Lomerizine Hydrochloride Tablets

Dissolution *<6.10>* Perform the test with 1 tablet of Lomerizine Hydrochloride Tablets at 50 revolutions per minute according to the Paddle method, using 900 mL of 0.05 mol/L acetic acid-sodium acetate buffer solution, pH 4.0 as the dissolution medium. Withdraw not less than 20 mL of the medium at the specified minute after starting the test, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 10 mL of the filtrate, pipet V mL of the subsequent filtrate, add 0.05 mol/L acetic acid-sodium acetate buffer solution, pH 4.0 to make V' mL so that each mL contains about 5.6 μg of lomerizine hydrochloride ($C_{27}H_{30}F_2N_2O_3.2HCl$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 28 mg of Lomerizine Hydrochloride RS, previously dried in vacuum at room temperature for 3 hours, and dissolve in methanol to make exactly 100 mL. Pipet 2 mL of this solution, add 0.05 mol/L acetic acid-sodium acetate buffer solution, pH 4.0 to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 20 μL each of the sample solution and standard solution as directed under Liquid Chromatography *<2.01>* according to the following conditions, and determine the peak areas, A_T and A_S, of lomerizine in each solution.

The requirements are met if Lomerizine Hydrochloride Tables conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of lomerizine hydrochloride ($C_{27}H_{30}F_2N_2O_3.2HCl$)

$= M_S \times A_T/A_S \times V'/V \times 1/C \times 18$

M_S: Amount (mg) of Lomerizine Hydrochloride RS

C: Labeled amount (mg) of lomerizine hydrochloride ($C_{27}H_{30}F_2N_2O_3.2HCl$) in 1 tablet

Operating conditions —

Detector: An ultraviolet absorption photometer (wavelength: 225 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 50ºC.

Mobile phase: Dissolve 5 g of sodium lauryl sulfate in 1000 mL of water, and adjust to pH 2.5 with phosphoric acid. To 250 mL of this solution add 750 mL of methanol.

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

System suitability —

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of

lomerizine are not less than 2000 and not more than 2.0, respectively.

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 the peak area of lomerizine is not more than 1.0%.

Dissolution Requirements

Labeled amount	Specified minute	Dissolution rate
5 mg	15 minutes	Not less than 80%

Lomerizine Hydrochloride RS $C_{27}H_{30}F_2N_2O_3.2HCl$: 541.46

1-[Bis(4-fluorophenyl)methyl]-4-(2,3,4-trimethoxybenzyl)piperazine dihydrochloride. It meets the following requirements.

Description－Lomerizine Hydrochloride RS occurs as a white crystalline powder.

Identification: (1) Determine the absorption spectrum of a solution of Lomerizine Hydrochloride RS in methanol (1 in 4000) as directed under Ultraviolet-visible Spectrophotometry <*2.24*>: it exhibits maxima between 263 nm and 267 nm, and between 270 nm and 274 nm.

(2) Determine the infrared absorption spectrum of Lomerizine Hydrochloride RS, previously dried, as directed in the potassium bromide disk method under Infrared Spectrophotometry <*2.25*>: it exhibits absorption at the wave numbers of about 2320 cm^{-1} and 1512 cm^{-1}.

Purity (1) Related substances－Dissolve 0.50 g of Lomerizine Hydrochloride RS in 50 mL of the mobile phase, and use this solution as the sample solution. Pipet 1 mL of this solution, add the mobile phase to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions, and determine each peak area by the automatic integration method: the total area of peaks other than lomerizine obtained from the sample solution is not larger than 7/10 times the peak area of lomerizine from the standard solution.

Operating conditions

Detector: An ultraviolet absorption photometer (wavelength: 265 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 50ºC.

Mobile phase: Dissolve 5 g of sodium lauryl sulfate in 1000 mL of water, and adjust to pH 2.5 with phosphoric acid. To 250 mL of this solution add 750 mL of methanol.

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

Time span of measurement: About 2 times as long as the retention time of lomerizine beginning after the solvent peak.

System suitability

Test for required detectability: To exactly 7 mL of the standard solution add the mobile phase to make exactly 10 mL. Confirm that the peak area of lomerizine obtained from 10 μL of this solution is equivalent to 65 to 75% of that from 10 μL of the standard solution.

System performance: When the procedure is run with 10 μL of the sample solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of lomerizine are not less than 3000 and between 0.4 and 1.2, respectively.

System repeatability: When the test is repeated 6 times with 10 μL of the sample solution under the above operating conditions, the relative standard deviation of the peak area of lomerizine is not more than 5.0%.

(2) Acetonitrile－Weigh accurately 0.1 g of Lomerizine Hydrochloride RS, add exactly 1 mL of the internal standard solution to dissolve, and use this solution as the sample solution. Separately, weigh exactly 6 mL of acetonitrile, and add the internal standard solution to make exactly 100 mL. Pipet 1 mL of this solution, and add the internal standard solution to make exactly 100 mL. Pipet 1 mL of this solution, add the internal standard solution to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 0.5 μL each of the sample solution and standard solution as directed under Gas Chromatography *<2.02>* according to the following conditions, and determine the ratios, Q_T and Q_S, of the peak area of acetonitrile to that of the internal standard (not more than 50 ppm).

Amount (ppm) of acetonitrile = $M_T \times Q_T/Q_S \times (0.782 \times 6)$

M_T: Amount (g) of sample

0.782: Density (g/mL) of acetonitrile

Internal standard solution: A solution of dodecane in *N,N*-dimethylformamide (1 in 100,000).

Operating conditions

Detector: A hydrogen flame-ionization detector.

Column: A glass column 0.75 mm in inside diameter and 60 m in length, coated inside surface with ethylene glycol polymer for gas chromatography 1.0 μm in thickness.

Column temperature: A constant temperature of about 100ºC.

Injection port temperature: A constant temperature of about 140ºC.

Detector temperature: A constant temperature of about 220ºC.

Carrier gas: Helium.

Flow rate: Adjust the flow rate so that the retention time of acetonitrile is about 5 minutes.

System suitability

System performance: When the procedure is run with 3 μL of the standard solution under the above operating conditions, acetonitrile and the internal standard are eluted in this order with the resolution

between these peaks being not less than 8.5.

System repeatability: When the test is repeated 6 times with 3 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of acetonitrile to that of the internal standard is not more than 10.0%.

Loss on drying <2.41>: not more than 1.0% (1 g, in vacuum, room temperature, 3 hours).

Content: not less than 99.5%. Assay－Weigh accurately about 0.4 g of Lomerizine Hydrochloride RS, previously dried, add 100 mL of acetic anhydride to dissolve, and titrate <2.50> with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination in the same manner, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 27.07 mg of $C_{27}H_{30}F_2N_2O_3 \cdot 2HCl$

Reagents, Test Solutions

Dodecane $CH_3(CH_2)_{10}CH_3$ Clear and colorless liquid.

Density <2.56> (20ºC): 0.749 g/mL