

$C_6H_7N_3O$: 137.14

Pyridine-4-carbohydrazide [54-85-3]

Isoniazid, when dried, contains not less than 98.5% of $C_6H_7N_3O$.

Description Isoniazid occurs as colorless crystals or a white, crystalline powder. It is odorless.

It is freely soluble in water, sparingly soluble in ethanol (95), slightly soluble in acetic anhydride, and very slightly soluble in diethyl ether.

Identification (1) Dissolve about 0.02 g of Isoniazid in water to make 200 mL. To 5 mL of the solution add 1 mL of 0.1 mol/L hydrochloric acid TS and water to make 50 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 Isoniazid, 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.

pH Dissolve 1.0 g of Isoniazid in 10 mL of freshly boiled and cooled water: the pH of this solution is between 6.5 and 7.5.

Melting point 170 – 173°C

Purity (1) Clarity and color of solution—Dissolve 1.0 g of isoniazid in 20 mL of water: the solution is clear and colorless.

(2) Heavy metals—Proceed with 1.0 g of Isoniazid 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) Arsenic—Prepare the test solution with 0.40 g of Isoniazid according to Method 3, and perform the test using Apparatus B. In this case, add 10 mL of a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 50), then add 1.5 mL of hydrogen peroxide (30), and ignite the ethanol to burn (not more than 5 ppm).

(4) Hydrazine—Dissolve 0.10 g of isoniazid in 5 mL of water, add 0.1 mL of a solution of salicylaldehyde in ethanol (95) (1 in 20), shake immediately, and allow to stand for 5 minutes: no turbidity is produced.

Loss on drying Not more than 0.5% (1 g, 105°C, 2 hours).

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

Assay Weigh accurately about 0.3 g of isoniazid, previously dried, dissolve in 50 mL of acetic acid (100) and 10 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from yellow to green (indicator: 0.5 mL of *p*-naphtholbenzein TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 13.714 mg of $C_6H_7N_3O$

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

Isoniazid Injection

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Isoniazid Injection is an aqueous solution for injection. It contains not less than 95% and not more than 105% of the labeled amount of isoniazid ($C_6H_7N_3O$: 137.14).

Method of preparation Prepare as directed under Injections, with Isoniazid.

Description Isoniazid Injection occurs as a clear, colorless liquid. It has a slight, bitter taste.

pH: 6.5 – 7.5

Identification (1) To a volume of Isoniazid Injection, equivalent to 0.01 g of Isoniazid according to the labeled amount, and add water to make 2 mL. Add 1 mL of silver nitrate-ammonia TS to this solution: a dark turbidity is produced, and a silver mirror is formed on the wall of the test tube with effervescence.

(2) To a volume of Isoniazid Injection, equivalent to 0.1 g of Isoniazid according to the labeled amount, add water to make 4 mL. Add 0.1 g of vanillin and 4 mL of ethanol (95), dissolve by warming moderately, and allow to stand for 3 hours. Collect the precipitated yellow crystals by filtration, and dry at 105°C for 1 hour: the crystals melt between 225°C and 231°C.

Assay To an exactly measured volume of Isoniazid Injection, equivalent to about 0.025 g of isoniazid ($C_6H_7N_3O$), add water to make exactly 250 mL. Pipet 10 mL of the solution, add 10 mL of 1 mol/L hydrochloric acid TS and water to make exactly 100 mL, and use this solution as the sample solution. Dry isoniazid for assay at 105°C for 2 hours, weigh accurately about 0.025 g of the residue, and dissolve in water to make exactly 250 mL. Pipet 10 mL of the solution, add 10 mL of 1 mol/L hydrochloric acid TS and water to make exactly 100 mL, and use this solution as the standard solution. Perform the test as directed under the Ultraviolet-visible Spectrophotometry, and determine the absorbances, A_T and A_S , of the sample solution and the standard solution at the wavelength of 267 nm, respectively.

Amount (mg) of isoniazid ($C_6H_7N_3O$)

$$= \text{amount (mg) of isoniazid for assay} \times \frac{A_T}{A_S}$$

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

Storage—Light-resistant.

Isoniazid Tablets

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Isoniazid Tablets contain not less than 95% and not more than 105% of the labeled amount of isoniazid ($C_6H_7N_3O$: 137.14).

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

Identification Take a quantity of powdered Isoniazid Tablets, equivalent to 0.02 g of Isoniazid according to the labeled amount, add 200 mL of water, shake well, and filter. To 5 mL of the filtrate add 1 mL of 0.1 mol/L hydrochloric acid TS and water to make 50 mL, and determine the absorption spectrum of this solution as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 264 nm and 268 nm.

Dissolution test Perform the test with 1 tablet of Isoniazid Tablets at 50 revolutions per minute according to Method 2 under the Dissolution Test, using 900 mL of water as the test solution. Take 20 mL or more of the dissolved solution 20 minutes after starting the test, and filter through a membrane filter with pore size of not more than 0.45 μm . Discard the first 10 mL of the filtrate, pipet 5 mL of the subsequent, add water to make exactly 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.10 g of isoniazid for assay, previously dried at 105°C for 2 hours, dissolve in water to make exactly 100 mL, then pipet 5 mL of this solution, add water to make exactly 50 mL, and then pipet 5 mL of this solution, add water 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 267 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Isoniazid Tablets in 20 minutes is not less than 75%.

Dissolution rate (%) with respect to the labeled amount of isoniazid ($\text{C}_6\text{H}_7\text{N}_3\text{O}$)

$$= W_S \times \frac{A_T}{A_S} \times \frac{90}{C}$$

W_S : Amount (mg) of isoniazid for assay.

C : Labeled amount (mg) of isoniazid ($\text{C}_6\text{H}_7\text{N}_3\text{O}$) in 1 tablet.

Assay Weigh accurately and powder not less than 20 Isoniazid Tablets. Weigh accurately a quantity of the powder, equivalent to about 0.10 g of isoniazid ($\text{C}_6\text{H}_7\text{N}_3\text{O}$), add 150 mL of water, shake for 30 minutes, then add water to make exactly 200 mL, and filter. Discard the first 10 mL of the filtrate, pipet 5 mL of the subsequent filtrate, add the mobile phase to make exactly 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.05 g of isoniazid for assay, previously dried at 105°C for 2 hours, dissolve in water to make exactly 100 mL. Pipet 5 mL of this solution, add the mobile phase to make exactly 50 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following operating conditions. Determine the peak areas, A_T and A_S , of isoniazid of the sample solution and the standard solution.

Amount (mg) of $\text{C}_6\text{H}_7\text{N}_3\text{O}$

$$= \text{amount (mg) of isoniazid for assay} \times \frac{A_T}{A_S} \times 2$$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 265 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in parti-

cle diameter).

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

Mobile phase: Dissolve 6.80 g of potassium dihydrogenphosphate in water to make 1000 mL. Separately, to 5.76 g of phosphoric acid add water to make 1000 mL. Mix these solutions to adjust the pH to 2.5. To 400 mL of this solution add 600 mL of methanol, and dissolve 2.86 g of sodium tridecanesulfonate in this.

Flow rate: Adjust the flow rate so that the retention time of isoniazid is about 5 minutes.

Selection of column: Dissolve 5 mg of Isoniazid and 5 mg of isonicotinic acid in 100 mL of the mobile phase. Proceed with 10 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of isonicotinic acid and isoniazid in this order with the resolution between these peaks being not less than 1.5.

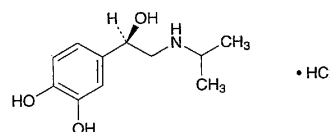
Containers and storage Containers—Tight containers.

Storage—Light-resistant.

l-Isoprenaline Hydrochloride

l-Isoproterenol Hydrochloride

l-塩酸イソプレナリン



$\text{C}_{11}\text{H}_{17}\text{NO}_3 \cdot \text{HCl}$: 247.72

(1*R*)-1-(3,4-Dihydroxyphenyl)-2-(isopropylamino)ethanol monohydrochloride [51-30-9]

l-Isoprenaline Hydrochloride, when dried, contains not less than 98.0% of $\text{C}_{11}\text{H}_{17}\text{NO}_3 \cdot \text{HCl}$.

Description *l*-Isoprenaline Hydrochloride occurs as a white, crystalline powder. It is odorless.

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

It gradually changes in color by air and by light.

Identification (1) Dissolve 0.01 g of *l*-Isoprenaline Hydrochloride in 5 mL of water, and add 1 drop of iron (III) chloride TS: a deep green color develops, and changes through yellow-green to brown on standing.

(2) Dissolve 1 mg each of *l*-Isoprenaline Hydrochloride in 1 mL of water in the test tubes A and B. Add 10 mL of potassium hydrogen phthalate buffer solution, pH 3.5 to A, and add 10 mL of phosphate buffer solution, pH 6.5 to B. To each of the test tubes add 1 mL of iodine TS, allow to stand for 5 minutes, and add 2 mL each of sodium thiosulfate TS: a red color develops in the test tube A, and a deep red color develops in the test tube B.

(3) Dissolve 0.01 g of *l*-Isoprenaline Hydrochloride in 1 mL of water, and add 1 mL of phosphotungstic acid TS: a light brown precipitate is produced.