

$$\begin{aligned} &\text{Amount (mg) of mefruside (C}_{13}\text{H}_{19}\text{ClN}_2\text{O}_5\text{S}_2) \\ &= \text{amount (mg) of mefruside for assay} \\ &\quad \times \frac{A_T}{A_S} \end{aligned}$$

**Containers and storage** Containers—Tight containers.

## Meglumine Amidotrizoate Injection

アミドトリゾ酸メグルミン注射液

Meglumine Amidotrizoate Injection is an aqueous solution for injection. It contains not less than 46.9 w/v% and not more than 51.8 w/v% of amidotrizoic acid (C<sub>11</sub>H<sub>9</sub>I<sub>3</sub>N<sub>2</sub>O<sub>4</sub>; 613.91).

### Method of preparation

Amidotrizoic Acid (anhydrous)	493.2 g
Meglumine	156.8 g
Water for Injection	a sufficient quantity
To make 1000 mL	

Prepare as directed under Injections, with the above ingredients.

**Description** Meglumine Amidotrizoate 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 Amidotrizoate Injection 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 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.

**Optical rotation**  $\alpha_D^{20}$ : -3.63 - -4.20° (100 mm).

**pH** 6.0 - 7.7

**Purity (1)** Primary aromatic amines—Mix 0.40 mL of Meglumine Amidotrizoate Injection with 6 mL of water, 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 0.50 mL of Meglumine Amidotrizoate Injection add water to make 20 mL, shake with 5 mL of dilute nitric acid, 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.

roform and 1 mL of hydrogen peroxide (30), and shake vigorously.

**Pyrogen** Prepare a solution with isotonic sodium chloride solution so as to contain 0.40 mL of Meglumine Amidotrizoate Injection per 1 mL, and perform the test: it meets the requirements of the Pyrogen Test.

**Assay** To an exactly measured 1 mL of Meglumine Amidotrizoate Injection 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. 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  $\mu$ 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.

$$\begin{aligned} &\text{Amount (mg) of amidotrizoic acid (C}_{11}\text{H}_9\text{I}_3\text{N}_2\text{O}_4) \\ &= \text{amount (mg) of amidotrizoic acid for assay,} \\ &\quad \text{calculated on the dried basis} \\ &\quad \times \frac{Q_T}{Q_S} \times 2 \end{aligned}$$

**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  $\mu$ 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  $\mu$ 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  $\mu$ 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.