(4) Related substances—Conduct this procedure without exposure to daylight, using light-resistant vessels. Dissolve 0.10 g of Naproxen in 10 mL of a mixture of chloroform and ethanol (99.5) (1:1), and use this solution as the sample solution. Pipet 2 mL of the sample solution, and add a mixture of chloroform and ethanol (99.5) (1:1) to make exactly 100 mL. Pipet 5 mL of this solution, add a mixture of chloroform and ethanol (99.5) (1:1) to make exactly 50 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 hexane, dichloromethane, tetrahydrofuran and acetic acid (100) (50:30:17:3) to a distance of about 12 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot and the spot of the starting point 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, 3 hours).

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

Assay Weigh accurately about 0.5g of Naproxen, previously dried, add 100 mL of diluted methanol (4 in 5), dissolve by gentle warming if necessary, and titrate with 0.1 mol/L sodium hydroxide VS (indicator: 3 drops of phenolphthalein TS). Perform a blank determination, and make any necessary correction.

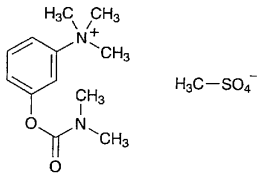
Each mL of 0.1 mol/L sodium hydroxide VS
= 23.026 mg of $C_{14}H_{14}O_3$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Neostigmine Methylsulfate

メチル硫酸ネオスチグミン



$C_{13}H_{22}N_2O_6S$: 334.39

N-(3-Dimethylcarbamoyloxyphenyl)-*N*,*N*,*N*-trimethylammonium methyl sulfate [*51-60-5*]

Neostigmine Methylsulfate, when dried, contains not less than 98.0% and not more than 102.0% of $C_{13}H_{22}N_2O_6S$.

Description Neostigmine Methylsulfate occurs as a white, crystalline powder.

It is very soluble in water, and freely soluble in acetonitrile and in ethanol (95).

Identification (1) Determine the absorption spectrum of a solution of Neostigmine Methylsulfate (1 in 2000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Neostigmine Methylsulfate Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Neostigmine Methylsulfate, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of dried Neostigmine Methylsulfate Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

pH Dissolve 1.0 g of Neostigmine Methylsulfate in 10 mL of freshly boiled and cooled water: the pH of the solution is between 3.0 and 5.0.

Melting point 145 - 149°C

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

(2) Sulfate—Dissolve 0.20 g of Neostigmine Methylsulfate in 10 mL of water, add 1 mL of dilute hydrochloric acid and 1 mL of barium chloride TS: no turbidity is produced immediately.

(3) Dimethylaminophenol—Dissolve 0.10 g of Neostigmine Methylsulfate in 5 mL of water, add 1 mL of sodium hydroxide TS, and while cooling with ice, add 1 mL of diazobenzenesulfonic acid TS: no color develops.

Loss on drying Not more than 1.0% (1 g, 105°C, 3 hours).

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

Assay Weigh accurately about 0.025 g each of Neostigmine Methylsulfate and Neostigmine Methylsulfate Reference Standard, previously dried, dissolve each in the mobile phase to make exactly 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 determine the peak areas, A_T and A_S, of neostigmine methylsulfate in each solution.

Amount (mg) of $C_{13}H_{22}N_2O_6S$
= amount (mg) of Neostigmine Methylsulfate Reference Standard $\times \frac{A_T}{A_S}$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 259 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: Dissolve 3.12 g of sodium dihydrogenphosphate dihydrate in 1000 mL of water, adjust to pH 3.0 with phosphoric acid, and add 0.871 g of sodium 1-pentanesulfonate to dissolve. To 890 mL of this solution add 110 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time

of neostigmine methylsulfate is about 9 minutes.

System suitability—

System performance: Dissolve 0.025 g of Neostigmine Methylsulfate and 4 mg of dimethylaminophenol in 50 mL of the mobile phase. When the procedure is run with 10 μL of this solution under the above operating conditions, dimethylaminophenol and neostigmine methylsulfate 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 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of neostigmine methylsulfate is not more than 1.0%.

Containers and storage Containers—Tight containers.

Neostigmine Methylsulfate Injection

メチル硫酸ネオスチグミン注射液

Neostigmine Methylsulfate Injection is an aqueous solution for injection. It contains not less than 93% and not more than 107% of the labeled amount of neostigmine methylsulfate ($C_{13}H_{22}N_2O_6S$: 334.39).

Method of preparation Prepare as directed under Injections, with Neostigmine Methylsulfate.

Description Neostigmine Methylsulfate Injection is a clear, colorless liquid.

It is slowly affected by light.

pH: 5.0 - 6.5

Identification Take a volume of Neostigmine Methylsulfate Injection equivalent to 5 mg of neostigmine methylsulfate according to the labeled amount, add water to make 10 mL if necessary, and determine the absorption spectrum of this solution as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 257 nm and 261 nm.

Bacterial endotoxins Less than 5 EU/mg.

Assay Use Neostigmine Methylsulfate Injection as the sample solution. Separately, weigh accurately about 0.025 g of Neostigmine Methylsulfate Reference Standard, previously dried at 105°C for 3 hours, dissolve in the mobile phase to make exactly 50 mL, and use this solution as the standard solution. Proceed as directed in the Assay under Neostigmine Methylsulfate.

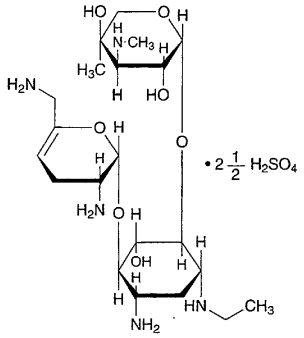
Amount (mg) of neostigmine methylsulfate ($C_{13}H_{22}N_2O_6S$) = amount (mg) of Neostigmine Methylsulfate Reference Standard $\times \frac{A_T}{A_S}$

Containers and storage Containers—Hermetic containers.

Storage—Light-resistant.

Netilmicin Sulfate

硫酸ネチルマイシン



$C_{21}H_{41}N_5O_7.2½H_2SO_4$: 720.78

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-1-*N*-ethyl-D-streptamine hemiheptasulfate

[*56391-57-2*]

Netilmicin Sulfate contains not less than 595 μg (potency) per mg, calculated on the dried basis. The potency of Netilmicin Sulfate is expressed as mass (potency) of netilmicin ($C_{21}H_{41}N_5O_7$: 475.58).

Description Netilmicin 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 0.03 g of Netilmicin Sulfate in 3 mL of water, and add 0.2 mL of bromine TS: the solution is immediately decolorized.

(2) Dissolve 0.015 g each of Netilmicin Sulfate and Netilmicin 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 saturated 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 Netilmicin Sulfate (1 in 100) responds to the Qualitative Test (1) for sulfate.

Optical rotation $[\alpha]_D^{20}$: +88 - +96° (0.1 g calculated on the dried basis, water, 10 mL, 100 mm).

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

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