drops of barium chloride TS: a white precipitate is produced.

(4) Determine the absorption spectrum of a solution of Furosemide in dilute sodium hydroxide TS (1 in 25,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 1: both spectra exhibit similar intensities of absorption at the same wavelengths. Separately, determine the absorption spectrum of a solution of Furosemide in methanol (1 in 250,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 2: both spectra exhibit similar intensities of absorption at the same wavelengths.

Purity **(1)** Clarity and color of solution—Dissolve 0.10 g of Furosemide in 10 mL of ethanol (95) by warming, and allow to cool to room temperature: the solution is colorless and clear. Dissolve 0.5 g of Furosemide in 10 mL of a solution of sodium hydroxide (1 in 50): the solution is also colorless and clear.

(2) Chloride—Dissolve 0.5 g of Furosemide in 30 mL of dilute sodium hydroxide TS, add 1 mL of nitric acid, and filter. To 10 mL of the filtrate add 6 mL of dilute nitric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 0.25 mL of 0.01 mol/L hydrochloric acid VS, 6 mL of dilute nitric acid and water to make 50 mL (not more than 0.055%).

(3) Sulfate—Dissolve 0.20 g of Furosemide in 10 mL of dilute sodium hydroxide TS, add 1 mL of nitric acid, and filter. Add 2 mL of barium chloride TS, and allow to stand for 10 minutes: no turbidity is produced.

(4) Heavy metals—Proceed with 2.0 g of Furosemide 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).

(5) Primary aromatic amines—Dissolve 0.080 g of Furosemide in acetone to make exactly 100 mL. Measure 1.0 mL of the solution, add 3 mL of water, cool with ice, add 3.0 mL of dilute hydrochloric acid and 0.15 mL of sodium nitrite TS, shake, and allow to stand for 1 minute. Shake well this solution with 1.0 mL of ammonium amidosulfate TS, allow to stand for 3 minutes, then add 1.0 mL of *N*-(1-naphthyl)-*N'*-diethylethylenediamine oxalate TS, shake well, and allow to stand for 5 minutes. Determine the absorbance of this solution at 530 nm as directed under the Ultraviolet-visible Spectrophotometry, using a solution, prepared with 1.0 mL of acetone in the same manner, as the blank: the absorbance is not more than 0.10.

Loss on drying Not more than 0.5% (1 g, 105°C, 4 hours).

Residue on ignition Not more than 0.10% (1 g).

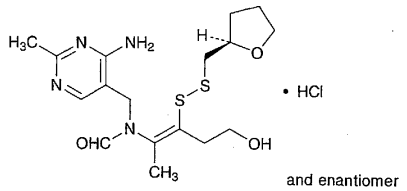
Assay Weigh accurately about 0.5 g of Furosemide, previously dried, dissolve in 50 mL of *N,N*-dimethylformamide, and titrate with 0.1 mol/L sodium hydroxide VS until the color of the solution changes from yellow to blue (indicator: 3 drops of bromothymol blue TS). Perform a blank determination with a mixture of 50 mL of *N,N*-dimethylformamide and 15 mL of water.

Each mL of 0.1 mol/L sodium hydroxide VS
= 33.075 mg of $C_{12}H_{11}ClN_2O_5S$

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

Fursultiamine Hydrochloride

塩酸フルスルチアミン



$C_{17}H_{26}N_4O_3S_2.HCl$: 435.00
N-(4-Amino-2-methylpyrimidin-5-ylmethyl)-*N*-{4-hydroxy-1-methyl-2-[(*RS*)-tetrahydrofuran-2-ylmethyldisulfanyl]-but-1-en-1-yl}formamide monohydrochloride
[*804-30-8*, Fursultiamine]

Fursultiamine Hydrochloride contains not less than 98.5% of $C_{17}H_{26}N_4O_3S_2.HCl$, calculated on the dried basis.

Description Fursultiamine Hydrochloride occurs as white crystals or crystalline powder. It is odorless or has a characteristic odor, and has a bitter taste.

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

Identification **(1)** Dissolve 5 mg of Fursultiamine Hydrochloride in 6 mL of 0.1 mol/L hydrochloric acid TS, add 0.1 g of zinc powder, allow to stand for several minutes, and filter. To 3 mL of the filtrate, add 3 mL of sodium hydroxide TS and 0.5 mL of potassium hexacyanoferrate (III) TS, then add 5 mL of 2-methyl-1-propanol, shake vigorously for 2 minutes, allow to stand to separate the 2-methyl-1-propanol layer, and examine under ultraviolet light (main wavelength: 365 nm): the 2-methyl-1-propanol layer shows a blue-purple fluorescence. The fluorescence disappears by acidifying, and appears again by alkalifying.

(2) Determine the infrared absorption spectrum of a solution of Fursultiamine Hydrochloride, previously dried in a desiccator (in vacuum, phosphorus (V) oxide) for 24 hours, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum, or with the spectrum of Fursultiamine Hydrochloride Reference Standard, previously dried in a desiccator (in vacuum, phosphorus (V) oxide) for 24 hours: both spectra exhibit similar intensities of absorption at the same wave numbers. If any differences appear, dissolve the Fursultiamine Hydrochloride in water, evaporate the water, and dry the residue in a desiccator (in vacuum, phosphorus (V) oxide) for 24 hours, and repeat the test.

(3) A solution of Fursultiamine Hydrochloride (1 in 50) responds to the Qualitative Tests (2) for chloride.

Purity **(1)** Clarity of solution—Dissolve 1.0 g of Fursultiamine Hydrochloride in 20 mL of water: the solution is clear and colorless.

(2) Sulfate—Proceed with 1.5 g of Fursultiamine Hydrochloride, and perform the test. Prepare the control solution with 0.35 mL of 0.005 mol/L sulfuric acid VS (not more than 0.011%).

(3) Heavy metals—Proceed with 1.0 g of Fursultiamine

Hydrochloride according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(4) Related substances—Dissolve 0.10 g of Fursultiamine Hydrochloride in 100 mL of the mobile phase, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase to make exactly 100 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 condition. Determine each peak area of each solution by the automatic integration method: the total area of the peaks other than the peak of fursultiamine from the sample solution is not larger than the peak area of fursultiamine from the standard solution.

Operating conditions—

Detector, column, column temperature, mobile phase, flow rate, and selection of column: Proceed as directed in the operating conditions in the Assay.

Detector sensitivity: Adjust the detection sensitivity so that the peak height of fursultiamine from 10 μL of the standard solution is between 20 mm and 30 mm.

Time span of measurement: About 3 times as long as the retention time of fursultiamine.

Water Not more than 5.0% (0.3 g, direct titration).

Residue on ignition Not more than 0.10% (1 g).

Assay Weigh accurately about 0.055 g each of Fursultiamine Hydrochloride and Fursultiamine Hydrochloride Reference Standard, separately determined for water, and dissolve each in 50 mL of water, and add exactly 10 mL each of the internal standard solution, then add water to make exactly 100 mL. To 8 mL each of the solution add water to make 50 mL, and use these solutions as the sample solution and the standard solution, respectively. 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 fursultiamine to that of the internal standard, respectively.

Amount (mg) of $C_{17}H_{26}N_4O_3S_2$.HCl
= amount (mg) of Fursultiamine Hydrochloride Reference Standard, calculated on the anhydrous basis
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of isopropyl 4-aminobenzoate in ethanol (95) (3 in 400).

Operating conditions—

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

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

Column temperature: A constant temperature of about 50°C.

Mobile phase: Dissolve 1.01 g of sodium 1-heptane sulfonate in 1000 mL of diluted acetic acid (100) (1 in 100). To 675 mL of this solution add 325 mL of a mixture of methanol and acetonitrile (3:2).

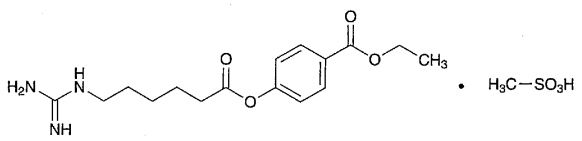
Flow rate: Adjust the flow rate so that the retention time of Fursultiamine is about 9 minutes.

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 fursultiamine and the internal standard in this order with the resolution between these peaks being not less than 10.

Containers and storage Containers—Tight containers.

Gabexate Mesilate

メシル酸ガベキサート



$C_{16}H_{23}N_3O_4.CH_4O_3S$: 417.48
Ethyl 4-(6-guanidinohexanoyloxy)benzoate monomethanesulfonate [*56974-61-9*]

Gabexate Mesilate, when dried, contains not less than 98.5% of $C_{16}H_{23}N_3O_4.CH_4O_3S$.

Description Gabexate Mesilate occurs as white crystals or crystalline powder.

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

Identification **(1)** To 4 mL of a solution of Gabexate Mesilate (1 in 2000) add 2 mL of 1-naphthol TS and 1 mL of diacetyl TS, and allow to stand for 10 minutes: a red color develops.

(2) Dissolve 1 g of Gabexate Mesilate in 5 mL of water, add 2 mL of sodium hydroxide TS, and heat in a water bath for 5 minutes. After cooling, add 2 mL of dilute nitric acid and 5 mL of ethanol (95), shake, add 5 drops of iron (III) chloride TS, and shake: a purple color develops.

(3) Determine the absorption spectrum of a solution of Gabexate Mesilate (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Gabexate Mesilate Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(4) To 0.1 g of Gabexate Mesilate add 0.2 g of sodium hydroxide, fuse by heating gently, and continue the heating for 20 to 30 seconds. After cooling, add 0.5 mL of water and 3 mL of dilute hydrochloric acid, and warm: the gas evolved changes a potassium iodate-starch paper to blue.

pH Dissolve 1.0 g of Gabexate Mesilate in 10 mL of water: the pH of the solution is between 4.5 and 5.5.

Melting point 90 - 93°C

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Gabexate Mesilate in 10 mL of water: the solution is clear and colorless.

(2) Heavy metals—Proceed with 2.0 g of Gabexate Mesi-