pare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Mefruside, 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.

(3) Perform the test with Mefruside as directed under the Flame Coloration Test (2): a green color appears.

Melting point 149 - 152°C

Purity (1) Heavy metals—Dissolve 1.0 g of Mefruside in 30 mL of acetone, and add 2 mL of dilute acetic acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 2.0 mL of Standard Lead Solution add 30 mL of acetone, 2 mL of dilute acetic acid and water to make 50 mL (not more than 20 ppm).

(2) Arsenic—Prepare the test solution with 1.0 g of Mefruside according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(3) Related substances—Dissolve 0.20 g of Mefruside in 10 mL of acetone, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add acetone to make exactly 200 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of chloroform and acetone (5:2) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

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 0.5 g of Mefruside, previously dried, dissolve in 80 mL of *N,N*-dimethylformamide, and titrate with 0.1 mol/L tetramethylammonium hydroxide VS (potentiometric titration). Separately, perform a blank determination with a solution prepared by adding 13 mL of water to 80 mL of *N,N*-dimethylformamide, and make any necessary correction.

Each mL of 0.1 mol/L tetramethylammonium hydroxide VS
= 38.289 mg of $C_{13}H_{19}ClN_2O_5S_2$

Containers and storage Containers—Well-closed containers.

Mefruside Tablets

メフルシド錠

Mefruside Tablets contain not less than 95% and not more than 105% of the labeled amount of mefruside ($C_{13}H_{19}ClN_2O_5S_2$: 382.88).

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

Identification (1) Weigh a quantity of powdered Mefruside Tablets, equivalent to 0.3 g of Mefruside according to the labeled amount, shake with 15 mL of heated methanol for 20 minutes, and filter. Add 25 mL of water to the filtrate, and allow to stand while ice-cooling for 30 minutes. Filter the white precipitate formed, wash with water, and dry at 105°C for 2 hours: the precipitate melts between 149°C and 152°C.

(2) Weigh a quantity of powdered Mefruside Tablets, equivalent to 0.01 g of Mefruside according to the labeled amount, shake with 70 mL of methanol strongly for 15 minutes, add methanol to make 100 mL, and filter. Determine the absorption spectrum of the filtrate as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 274 nm and 278 nm, and between 283 nm and 287 nm.

Dissolution test Perform the test with 1 tablet of Mefruside 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 45 minutes after starting the test, and filter through a filter paper for quantitative analysis (5C). Discard the first 5 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.070 g of mefruside for assay, previously dried at 105°C for 2 hours, dissolve in methanol to make exactly 50 mL. Pipet 2 mL of this solution, add water to make exactly 100 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 285 nm in a layer of 5 cm in length as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Mefruside Tablets in 45 minutes is not less than 85%.

Dissolution rate (%) with respect to the labeled amount of mefruside ($C_{13}H_{19}ClN_2O_5S_2$)

$$= W_S \times \frac{A_T}{A_S} \times \frac{1}{C} \times 36$$

W_S: Amount (mg) of mefruside for assay.
C: Labeled amount (mg) of mefruside ($C_{13}H_{19}ClN_2O_5S_2$) in 1 tablet.

Assay Weigh accurately not less than 20 Mefruside Tablets, and powder. Weigh accurately a portion of the powder, equivalent to about 0.065 g of mefruside ($C_{13}H_{19}ClN_2O_5S_2$), shake with 70 mL of methanol for 15 minutes, then add methanol to make exactly 100 mL, and filter. Discard the first 20 mL of the filtrate, take exactly 10 mL of the subsequent filtrate, add methanol to make exactly 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.065 g of mefruside for assay, previously dried at 105°C for 2 hours, and dissolve in methanol to make exactly 100 mL. Pipet 10 mL of this solution, add methanol 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 285 nm as directed under the Ultraviolet-visible Spectrophotometry.

Amount (mg) of mefruside ($C_{13}H_{19}ClN_2O_5S_2$)
= amount (mg) of mefruside for assay
$\times \frac{A_T}{A_S}$

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 ($C_{11}H_9I_3N_2O_4$: 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 α_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.

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 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 amidotrizoic acid to that of the internal standard.

Amount (mg) of amidotrizoic acid ($C_{11}H_9I_3N_2O_4$)
= amount (mg) of amidotrizoic acid for assay, calculated on the dried basis
$\times \frac{Q_T}{Q_S} \times 2$

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 μm 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 μL 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 μL 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.