

the Assay under Thiamylal Sodium.

Each mL of 0.1 mol/L potassium hydroxide-ethanol VS  
= 27.634 mg of  $C_{12}H_{17}N_2NaO_2S$

(2) Sodium—Weigh accurately about 0.5 g of the dried material, obtained in the Assay (1), dissolve in 40 mL of water, and titrate with 0.1 mol/L hydrochloric acid VS until a persistent orange to orange-red color is observed when the solution is carefully boiled, loosely stoppered, and cooled (indicator: 3 drops of methyl red TS).

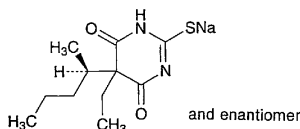
Each mL of 0.1 mol/L hydrochloric acid VS  
= 2.2990 mg of Na

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

Storage—Light-resistant.

## Thiopental Sodium

チオペンタールナトリウム



$C_{11}H_{17}N_2NaO_2S$ : 264.32

Monosodium 5-ethyl-1,4,5,6-tetrahydro-5-[(*RS*)-1-methylbutyl]-4,6-dioxypyrimidine-2-thiolate [71-73-8]

Thiopental Sodium, when dried, contains not less than 97.0% of  $C_{11}H_{17}N_2NaO_2S$ .

**Description** Thiopental Sodium occurs as a light yellow powder. It has a faint, characteristic odor.

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

A solution of Thiopental Sodium (1 in 10) is alkaline.

It is hygroscopic.

Its solution gradually decomposes on standing.

**Identification** (1) Dissolve 0.2 g of Thiopental Sodium in 5 mL of sodium hydroxide TS, and add 2 mL of lead (II) acetate TS: a white precipitate, which dissolves upon heating, is produced. Boil the solution thus obtained: a black precipitate forms gradually, and the precipitate responds to the Qualitative tests for sulfide.

(2) Dissolve 0.5 g of Thiopental Sodium in 15 mL of water, add 10 mL of dilute hydrochloric acid to produce white precipitate, and extract with four 25-mL portions of chloroform. Combine the chloroform extracts, evaporate on a water bath, and dry at 105°C for 2 hours: the residue melts between 157°C and 162°C.

(3) A solution of Thiopental Sodium (1 in 10) responds to the Qualitative Tests (1) and (2) for sodium salt.

**Purity** (1) Clarity and color of solution—Dissolve 1.0 g of Thiopental Sodium in 10 mL of freshly boiled and cooled water: the solution is clear and light yellow.

(2) Heavy metals—Dissolve 2.0 g of Thiopental Sodium in 76 mL of water, add 4 mL of dilute hydrochloric acid, shake, and filter through a glass filter (G4). To 40 mL of the

filtrate add 2 mL of ammonium acetate TS, dilute with water to 50 mL, and perform the test using this solution as the test solution. Prepare a control solution as follows: to 2.0 mL of Standard Lead Solution add 2 mL of dilute acetic acid, 2 mL of ammonium acetate TS and water to make 50 mL (not more than 20 ppm).

(3) Neutral and basic substances—Weigh accurately about 1 g of Thiopental Sodium, dissolve in 10 mL of water and 5 mL of sodium hydroxide TS, and shake vigorously with 40 mL of chloroform. Separate the chloroform layer, wash with two 5-mL portions of water, filter, and evaporate the filtrate on a water bath to dryness. Dry the residue at 105°C for 1 hour: the amount of the residue is not more than 0.50%.

(4) Related substances—Dissolve 0.050 g of Thiopental Sodium in 50 mL of the mobile phase, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase to make exactly 200 mL, and use this solution as the standard solution. Perform the test with 20  $\mu$ L each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Measure each peak area of each solution by the automatic integration method: the total area of peaks other than those of thiopental in the sample solution is not larger than the peak area of thiopental in the standard solution.

**Operating conditions**—

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

**Column:** A stainless steel column about 4 mm in inside diameter and 15 to 25 cm in length, packed with octadecylsilanized silica gel (5  $\mu$ m in particle diameter).

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

**Mobile phase:** Dissolve 1 g of potassium dihydrogenphosphate in 1000 mL of water, and adjust with phosphoric acid to a pH of 3.0. To 700 mL of this solution add 300 mL of acetonitrile.

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

**Selection of column:** Dissolve 5 mg each of isopropyl parahydroxybenzoate and propyl parahydroxybenzoate in 50 mL of acetonitrile, and add water to make 100 mL. Proceed with 20  $\mu$ L of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of isopropyl parahydroxybenzoate and propyl parahydroxybenzoate in this order with the resolution between these peaks being not less than 1.9.

**Detection sensitivity:** Adjust the detection sensitivity so that the peak height of thiopental obtained from the standard solution is 2 to 6 mm.

**Time span of measurement:** 1.5 times as long as the retention time of thiopental.

**Loss on drying** Not more than 2.0% (1 g, in vacuum, 80°C, 4 hours).

**Assay** Weigh accurately about 0.5 g of Thiopental Sodium, previously dried, transfer to a separator, dissolve in 20 mL of water, add 5 mL of ethanol (95) and 10 mL of dilute hydrochloric acid, and extract with 50 mL of chloroform, then with three 25-mL portions of chloroform. Combine the chloroform extracts, wash with two 5-mL portions of water, and extract the washings with two 10-mL portions of chlo-

roform. Filter the combined chloroform extracts into a conical flask, and wash the filter paper with three 5-mL portions of chloroform. Combine the filtrate and the washings, and add 10 mL of ethanol (95). Titrate with 0.1 mol/L potassium hydroxide-ethanol VS until the color of the solution changes from yellow through light blue to purple (indicator: 2 mL of alizarin yellow GG-thymolphthalein TS). Perform a blank determination with a mixture of 160 mL of chloroform and 30 mL of ethanol (95), and make any necessary correction.

Each mL of 0.1 mol/L potassium hydroxide-ethanol VS = 26.432 mg of  $C_{11}H_{17}N_2NaO_2S$

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

## Thiopental Sodium for Injeciton

注射用チオペンタールナトリウム

Thiopental Sodium for Injection is a preparation for injection which is dissolved before use. It contains not less than 93% and not more than 107% of the labeled amount of thiopental sodium ( $C_{11}H_{17}N_2NaO_2S$ ; 264.32).

**Method of preparation** Prepare as directed under Injections, with 100 parts of Thiopental Sodium and 6 parts of Dried Sodium Carbonate in mass.

**Description** Thiopental Sodium for Injection is a light yellow powder or mass, and has a slight, characteristic odor.

It is very soluble in water, and practically insoluble in dehydrated diethyl ether.

It is hygroscopic.

**Identification (1)** Dissolve 0.1 g of Thiopental Sodium for Injection in 10 mL of water, and add 0.5 mL of barium chloride TS: a white precipitate is formed. Collect the precipitate, and add dilute hydrochloric acid dropwise: the precipitate dissolves with effervescence.

(2) Proceed as directed in the Identification under Thiopental Sodium.

**pH** Dissolve 1 g of Thiopental Sodium for Injection in 40 mL of water: the pH of this solution is between 10.2 and 11.2.

**Purity** Proceed as directed in the Purity under Thiopental Sodium.

**Loss on drying** Not more than 2.0% (1 g, in vacuum, 80°C, 4 hours).

**Sterility** Perform the test according to the Membrane filtration method: it meets the requirements of the Sterility Test.

**Assay** Take 10 samples of Thiopental Sodium for Injection, and open each container carefully. Dissolve each content with water, wash each container with water, combine the washings with the former solution, and add water to make exactly 1000 mL. Pipet 10 mL of this solution, and add water to make exactly 100 mL. Measure exactly a volume ( $V$  mL) of this solution, equivalent to about 0.015 g of thiopental sodium ( $C_{11}H_{17}N_2NaO_2S$ ), and add water to

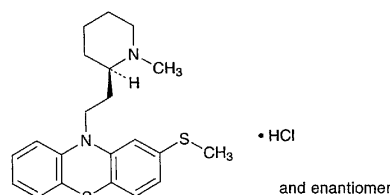
make exactly 1000 mL. Pipet 10 mL of this solution, add 15 mL of diluted dilute sodium hydroxide TS (1 in 100), add water to make exactly 30 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.046 g of thiopental for assay, previously dried at 105°C for 3 hours, dissolve in 50 mL of dilute sodium hydroxide TS, and add water to make exactly 200 mL. Pipet 2 mL of this solution, add water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with the sample solution and the standard solution as directed under the Ultraviolet-visible Spectrophotometry, and determine the absorbances,  $A_T$  and  $A_S$ , at 304 nm.

Amount (mg) of thiopental sodium ( $C_{11}H_{17}N_2NaO_2S$ ) in each sample of Thiopental Sodium for Injection = amount (mg) of thiopental sodium for assay  $\times \frac{A_T}{A_S} \times \frac{300}{V} \times 1.0907$

**Containers and storage** Containers—Hermetic containers.  
Storage—Light-resistant.

## Thioridazine Hydrochloride

塩酸チオリダジン



$C_{21}H_{26}N_2S_2 \cdot HCl$ : 407.04  
10- $\{2-[(1S)-1\text{-Methylpiperidin-2-yl}]ethyl\}$ -2-methylsulfanylphenothiazine monohydrochloride  
[130-61-0]

Thioridazine Hydrochloride, when dried, contains not less than 99.0% of  $C_{21}H_{26}N_2S_2 \cdot HCl$ .

**Description** Thioridazine Hydrochloride occurs as a white to pale yellow, crystalline powder. It is odorless, and has a bitter taste.

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

The pH of a solution of Thioridazine Hydrochloride (1 in 100) is between 4.2 and 5.2.

It is gradually colored by light.

**Identification (1)** Dissolve 0.01 g of Thioridazine Hydrochloride in 2 mL of sulfuric acid: a deep blue color develops.

(2) Dissolve 0.01 g of Thioridazine Hydrochloride in 2 mL of water, and add 1 drop of cerium (IV) tetraammonium sulfate TS: a blue color develops, and the color disappears on the addition of excess of the reagent.

(3) Determine the infrared absorption spectrum of Thioridazine Hydrochloride, previously dried, as directed in the potassium chloride disk method under the Infrared Spectrophotometry, and compare the spectrum with the Refer-