$C_9H_{11}IN_2O_5$: 354.10
5-Iodo-2′-deoxyuridine [*54-42-2*]

Idoxuridine, when dried, contains not less than 98.0% of $C_9H_{11}IN_2O_5$.

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

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

It dissolves in sodium hydroxide TS.

Melting point: about 176°C (with decomposition).

Identification (1) Dissolve 0.01 g of Idoxuridine in 5 mL of water by warming, add 5 mL of diphenylamine-acetic acid TS, and heat for 5 minutes: a blue color develops.

(2) Heat 0.1 g of Idoxuridine: a purple gas evolves.

(3) Dissolve 2 mg of Idoxuridine in 50 mL of 0.01 mol/L sodium hydroxide. Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Idoxuridine Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

Optical rotation $[\alpha]_D^{20}$: +28 – +31° (after drying, 0.20 g, sodium hydroxide TS, 20 mL, 100 mm).

Purity (1) Clarity and color of solution—Dissolve 0.20 g of Idoxuridine in 5 mL of a solution of sodium hydroxide (1 in 200): the solution is clear and colorless.

(2) Heavy metals—Proceed with 2.0 g of Idoxuridine 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).

(3) Related substances—Dissolve 0.10 g of Idoxuridine in exactly 10 mL of a mixture of dilute ethanol and ammonia solution (28) (99:1), and use this solution as the sample solution. Perform the test with the sample solution as directed under the Thin-layer Chromatography. Spot 50 μL of the sample solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of ethyl acetate and diluted 2-propanol (2 in 3) (4:1) to a distance of about 10 cm, and air-dry the plate. Then develop two-dimensionally at right angles to the first, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): any spot other than the principal spot does not appear.

(4) Iodine and iodide—Dissolve 0.10 g of Idoxuridine in 20 mL of water and 5 mL of sodium hydroxide TS, and add immediately 5 mL of dilute sulfuric acid under ice-cooling. Allow to stand for 10 minutes with occasional shaking, and filter. Transfer the filtrate into a Nessler tube, add 10 mL of chloroform and 3 drops of a solution of potassium iodate (1 in 100), shake for 30 seconds, and allow to stand: the chloroform layer has no more color than the following control solution.

Control solution: Weigh accurately 0.111 g of potassium iodide, and dissolve in water to make 1000 mL. To exactly 1 mL of this solution add 19 mL of water, 5 mL of sodium hydroxide TS and 5 mL of dilute sulfuric acid, mix, and filter. Transfer the filtrate to a Nessler tube, and proceed in the same manner.

Loss on drying Not more than 0.5% (2 g, in vacuum, 60°C, 3 hours).

Residue on ignition Not more than 0.30% (1 g).

Assay Weigh accurately about 0.7 g of Idoxuridine, previously dried, dissolve in 80 mL of *N,N*-dimethylformamide, and titrate with 0.1 mol/L tetramethylammonium hydroxide VS until the color of the solution changes from yellow through yellow-green to blue (indicator: 5 drops of thymol blue-dimethylformamide TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L tetramethylammonium hydroxide VS
= 35.410 mg of $C_9H_{11}IN_2O_5$

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

Idoxuridine Ophthalmic Solution

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Idoxuridine Ophthalmic Solution contains not less than 90% and not more than 110% of the labeled amount of idoxuridine ($C_9H_{11}IN_2O_5$: 354.10).

Method of preparation Prepare as directed under Ophthalmic Solutions, with Idoxuridine.

Description Idoxuridine Ophthalmic Solution is a clear, colorless liquid.

Identification (1) To a volume of Idoxuridine Opthalmic Solution, equivalent to 5 mg of Idoxuridine according to the labeled amount, add 5 mL of diphenylamine-acetic acid TS, and heat for 20 minutes: a light blue color develops.

(2) Place a volume of Idoxuridine Ophthalmic Solution, equivalent to 5 mg of Idoxuridine according to the labeled amount, in a porcelain crucible, add 0.1 g of anhydrous sodium carbonate, heat slowly, evaporate to dryness and ignite until the residue is incinerated. Dissolve the residue in 5 mL of water, acidify with hydrochloric acid, and add 2 to 3 drops of sodium nitrite TS: a yellow-brown color develops. Then add 2 to 3 drops of starch TS: a deep blue color develops.

(3) To a volume of Idoxuridine Ophthalmic Solution, equivalent to 2 mg of Idoxuridine according to the labeled amount, add 0.01 mol/L sodium hydroxide TS to make 50 mL. Determine the absorption spectrum of this solution as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 277 nm and 281 nm.

pH 4.5 – 7.0

Purity 5-Iodouracil and 2′-deoxyuridine—To a volume of Idoxuridine Ophthalmic Solution, equivalent to 4.0 mg of Idoxuridine according to the labeled amount, add water to make exactly 5 mL, and use this solution as the sample solution. Separately, dissolve 12.0 mg of 5-iodouracil for liquid chromatography and 4.0 mg of 2′-deoxyuridine for liquid chromatography in water to make exactly 200 mL. Measure exactly 5 mL of this solution, add water to make exactly 25 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 conditions, and determine the peak areas of 5-iodouracil and 2′-deoxyuridine: the peak areas of 5-iodouracil and 2′-deoxyuridine of the sample solution are not more than the peak areas of 5-iodouracil and 2′-deoxyuridine of 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 30 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 to 10 μm in particle diameter).

Column temperature: Room temperature.

Mobile phase: A mixture of water and methanol (24:1).

Flow rate: Adjust the flow rate so that the retention time of 2′-deoxyuridine is about 6 minutes.

Selection of column: Proceed with 10 μL of the standard solution under the above operating conditions. Use a column giving elution of 2′-deoxyuridine and 5-iodouracil in this order with the resolution between these peaks being not less than 2.0.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of 2′-deoxyuridine from 10 μL of the standard solution is between 5 mm and 15 mm.

Assay Measure exactly a volume of Idoxuridine Ophthalmic Solution, equivalent to 3 mg of idoxuridine ($C_9H_{11}IN_2O_5$) according to the labeled amount, add exactly 2 mL of the internal standard solution, then add water to make 10 mL, and use this solution as the sample solution. Separately weigh accurately about 0.01 g of Idoxuridine Reference Standard, previously dried at 60°C for 3 hours, dissolve in water to make exactly 10 mL. Measure exactly 3 mL of this solution, add exactly 2 mL of the internal standard solution, then add water to make 10 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 conditions, and calculate the ratios, Q_T and Q_S, of the peak area of idoxuridine to that of the internal standard, respectively.

$$\text{Amount (mg) of idoxuridine } (C_9H_{11}IN_2O_5) = \text{amount (mg) of Idoxuridine Reference Standard} \times \frac{Q_T}{Q_S} \times \frac{3}{10}$$

Internal standard solution—A solution of sulfathiazole in mobile phase (1 in 4000).

Operating conditions—

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

Column: A stainless steel column about 4 mm in inside diameter and 15 to 30 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 to 10 μm in particle diameter).

Column temperature: Room temperature.

Mobile phase: A mixture of water and methanol (87:13).

Flow rate: Adjust the flow rate so that the retention time of idoxuridine is about 9 minutes.

Selection of column: Proceed with 10 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of idoxuridine and the internal standard in this order with the resolution between these peaks being not less than 2.0.

Containers and storage Containers—Tight containers.

Storage—Light-resistant, in a cold place, and avoid freezing.

Ifenprodil Tartrate

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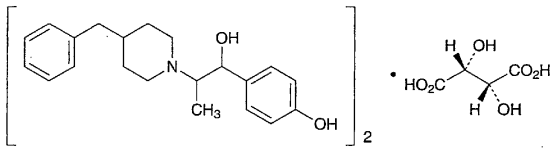

$(C_{21}H_{27}NO_2)_2.C_4H_6O_6$: 800.98

(1*RS*,2*SR*)-4-[2-(4-Benzylpiperidin-1-yl)-1-hydroxypropylphenol hemi-(2*R*,3*R*)-tartrate [*23210-58-4*]

Ifenprodil Tartrate contains not less than 98.5% of $(C_{21}H_{27}NO_2)_2.C_4H_6O_6$, calculated on the anhydrous basis.

Description Ifenprodil Tartrate occurs as a white crystalline powder. It is odorless.

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

Optical rotation $[\alpha]_D^{20}$: +11 – +15° (1.0 g, calculated on the anhydrous basis, ethanol (95), 20 mL, 100 mm).

Melting point: about 148°C (with decomposition).

Identification (1) Determine the absorption spectrum of a solution of Ifenprodil Tartrate in methanol (1 in 100,000) 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.

(2) Determine the infrared absorption spectrum of Ifenprodil Tartrate 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) Dissolve 0.4 g of Ifenprodil Tartrate in 40 mL of water by warming. After cooling, add 0.5 mL of ammonia TS to this solution, extract with two 40-mL portions of chloroform, and collect the water layer. Evaporate 30 mL of the water layer on a water bath to dryness, and after cooling, dissolve the residue in 6 mL of water: the solution responds to the Qualitative Tests for tartrate.

Purity (1) Heavy metals—Proceed with 2.0 g of Ifenprodil Tartrate 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).

(2) Related substances—Dissolve 0.30 g of Ifenprodil Tartrate in 10 mL of diluted ethanol (95) (3 in 4), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add diluted ethanol (95) (3 in 4) to make exactly 200 mL, and use this solution as the standard solution.