Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 281 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: Room temperature.

Mobile phase: A mixture of water and acetonitrile (1:1).

Flow rate: Adjust the flow rate so that the retention time of 4-chlorophenol is about 7 minutes.

Selection of column: Proceed with 20 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of the internal standard and 4-chlorophenol in this order, and showing complete separation between these peaks.

Loss on drying Not more than 0.5% (1 g, in vacuum, phosphorus (V) oxide, 4 hours).

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

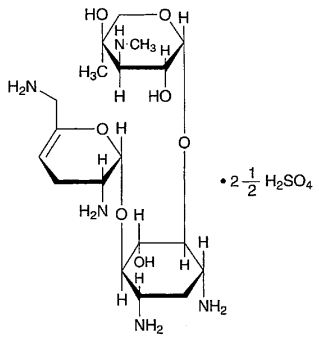
Assay Weigh accurately about 0.8 g of Simfibrate, previously dried, add exactly 50 mL of 0.1 mol/L potassium hydroxide-ethanol VS, and boil gently under a reflux condenser with a carbon dioxide absorption tube (soda lime) on a water bath for 60 minutes. After cooling, titrate the excess potassium hydroxide immediately with 0.1 mol/L hydrochloric acid VS (indicator: 3 drops of phenolphthalein TS). Perform a blank determination.

Each mL of 0.1 mol/L potassium hydroxide-ethanol VS
= 23.468 mg of $C_{23}H_{26}Cl_2O_6$

Containers and storage Containers—Well-closed containers.

Sisomicin Sulfate

硫酸シソマイシン



$C_{19}H_{37}N_5O_7.2½H_2SO_4$: 692.72

O-3-Deoxy-4-*C*-methyl-3-methylamino-β-L-arabinopyranosyl-(1→6)-*O*-[2,6-diamino-4,5-dehydro-2,3,4,6-tetradeoxy-α-D-*glycero*-hexopyranosyl-(1→4)]-2-deoxy-D-streptamine hemiheptasulfate [*53179-09-2*]

Sisomicin Sulfate contains not less than 590 μg (potency) per mg, calculated on the dried basis. The potency of Sisomicin Sulfate is expressed as mass (potency) of sisomicin ($C_{19}H_{37}N_5O_7$: 447.53).

Description Sisomicin Sulfate occurs as a white to light yellowish white powder.

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

It is hygroscopic.

Identification (1) Dissolve 0.05 g of Sisomicin Sulfate in 5 mL of water, and add 0.3 mL of bromine TS: the solution is immediately decolorized.

(2) Dissolve 0.015 g each of Sisomicin Sulfate and Sisomicin Sulfate Reference Standard in 5 mL of water, and use these solutions as the sample solution and the standard solution. Perform the test with these solutions as directed under the Thin-layer chromatography. Spot 5 μL each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of methanol, chloroform, ammonia water (28) and acetone (2:2:1:1) to a distance of about 15 cm, and air-dry the plate. Spray evenly 0.2% ninhydrin-water satutated 1-butabol TS on the plate, and heat at 100°C for 5 minutes: the principal spots from the sample solution and the standard solution exhibit a red-purple to red-brown color and show the same *R*f value.

(3) A solution of Sisomicin Sulfate (1 in 100) responds to the Qualitative Test (1) for sulfate.

Optical rotation $[\alpha]_D^{20}$: +100 – +110° (0.25 g calculated on the dried basis, water, 25 mL, 100 mm).

pH Dissolve 0.5 g of Sisomicin Sulfate in 5 mL of water: the pH of the solution is between 3.5 and 5.5.

Purity (1) Clarity and color of solution—Dissolve 0.5 g of Sisomicin Sulfate in 5 mL of water: the solution is clear and colorless to light yellow.

(2) Heavy metals—Proceed with 1.0 g of Sisomicin Sulfate 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).

(3) Related substances—Dissolve 0.05 g of Sisomicin Sulfate, calculated on the dried basis, in water to make 10 mL, and use this solution as the sample solution. Separately, weigh accurately an amount of Sisomicin Sulfate Reference Standard, equivalent to 0.025 g (potency), dissolve in water to make exactly 50 mL. Pipet 1 mL, 2 mL and 3 mL of this solution, add water to each to make exactly 10 mL, and use these solutions as the standard solution (1), the standard solution (2) and the standard solution (3), respectively. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL each of the sample solution and the standard solutions (1), (2), and (3) on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of methanol, chloroform, ammonia water (28) and acetone (2:2:1:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly 0.2% ninhydrin-water saturated 1-butabol TS on the plate, and heat at 100° C for 5 minutes. The spots corresponding to *R*f about 0.35 and *R*f about 0.30 are not more intense than that of the spot from the standard solution (3), and the spot of gallamine corresponding to *R*f about 0.25 is not more intense than the spot from the standard solution (1). The total amount of the intensity of the spots other than the principal spot from the sample solution is not more than 6%.

Loss on drying Not more than 15.0% (0.15 g, in vacuum not exceeding 0.67 kPa, 110°C, 3 hours). Sampling should

be carried out in a manner to avoid moisture absorption.

Residue on ignition Not more than 1.0% (1 g).

Assay Perform the test according to the Cylinder-plate method as directed under the Microbial Assay for Antibiotics according to the following conditions.

(1) Test organism—*Staphylococcus epidermidis* ATCC 12228

(2) Culture medium—Use the medium ii in 3) Medium for other organisms under (1) Agar media for seed and base layer. Adjust the pH of the medium so that it will be 7.8 to 8.0 after sterilization.

(3) Standard solution—Weigh accurately an amount of Sisomicin Sulfate Reference Standard equivalent to about 0.025 g (potency), add 0.1 mol/L phosphate buffer solution, pH 8.0 to make exactly 25 mL, and use this solution as the standard stock solution. Keep the standard stock solution at 5°C or below and use within 7 days. Take exactly a suitable amount of the standard stock solution before use, add 0.1 mol/L phosphate buffer solution, pH 8.0 to make solutions so that each mL contains 1 μg (potency) and 0.25 μg (potency), and use these solutions as the high concentration standard solution and the low concentration standard solution, respectively.

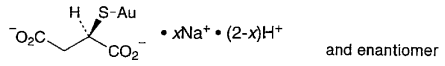
(4) Sample solution—Weigh accurately an amount of Sisomicin sulfate equivalent to about 0.025 g (potency), add 0.1 mol/L phosphate buffer solution, pH 8.0 to make exactly 25 mL. Take exactly a suitable amount of the solution, add 0.1 mol/L phosphate buffer solution, pH 8.0 to make solutions so that each mL contains 1 μg (potency) and 0.25 μg (potency), and use these solutions as the high concentration sample solution and the low concentration sample solution, respectively.

Containers and storage Containers—Tight containers.

Storage—Light-resistant, not exceeding −20°C, under nitrogen or argon atmosphere.

Sodium Aurothiomalate

金チオリンゴ酸ナトリウム



and enantiomer

Mixture of $C_4H_3AuNa_2O_4S$: 390.08 and $C_4H_4AuNaO_4S$: 368.09

Monogold monosodium monohydrogen (*RS*)-1-sulfidobutane-1,2-dioate

Monogold disodium (*RS*)-1-sulfidobutane-1,2-dioate

[*12244-57-4*, Sodium Aurothiomalate]

Sodium Aurothiomalate is a mixture of the monosodium salt of aurothiomalic acid ($C_4H_4AuNaO_4S$: 368.10) and disodium salt of aurothiomalic acid ($C_4H_3AuNa_2O_4S$: 390.08).

Sodium Aurothiomalate, when dried, contains not less than 49.0 % and not more than 52.5% of gold (Au: 196.97).

Description Sodium Aurothiomalate occurs as white to light yellow powder or granules. It is odorless.

It is very soluble in water, slightly soluble in ethanol (95), and very slightly soluble in diethyl ether.

It is hygroscopic.

It is affected by light.

Identification **(1)** To 2 mL of a solution of Sodium Aurothiomalate (1 in 10) add 1 mL of a solution of calcium nitrate tetrahydrate (1 in 10): a white precipitate is produced, and it dissolves in dilute nitric acid and reappears on the addition of ammonium acetate TS.

(2) To 2 mL of a solution of Sodium Aurothiomalate (1 in 10) add 3 mL of silver nitrate TS: a yellow precipitate is produced, and it dissolves in an excess of ammonia TS.

(3) Place 2 mL of a solution of Sodium Aurothiomalate (1 in 10) in a porcelain crucible, add 1 mL of ammonia TS and 1 mL of hydrogen peroxide (30), evaporate to dryness, and ignite. Add 20 mL of water to the residue, and filter: the residue on the filter paper occurs as a yellow or dark yellow powder, or yellow or dark yellow granules, and the filtrate responds to the Qualitative Tests for sodium salt and for sulfate.

pH Dissolve 1.0 g of Sodium Aurothiomalate in 10 mL of water: the pH of this solution is between 5.8 and 6.5.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Sodium Aurothiomalate in 10 mL of water: the solution is clear and light yellow.

(2) Heavy metals—Proceed with 1.0 g of Sodium Aurothiomalate according to Method 2, and perform the test. Prepare the control solution with 3.0 mL of Standard Lead Solution (not more than 30 ppm).

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

Loss on drying Not more than 8.0% (1 g, in vacuum, phosphorus (V) oxide, 80°C, 4 hours).

Assay Weigh accurately about 0.025 g of Sodium Aurothiomalate, previously dried, dissolve in 2 mL of aqua regia by heating, and add water to make exactly 100 mL. Pipet 2 mL of the solution, add water to make exactly 25 mL, and use this solution as the sample solution. Pipet 5, 10 and 15 mL of Standard Gold Solution for the Atomic Absorption Spectrophotometry, add water to make exactly 25 mL, and use these solutions as the standard solutions. Perform the test with the sample solution and the standard solutions as directed under the Atomic Absorption Spectrophotometry under the following conditions. Determine the amount of gold in the sample solution using the calibration curve obtained from the absorbances of the standard solutions.

Gas: Combustible gas—Acetylene gas
Supporting gas—Air

Lamp: Gold hollow-cathode lamp

Wavelength: 242.8 nm

Containers and storage Containers—Tight containers.

Storage—Light-resistant.