

Meglumine Sodium Amidotrizoate Injection

アミドトリゾ酸ナトリウムメグルミン注射液

Meglumine Sodium Amidotrizoate Injection is an aqueous solution for injection. It contains not less than 95% and not more than 105% of the labeled amount of amidotrizoic acid ($C_{11}H_9I_3N_2O_4$: 613.91).

Method of preparation

(1)	
Amidotrizoic Acid (anhydrous)	522.77 g
Sodium Hydroxide	25.16 g
Meglumine	43.43 g
Water for Injection	a sufficient quantity
To make 1000 mL	
(2)	
Amidotrizoic Acid (anhydrous)	471.78 g
Sodium Hydroxide	5.03 g
Meglumine	125.46 g
Water for Injection	a sufficient quantity
To make 1000 mL	
(3)	
Amidotrizoic Acid (anhydrous)	597.30 g
Sodium Hydroxide	6.29 g
Meglumine	159.24 g
Water for Injection	a sufficient quantity
To make 1000 mL	

Prepare as directed under Injections, with the above ingredients (1), (2) or (3).

Description Meglumine Sodium Amidotrizoate Injection is a clear, colorless to pale yellow, slightly viscous liquid.

It gradually changes in color by light.

Identification (1) To a volume of Meglumine Sodium Amidotrizoate Injection, equivalent to 1 g of Amidotrizoic Acid according to the labeled amount, add 25 mL of water, and add 2.5 mL of dilute hydrochloric acid with stirring; a white precipitate is produced. Filter the precipitate by suction through a glass filter (G4), wash with two 10-mL portions of water, and dry at 105°C for 1 hour. Proceed with the precipitate so obtained as directed in the Identification (2) under Amidotrizoic Acid.

(2) To 1 mL of Meglumine Sodium Amidotrizoate Injection add 1 mL of potassium 1,2-naphthoquinone-4-sulfonate TS and 0.2 mL of sodium hydroxide TS: a deep red color develops.

(3) Meglumine Sodium Amidotrizoate Injection responds to the Qualitative Tests (1) for sodium salt.

Optical rotation

Method of preparation (1) α_D^{20} : $-1.01 - -1.17^\circ$ (100 mm).

Method of preparation (2) α_D^{20} : $-2.91 - -3.36^\circ$ (100 mm).

Method of preparation (3) α_D^{20} : $-3.69 - -4.27^\circ$ (100 mm).

pH 6.0 - 7.7

Purity (1) Primary aromatic amines—To a volume of Meglumine Sodium Amidotrizoate Injection, equivalent to 0.20 g of Amidotrizoic Acid according to the labeled amount, add 6 mL of water, mix, add 4 mL of a solution of sodium nitrite (1 in 100) and 10 mL of 1 mol/L hydrochloric acid TS, and shake. Proceed as directed in the Purity (2) under Amidotrizoic Acid: the absorbance is not more than 0.19.

(2) Iodine and iodide—To a volume of Meglumine Sodium Amidotrizoate Injection, equivalent to 0.25 g of Amidotrizoic Acid according to the labeled amount, add water to make 20 mL, add 5 mL of dilute nitric acid, shake well, and filter by suction through a glass filter (G4). Add 5 mL of chloroform to the filtrate, and shake vigorously: no color develops in the chloroform layer. Then add 1 mL of hydrogen peroxide (30), and shake vigorously: the chloroform layer has no more color than the following control solution.

Control solution: Dissolve 0.10 g of potassium iodide in water to make 100 mL. Add 20 mL of water to 0.10 mL of this solution, add 5 mL of dilute nitric acid, 5 mL of chloroform and 1 mL of hydrogen peroxide (30), and shake vigorously.

Pyrogen Dilute Meglumine Sodium Amidotrizoate Injection with isotonic sodium chloride solution so as to contain 0.20 g of amidotrizoic acid ($C_{11}H_9I_3N_2O_4$) per mL according to the labeled amount, and perform the test: it meets the requirements of the Pyrogen Test.

Assay To an exactly measured volume of Meglumine Sodium Amidotrizoate Injection, equivalent to about 0.5 g of amidotrizoic acid ($C_{11}H_9I_3N_2O_4$), add water to make exactly 200 mL. Pipet 2 mL of this solution, add exactly 10 mL of the internal standard solution and water to make 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.25 g of amidotrizoic acid for assay, separately determined its loss on drying (105°C, 4 hours), dissolve in a solution of meglumine (3 in 1000) to make exactly 100 mL, then pipet 2 mL of this solution, add exactly 10 mL of the internal standard solution and water to make 100 mL, and use this solution as the standard solution. Perform the test with 5 μ L 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 amidotrizoic acid to that of the internal standard.

$$\begin{aligned} & \text{Amount (mg) of amidotrizoic acid (C}_{11}\text{H}_9\text{I}_3\text{N}_2\text{O}_4\text{)} \\ &= \text{amount (mg) of amidotrizoic acid for assay,} \\ & \quad \text{calculated on the dried basis} \\ & \quad \times \frac{Q_T}{Q_S} \end{aligned}$$

Internal standard solution—Dissolve 0.06 g of acetrizoic acid in a solution of meglumine (3 in 1000) to make 100 mL.

Operating conditions—

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

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μ m in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: Dissolve 1.7 g of tetrabutylammonium phosphate and 7.0 g of dipotassium hydrogenphosphate in 750 mL of water, adjust the pH to 7.0 with diluted phosphoric acid (1 in 10), add water to make 800 mL, then add 210 mL of acetonitrile, and mix.

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

System suitability—

System performance: When the procedure is run with 5 μ L of the standard solution under the above operating conditions, amidotrizoic acid and the internal standard are eluted in this order with the resolution between these peaks being not less than 6.

System repeatability: When the test is repeated 6 times with 5 μ L of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of amidotrizoic acid to that of the internal standard is not more than 1.0%.

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

Storage—Light-resistant.

Meglumine Sodium Iodamide Injection

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Meglumine Sodium Iodamide Injection is an aqueous solution for injection. It contains not less than 59.7 w/v% and not more than 65.9 w/v% of iodamide ($C_{12}H_{11}I_3N_2O_4$; 627.94).

Method of preparation

Iodamide	627.9 g
Sodium Hydroxide	6.0 g
Meglumine	165.9 g
Water for Injection	a sufficient quantity
To make 1000 mL	

Prepare as directed under Injections, with the above ingredients.

Description Meglumine Sodium Iodamide Injection is a clear, colorless to pale yellow, slightly viscous liquid.

It gradually changes in color by light.

Identification (1) To 2 mL of Meglumine Sodium Iodamide Injection add 25 mL of water, and add 3 mL of dilute hydrochloric acid with thorough stirring: a white precipitate is formed. Filter the precipitate by suction through a glass filter (G3), and wash with two 10-mL portions of water. Transfer the precipitate to a suitable flask, add 100 mL of water, dissolve by heating, and gently boil until the volume becomes about 30 mL. After cooling, collect the separated crystals by filtration, dry at 105°C for 1 hour, and proceed as directed in the Identification (1) and (2) under Iodamide.

(2) Determine the infrared absorption spectrum of the dried crystals obtained in (1) as directed in the potassium bromide disk method under the Infrared Spectrophotometry: it exhibits absorption at the wave numbers of about

3390 cm^{-1} , 1369 cm^{-1} , 1296 cm^{-1} , 1210 cm^{-1} and 1194 cm^{-1} .

(3) To 1 mL of Meglumine Sodium Iodamide Injection add 1 mL of potassium 1,2-naphthoquinone-4-sulfonate TS and 0.2 mL of sodium hydroxide TS: a deep red color is produced.

(4) Meglumine Sodium Iodamide Injection responds to the Qualitative Test (1) for sodium salt.

Optical rotation α_D^{20} : $-3.84 - -4.42^\circ$ (100 mm).

pH 6.5 – 7.5

Purity (1) Primary aromatic amines—Mix 0.30 mL of Meglumine Sodium Iodamide Injection and 6 mL of water, then add 4 mL of a solution of sodium nitrite (1 in 100) and 10 mL of 1 mol/L hydrochloric acid TS, shake well, and proceed as directed in the Purity (2) under Iodamide: the absorbance is not more than 0.22.

(2) Iodine and iodide—To 0.40 mL of Meglumine Sodium Iodamide Injection add water to make 20 mL, then add 5 mL of dilute nitric acid, shake well, filter by suction through a glass filter (G3). To the filtrate add 5 mL of chloroform, and shake vigorously: no color develops in the chloroform layer. Then add 1 mL of a strong hydrogen peroxide solution, and shake vigorously: the chloroform layer has no more color than the control solution.

Control solution: Dissolve 0.10 g of potassium iodide in water to make 100 mL. To a 0.10-mL portion of this solution add 20 mL of water, 5 mL of dilute nitric acid, 5 mL of chloroform and 1 mL of strong hydrogen peroxide solution, and shake vigorously.

Pyrogen Dilute Meglumine Sodium Iodamide Injection with isotonic sodium chloride solution so as to contain 0.30 mL of Meglumine Sodium Iodamide Injection per mL according to the labeled amount, and perform the test: it meets the requirements of the Pyrogen Test.

Assay To an exactly measured 8 mL of Meglumine Sodium Iodamide Injection add sodium hydroxide TS to make exactly 100 mL, and use this solution as the sample solution. Pipet 10 mL of the sample solution into a saponification flask, add 30 mL of sodium hydroxide TS and 1 g of zinc powder, and proceed as directed in the Assay under Iodamide.

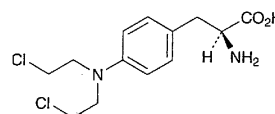
Each mL of 0.1 mol/L silver nitrate VS
= 20.931 mg of $C_{12}H_{11}I_3N_2O_4$

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

Storage—Light-resistant.

Melphalan

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$C_{13}H_{18}Cl_2N_2O_2$: 305.20
4-Bis(2-chloroethyl)amino-L-phenylalanine [148-82-3]