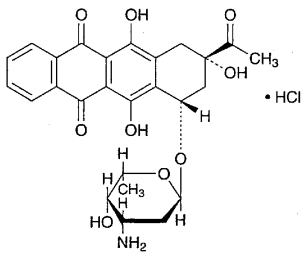
Idarubicin Hydrochloride

塩酸イダルビシン



$C_{26}H_{27}NO_9$.HCl: 533.95
(2*S*,4*S*)-2-Acetyl-4-(3-amino-2,3,6-trideoxy-α-L-*lyxo*-hexopyranosyloxy)-1,2,3,4-tetrahydro-2,5,12-trihydroxynaphthacene-6,11-dione monohydrochloride
[*57852-57-0*]

Idarubicin Hydrochloride contains not less than 960 μg (potency) per mg, calculated on the anhydrous basis. The potency of Idarubicin Hydrochloride is expressed as mass (potency) of idarubicin hydrochloride ($C_{26}H_{27}NO_9$.HCl).

Description Idarubicin Hydrochloride occurs as a yellow-red powder.

It is sparingly soluble in methanol, and slightly soluble in water and in ethanol (95).

Identification **(1)** Determine the absorption spectra of solutions of Idarubicin Hydrochloride and Idarubicin Hydrochloride Reference Standard in methanol (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare these spectra: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectra of Idarubicin Hydrochloride and Idarubicin Hydrochloride Reference Standard as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare these spectra: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) Dissolve 2 mg of Idarubicin Hydrochloride in 3 mL of water, and add 1 mL of dilute nitric acid and 3 drops of silver nitrate TS: a white turbidity is produced.

Absorbance $E^{1\%}_{1\,cm}$ (482 nm): 204 - 210 (0.02 g calculated on the anhydrous basis, methanol, 1000 mL).

Optical rotation $[\alpha]_D^{20}$: +191 - +197° (0.02 g calculated on the anhydrous basis, methanol, 20 mL, 100 mm).

pH The pH of a solution of Idarubicin Hydrochloride (1 in 200) is between 5.0 and 6.5.

Purity **(1)** Clarity and color of solution—Being specified separately.

(2) Heavy metals—Being specified separately.

(3) Related substances—Being specified separately.

(4) Residual solvent—Being specified separately.

Water Not more than 5.0% (0.5 g, volumetric titration, direct titration).

Residue on ignition Being specified separately.

Bacterial endotoxins Less than 8.9 EU/mg (potency).

Assay Weigh accurately an amount of Idarubicin Hydrochloride and Idarubicin Hydrochloride Reference Standard, equivalent to about 0.01 g (potency), dissolve each in the mobile phase containing no sodium lauryl sulfate to make exactly 50 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with exactly 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and determine peak areas, A_T and A_S, of idarubicin of these solutions.

Amount [μg (potency)] of $C_{26}H_{27}NO_9$.HCl
= amount [mg (potency)] of Idarubicin Hydrochloride Reference Standard $\times \frac{A_T}{A_S} \times 1000$

Operating conditions—

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

Column: A stainless steel column 3.9 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (4 μm in particle diameter).

Column temperature: A constant temperature of about 35°C.

Mobile phase: Dissolve 10.2 g of potassium dihydrogenphosphate in a suitable amount of water, add 1 mL of phosphoric acid and water to make 750 mL, and add 250 mL of tetrahydrofuran. To 500 mL of this solution add 0.72 g of sodium lauryl sulfate and 0.5 mL of *N,N*-dimethyl-*n*-octylamine, and adjust to pH 4 with 2 mol/L sodium hydroxide TS.

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

System suitability—

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, the number of theoretical steps of the peak of idarubicin is not less than 3000 steps.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of idarubicin is not more than 2.0%.

Containers and storage Containers—Tight containers.

Idoxuridine

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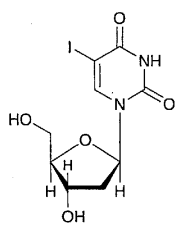

$C_9H_{11}IN_2O_5$: 354.10
5-Iodo-2′-deoxyuridine [*54-42-2*]

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