

proceed as directed in the Identification (1) under Protamine Sulfate.

(2) Dilute a volume of Protamine Sulfate Injection, equivalent to 5 mg of Protamine Sulfate according to the labeled amount, with water to make 1 mL, and proceed as directed in the Identification (2) under Protamine Sulfate.

(3) Protamine Sulfate Injection responds to the Qualitative Tests for sulfate.

**pH** 5.0 – 7.0

**Purity Nitrogen**—Transfer an exactly measured volume of Protamine Sulfate Injection, equivalent to about 0.010 g of Protamine Sulfate according to the labeled amount, to a Kjeldahl flask, and evaporate on a water bath with the aid of a current of air to dryness. Perform the test as directed under the Nitrogen Determination: 0.225 to 0.255 mg of nitrogen (N: 14.01) is found for each mg of the labeled amount of Protamine Sulfate.

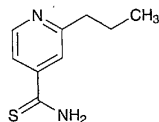
**Potency as antiheparin** Proceed as directed in the Potency as antiheparin under Protamine Sulfate, but use the following sample solution.

**Sample solution:** Dilute an exactly measured volume of Protamine Sulfate Injection, equivalent to 20.0 mg of Protamine Sulfate according to the labeled amount, with isotonic sodium chloride solution to make exactly 20 mL.

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

## Prothionamide

プロチオナミド



$C_9H_{12}N_2S$ : 180.27

2-Propylpyridine-4-carbothioamide [14222-60-7]

Prothionamide, when dried, contains not less than 98.0% of  $C_9H_{12}N_2S$ .

**Description** Prothionamide occurs as yellow crystals or crystalline powder. It has a slight, characteristic odor.

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

It dissolves in dilute hydrochloric acid and in dilute sulfuric acid.

**Identification (1)** Mix 0.05 g of Prothionamide with 0.1 g of 1-chloro-2,4-dinitrobenzene, transfer about 0.01 g of this mixture to a test tube, and heat for several seconds over a small flame until the mixture is fused. Cool, and add 3 mL of potassium hydroxide-ethanol TS: a red to orange-red color develops.

(2) Place 0.5 g of Prothionamide in a 100-mL beaker, and dissolve in 20 mL of sodium hydroxide TS by heating while shaking occasionally: the gas evolved turns a moistened red litmus paper to blue. Boil gently, and evaporate the solution to 3 to 5 mL. After cooling, add gradually 20 mL of acetic acid (100), and heat on a water bath: the gas evolved darkens moistened lead (II) acetate paper.

Evaporate the solution on a water bath to 3 to 5 mL with the aid of a current of air, cool, add 10 mL of water, and mix well. Filter the crystals by suction, recrystallize from water immediately, and dry in a desiccator (in vacuum, silica gel) for 6 hours: the crystals melt between 198°C and 203°C (with decomposition).

**Melting point** 142 – 145°C

**Purity (1)** Clarity and color of solution—Dissolve 0.5 g of Prothionamide in 20 mL of ethanol (95): the solution is clear, and shows a yellow color.

(2) **Acid**—Dissolve 3.0 g of Prothionamide in 20 mL of methanol with warming. Add 100 mL of water to the solution, cool in an ice water bath with agitation, and remove any precipitate by filtration. Allow 80 mL of the filtrate to cool to room temperature, and add 0.8 mL of cresol red TS and 0.20 mL of 0.1 mol/L sodium hydroxide VS: a red color develops.

(3) **Heavy metals**—Proceed with 1.0 g of Prothionamide 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 0.6 g of Prothionamide according to Method 3, and perform the test using Apparatus B. To the test solution add 10 mL of a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 50), then add 1.5 mL of strong hydrogen peroxide, and ignite to burn (not more than 3.3 ppm).

**Loss on drying** Not more than 0.5% (1 g, 80°C, 3 hours).

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

**Assay** Weigh accurately about 0.3 g of Prothionamide, previously dried, dissolve in 50 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from orange-red to dark orange-brown (indicator: 2 mL of *p*-naphtholbenzein TS). Perform a blank determination.

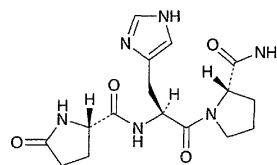
Each mL of 0.1 mol/L perchloric acid VS  
= 18.027 mg of  $C_9H_{12}N_2S$

**Containers and storage** Containers—Well-closed containers.

Storage—Light-resistant.

## Protirelin

プロチレリン



$C_{16}H_{22}N_6O_4$ : 362.38

5-Oxo-L-prolyl-L-histidyl-L-prolinamide [24305-27-9]

Protirelin contains not less than 98.5% of  $C_{16}H_{22}N_6O_4$ , calculated on the dehydrated basis.

**Description** Protirelin occurs as a white powder.

It is freely soluble in water, in methanol, in ethanol (95) and in acetic acid (100).