and dissolve in water to make 1000 mL. Pipet 1 mL of this solution, add 10 mL of dilute hydroxide TS, 14 mL of water and 5 mL of dilute sulfuric acid, and mix. Filter the mixture into a Nessler tube, and perform the test with the filtrate in the same manner as for the sample.

(3) Related substances—Dissolve 0.15 g of Liothyronine Sodium in 5 mL of diluted ammonia TS (1 in 3), and use this solution as the sample solution. Pipet 1 mL of this solution, add diluted ammonia TS (1 in 3) to make exactly 50 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 1  $\mu\text{L}$  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 *t*-butanol, *t*-amyl alcohol, water, ammonia solution (28) and 2-butanone (59:32:17:15:7) to a distance of about 12 cm, and air-dry the plate. Spray evenly a solution of 0.3 g of ninhydrin in 100 mL of a mixture of 1-butanol and acetic acid (100) (97:3) on the plate, and dry the plate at 100°C for 3 minutes: 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 4.0% (0.2 g, 105°C, 2 hours).

**Assay** Weigh accurately about 0.025 g of Liothyronine Sodium, and proceed as directed under the Oxygen Flask Combustion Method, using a mixture of 10 mL of a solution of