Clarithromycin contains not less than 900 μg (potency) per mg, calculated on the anhydrous basis. The potency of Clarithromycin is expressed as mass (potency) of clarithromycin ($C_{38}H_{69}NO_{13}$).

**Description** Clarithromycin occurs as a white crystalline powder and has a bitter taste.

It is soluble in acetone and in chloroform, slightly soluble in methanol and in ethanol (95), and practically insoluble in water.

**Identification** (1) To 5 mg of Clarithromycin add 2 mL of sulfuric acid, and shake gently: a red-brown color develops.

(2) Dissolve 3 mg of Clarithromycin in 2 mL of acetone, and add 2 mL of hydrochloric acid: an orange color develops and changes immediately to red to deep purple.

(3) Determine the infrared absorption spectra of Clarithromycin and Clarithromycin Reference Standard as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare these spectra: both spectra exhibit similar intensities of absorption at the same wave numbers.

(4) Dissolve 0.01 g each of Clarithromycin and Clarithromycin Reference Standard in 4 mL of chloroform, 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 with a mixture of chloroform, methanol and ammonia water (28) (100:5:1) to a distance of about 15 cm, and air-dry the plate. Spray evenly sulfuric acid on the plate, and heat at 105°C for 10 minutes: the principal spot from the sample solution and the spot from the standard solution show a dark purple color and have the same *Rf* value.

**Optical rotation** $[\alpha]_D^{20}$: −87 – −97° (0.25 g calculated on the anhydrous basis, chloroform, 25 mL, 100 mm).

**Melting point** Being specified separately.

**Purity** (1) Heavy metals—Proceed with 2.0 g of Clarithromycin according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(2) Arsenic—Being specified separately.

(3) Related substances—Being specified separately.

**Water** Not more than 2.0% (0.5 g, volumetric titration, direct titration).

**Residue on ignition** Not more than 0.10% (2.0 g).

**Assay** Weigh accurately an amount of Clarithromycin and Clarithromycin Reference Standard, equivalent to about 0.1 g (potency), and dissolve in the mobile phase to make exactly 20 mL. Pipet 2 mL each of these solutions, add exactly 2 mL of the internal standard solution, add the mobile phase to make 20 mL, and use these solutions as the sample solution and 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 conditions, and calculate the ratios, $Q_T$ and $Q_S$, of the peak area of clarithromycin to that of the internal standard.

Amount [μg (potency)] of clarithromycin ($C_{38}H_{69}NO_{13}$) = amount [mg (potency)] of Clarithromycin Reference Standard $\times \frac{Q_T}{Q_S} \times 1000$

*Internal standard solution*—A solution of butyl parahydroxybenzoate in the mobile phase (1 in 20,000).

*Operating conditions*—

Detector: An ultraviolet absorption photometer (wavelength: 210 nm).

Column: A stainless steel column 4 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 50°C.

Mobile phase: A mixture of diluted 0.2 mol/L potassium dihydrogenphosphate TS (1 in 3) and acetonitrile (13:7).

Flow rate: Adjust the flow rate so that the retention time of clarithromycin is about 8 minutes.

*System suitability*—

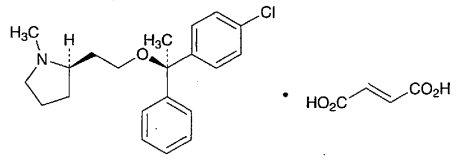
System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, clarithromycin and the internal standard are eluted in this order with the resolution between these peaks being not less than 3.

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 ratios of the peak area of clarithromycin to that of the internal standard is not more than 2.0%.

**Containers and storage** Containers—Well-closed containers.

# Clemastine Fumarate

フマル酸クレマスチン




$C_{21}H_{26}ClNO.C_4H_4O_4$: 459.96

(2*R*)-2-{2-[(1*R*)-1-(4-Chlorophenyl)-1-phenylethoxy]ethyl}-1-methylpyrrolidine monofumarate [*14976-57-9*]

Clemastine Fumarate, when dried, contains not less than 98.5% of $C_{21}H_{26}ClNO.C_4H_4O_4$.

**Description** Clemastine Fumarate occurs as a white, crystalline powder. It is odorless.

It is sparingly soluble in methanol and in acetic acid (100), slightly soluble in ethanol (95), very slightly soluble in diethyl ether, and practically insoluble in water.

**Identification** (1) To 5 mg of Clemastine Fumarate add 5 mL of sulfuric acid, and shake to dissolve: a yellow color develops. Slowly drop this solution into 10 mL of water: the yellow color immediately disappears.

(2) To 0.01 g of Clemastine Fumarate add 1 mL of fum-

ing nitric acid, and evaporate on a water bath to dryness. Then add 2 mL of diluted hydrochloric acid (1 in 2) and 0.2 g of zinc powder, heat for 10 minutes on a water bath, cool, and filter. Add 20 mL of water to the filtrate. The solution responds to the Qualitative Tests for primary aromatic amines.

**(3)** To 5 mL of a solution of Clemastine Fumarate (1 in 50,000), add 5 mL of 4-dimethylaminobenzaldehyde TS, and warm for 10 minutes: a red-purple color develops.

**(4)** Perform the test with Clemastine Fumarate as directed under the Flame Coloration Test (2): a green color appears.

**(5)** Dissolve 0.04 g of Clemastine Fumarate and 0.01 g of fumaric acid for thin-layer chromatography in 2 mL each of a mixture of ethanol (95) and water (4:1) by gentle warming, and use these solutions as the sample solution and the standard solution, respectively. 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 with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of isopropyl ether, formic acid and water (90:7:3) to a distance of about 10 cm, and air-dry the plate. Examine the plate under ultraviolet light (main wavelength: 254 nm): the spot with larger *Rf* value from the sample solution has the same *Rf* value as the spot from the standard solution.

**Optical rotation** $[\alpha]_D^{20}$: +16 – +18° (after drying, 0.1 g, methanol, 10 mL, 100 mm).

**Melting point** 176 - 180°C (with decomposition).

**Purity** **(1)** Clarity and color of solution—Dissolve 0.5 g of Clemastine Fumarate in 10 mL of methanol by warming: the solution is clear and colorless.

**(2)** Heavy metals—Perform the test with 1.0 g of Clemastine Fumarate according to Method 2. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

**(3)** Arsenic—Take 1.0 g of Clemastine Fumarate, prepare the test solution according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

**(4)** Related Substances—Dissolve 0.10 g of Clemastine Fumarate in 5 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add methanol to make exactly 250 mL, and use this solution as the standard solution (1). Pipet 5 mL of this solution, add methanol to make exactly 10 mL, and use this solution as the standard solution (2). Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μL each of the sample solution, the standard solution (1) and (2) on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of chloroform, methanol and ammonia solution (28) (90:10:1) to a distance of about 10 cm, and air-dry the plate. After spraying evenly Dragendorff's TS on the plate, immediately spray evenly hydrogen peroxide TS: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution (1), and not more than 2 spots from the sample solution are more intense than the spot from the standard solution (2).

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

**Residue on ignition** Not more than 0.20% (1 g).

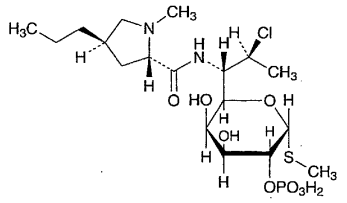
**Assay** Weigh accurately about 0.4 g of Clemastine Fumarate, previously dried, dissolved in 50 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 46.00 mg of $C_{21}H_{26}ClNO.C_4H_4O_4$

**Containers and storage** Containers—Tight containers.

# Clindamycin Phosphate

リン酸クリンダマイシン



$C_{18}H_{34}ClN_2O_8PS$: 504.96
Methyl 7-chloro-6,7,8-trideoxy-6-[(2*S*,4*R*)-1-methyl-4-propylpyrrolidine-2-carboxamido]-1-thio-L-*threo*-α-D-*galacto*-octopyranoside 2-dihydrogenphosphate
[*24729-96-2*]

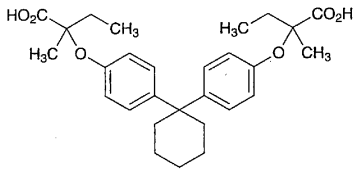
Clindamycin Phosphate conforms to the requirements of Clindamycin Phosphate in the Requirements for Antibiotic Products of Japan.

**Description** Clindamycin Phosphate occurs as a white to pale yellowish white, crystalline powder.

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

# Clinofibrate

クリノフィブラート



$C_{28}H_{36}O_6$: 468.58
2,2′-(4,4′-Cyclohexylidenediphenoxy)-2,2′-dimethyldibutanoic acid [*30299-08-2*]

Clinofibrate, when dried, contains not less than 98.5% of $C_{28}H_{36}O_6$.

**Description** Clinofibrate occurs as a white to yellowish white powder.

It is odorless and has no taste.

It is freely soluble in methanol, in ethanol (99.5), in acetone and in diethyl ether, and practically insoluble in water.