dition of 2 to 3 drops of sodium hydroxide TS.

(3) A solution of Migrenin (1 in 10) responds to the Qualitative Tests for citrate.

Melting point 104 - 110°C

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Migrenin in 40 mL of water: the solution is clear and colorless to pale yellow.

(2) Heavy metals—Proceed with 1.0 g of Migrenin according to Method 1, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

Loss on drying Not more than 0.5% (1 g, in vacuum, silica gel, 4 hours).

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

Assay **(1)** Antipyrine—Weigh accurately about 0.25 g of Migrenin, previously dried in an iodine flask, dissolve in 25 mL of sodium acetate TS, add exactly 30 mL of 0.05 mol/L iodine VS, and allow to stand for 20 minutes with occasional shaking. Add 15 mL of chloroform to dissolve the precipitate so obtained, and titrate the excess iodine with 0.1 mol/L sodium thiosulfate VS (indicator: 3 mL of starch TS). Perform a blank determination.

Each mL of 0.05 mol/L iodine VS
= 9.411 mg of $C_{11}H_{12}N_2O$

(2) Caffeine—To about 1 g of Migrenin, previously dried and accurately weighed, add exactly 5 mL of the internal standard solution, dissolve in chloroform to make 10 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.09 g of Caffeine Reference Standard, previously dried at 80°C for 4 hours, add exactly 5 mL of the internal standard solution, dissolve in chloroform to make 10 mL, and use this solution as the standard solution. Perform the test with 1 μL each of the sample solution and the standard solution as directed under the Gas Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of caffeine to that of the internal standard.

Amount (mg) of caffeine ($C_8H_{10}N_4O_2$)
= amount (mg) of Caffeine Reference Standard
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of ethenzamide in chloroform (1 in 50).

Operating conditions—

Detector: A hydrogen flame-ionization detector.

Column: A glass column about 3 mm in inside diameter and about 2 m in length, packed with siliceous earth for gas chromatography (180 to 250 μm in particle diameter) coated with 50% phenyl-methyl silicon polymer for gas chromatography at the ratio of 15%.

Column temperature: A constant temperature of about 210°C.

Carrier gas: Nitrogen

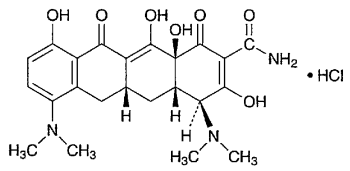
Flow rate: Adjust the flow rate so that the retention time of ethenzamide is about 4 minutes.

Selection of column: Dissolve 0.9 g of antipyrine and 0.09 g of caffeine in 10 mL of chloroform. Proceed with 1 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of caffeine and antipyrine in this order with the resolution between these peaks being not less than 1.5.

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

Minocycline Hydrochloride

塩酸ミノサイクリン



$C_{23}H_{27}N_3O_7$.HCl: 493.94
(4*S*,4a*S*,5a*R*,12a*S*)-4,7-Bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxonaphthacene-2-carboxamide monohydrochloride [*13614-98-7*]

Minocycline Hydrochloride contains not less than 890 μg (potency) per mg, calculated on the anhydrous basis. The potency of Minocycline Hydrochloride is expressed as mass (potency) of minocycline ($C_{23}H_{27}N_3O_7$: 457.48).

Description Minocycline Hydrochloride occurs as a yellow crystalline powder.

It is freely soluble in *N,N*-dimethylformamide, soluble in methanol, sparingly soluble in water, and slightly soluble in ethanol (95).

Identification **(1)** Determine the infrared absorption spectrum of Minocycline Hydrochloride as directed in the potassium chloride disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Minocycline Hydrochloride Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

(2) A solution of Minocycline Hydrochloride (1 in 100) responds to the Qualitative Test (2) for chloride.

Absorbance $E^{1\%}_{1\,cm}$ (358 nm): 296 - 328 (8 mg, a solution of hydrochloric acid in methanol (19 in 20,000), 500 mL).

pH Dissolve 1.0 g of Minocycline Hydrochloride in 100 mL of water: the pH of the solution is between 3.5 and 4.5.

Purity **(1)** Heavy metals—Proceed with 0.5 g of Minocycline Hydrochloride according to Method 2, and perform the test. Prepare the control solution with 2.5 mL of Standard Lead Solution (not more than 50 ppm).

(2) Related substances—Dissolve 0.05 g of Minocycline Hydrochloride in 100 mL of the mobile phase, and use this solution as the sample solution. Perform the test immediately after the preparation of the sample solution with 20 μL of the sample solution as directed under the Liquid Chromatography according to the following conditions, and measure each peak area by the automatic integration method. Calculate the amount of each peak area by the area percentage method: the amount of epiminocycline is not more than 1.2%, and the total area of the peaks other than

minocycline and the spot mentioned above is not more than 2.0%.

Operating conditions—

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

Flow rate: Adjust the flow rate so that the retention time of minocycline is about 12 minutes. The retention time of epiminocycline is about 10 minutes under this condition.

Time span of measurement: About 2.5 times as long as the retention time of minocycline after the solvent peak.

System suitability—

Test for required detection: Dissolve 0.02 g of Minocycline Hydrochloride Reference Standard in the mobile phase to make exactly 100 mL, then pipet 10 mL of this solution, and add the mobile phase to make exactly 100 mL. Adjust that the peak height of minocycline obtained from 20 μL of this solution is about 20 mm.

System performance: Proceed as directed in the system suitability in the Assay.

System repeatability: Dissolve 0.02 g of Minocycline Hydrochloride Reference Standard in the mobile phase to make exactly 100 mL, then pipet 10 mL of this solution, and add the mobile phase to make exactly 100 mL. When the test is repeated 6 times with 20 μL of this solution under the above operating conditions, the relative standard deviation of the peak areas of minocycline is not more than 2%.

Water Not less than 4.3% and not more than 8.0% (0.3 g, volumetric titration, direct titration).

Residue on ignition Not more than 0.5% (1 g).

Assay Weigh accurately an amount of Minocycline Hydrochloride and Minocycline Hydrochloride Reference Standard, equivalent to about 0.05 g (potency), dissolve each in the mobile phase to make exactly 100 mL, and use these solutions as the sample solution and the standard solution. Perform the test with exactly 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the peak areas, A_T and A_S, of minocycline of these solutions.

Amount [μg (potency)] of minocycline ($C_{23}H_{27}N_3O_7$) = amount [mg (potency)] of Minocycline Hydrochloride Reference Standard $\times \frac{A_T}{A_S} \times 1000$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 280 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 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: Adjust the pH of a mixture of a solution of ammonium oxalate monohydrate (7 in 250), *N,N*-dimethylformamide and 0.1 mol/L disodium dihydrogen ethylenediamine tetraacetate TS (11:5:4) to 6.2 with tetrabutylammonium hydroxide TS.

Flow rate: Adjust the flow rate so that the retention time of minocycline is about 12 minutes.

System suitability—

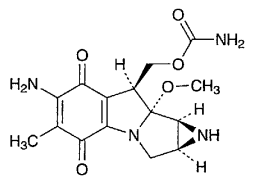
System performance: Dissolve 0.05 g (potency) of Minocycline Hydrochloride Reference Standard in 25 mL of water. Heat 5 mL of this solution on a water bath for 60 minutes, then add water to make 25 mL. When the procedure is run with 20 μL of this solution under the above operating conditions, epiminocycline and minocycline are eluted in this order with the resolution between these peaks being not less than 2.0.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of peak areas of minocycline is not more than 2.0%.

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

Mitomycin C

マイトマイシン C



$C_{15}H_{18}N_4O_5$: 334.33
(1a*S*,8*S*,8a*R*,8b*S*)-6-Amino-4,7-dioxo-1,1a,2,8,8a,8b-hexahydro-8a-methoxy-5-methylazirino[2′,3′:3,4]pyrrolo-[1,2-*a*]indol-8-ylmethyl carbamate [*50-07-7*]

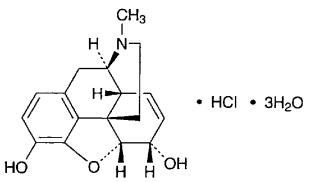
Mitomycin C conforms to the requirements of Mitomycin C in the Requirements for Antibiotic Products of Japan.

Description Mitomycin C occurs as blue-purple crystals or crystalline powder.

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

Morphine Hydrochloride

塩酸モルヒネ



$C_{17}H_{19}NO_3.HCl.3H_2O$: 375.84
(5*R*,6*S*)-7,8-Didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol monohydrochloride trihydrate [*6055-06-7*]

Morphine Hydrochloride contains not less than 98.0% and not more than 102.0% of $C_{17}H_{19}NO_3.HCl$: 321.80, calculated on the anhydrous basis.

Description Morphine Hydrochloride occurs as white crystals or crystalline powder.