Clarithromycin for Syrup

シロップ用クラリスロマイシン

Clarithromycin for Syrup is a preparation for syrup, which is suspended before use.

It contains not less than 90.0% and not more than 110.0% of the labeled potency of clarithromycin ($C_{38}H_{69}NO_{13}$: 747.95).

Method of preparation Prepare as directed under Preparations for Syrups, with Clarithromycin.

Identification To an amount of Clarithromycin for Syrup, equivalent to 0.1 g (potency) of Clarithromycin, add 5 mL of acetone, and sonicate for 15 minutes. After cooling with ice, centrifuge, take the supernatant liquid, and evaporate the solvent. Dissolve 10 mg of the residue and 2 mg of Clarithromycin RS in separate 2 mL of acetone, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with these solutions as directed under Thin-layer Chromatography *<2.03>*. Spot 10 μL each of the sample solution and standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of methanol, ethyl acetate and acetic acid (100) (90:10:1) to a distance of about 15 cm, and air-dry the plate. Spray evenly sulfuric acid on the plate, and heat at 105℃ for 10 minutes: the principal spot obtained from the sample solution and the spot from the standard solution show a black-purple color and the same *Rf* value.

Water *<2.48>* Not more than 3.0% (0.5 g, volumetric titration, direct titration).

Uniformity of dosage units *<6.02>* Perform the test according to the following method: Clarithromycin for Syrup in single-dose packages meet the requirement of the Content uniformity test.

To the total content of 1 package of Clarithromycin for Syrup add 3*V*/5 mL of ethanol (99.5), add exactly *V*/10 mL of the internal standard solution, sonicate for 30 minutes with occasional vigorous shaking, and add ethanol (99.5) to make *V* mL so that each mL contains about 0.5 mg (potency) of Clarithromycin. Centrifuge this solution, and filter the supernatant liquid through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 3 mL of the filtrate, and use the subsequent filtrate as the sample solution. Then, proceed as directed in the Assay.

Amount [mg (potency)] of clarithromycin ($C_{38}H_{69}NO_{13}$)
$= M_S \times Q_T / Q_S \times V / 100$

M_S: Amount [mg (potency)] of Clarithromycin RS taken

Internal standard solution — A solution of butyl parahydroxybenzoate in ethanol (99.5) (1 in 12,500).

Dissolution *<6.10>* When the test is performed at 50 revolutions per minute according to the Paddle method, using 900 mL of disodium hydrogen phosphate-citric acid buffer solution (pH 5.5) as the dissolution medium, the dissolution rate in 90 minutes of Clarithromycin for Syrup is not less than 75%.

Start the test with an accurately weighed amount of Clarithromycin for Syrup, equivalent to about 50 mg (potency) of Clarithromycin, 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 not less than 10 mL of the first filtrate, pipet 10 mL of the subsequent filtrate, add the mobile phase to make exactly 20 mL, and use this solution as the sample solution. Separately, weigh accurately an amount of Clarithromycin RS, equivalent to about 28 mg (potency), and dissolve in acetonitrile to make exactly 100 mL. Pipet 5 mL of this solution, add the mobile phase to make exactly 50 mL, and use this solution as the standard solution. Perform the test with exactly 100 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 clarithromycin in each solution.

Dissolution rate (%) with respect to the labeled amount of clarithromycin ($C_{38}H_{69}NO_{13}$)
$= M_S / M_T \times A_T / A_S \times 1 / C \times 180$

M_S: Amount [mg (potency)] of Clarithromycin RS taken
M_T: Amount (g) of Clarithromycin for Syrup taken
C: Labeled amount of [mg (potency)] of clarithromycin ($C_{38}H_{69}NO_{13}$) in 1 g

Operating conditions —

Proceed as directed in the operating conditions in the Assay.

System suitability —

System performance: When the procedure is run with 100 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of clarithromycin are not less than 3000 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 100 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of clarithromycin is not more than 2.0%.

Assay Weigh accurately an amount of crushed Clarithromycin for Syrup, equivalent to about 50 mg (potency) of Clarithromycin, add 60 mL of ethanol (99.5), add exactly 10 mL of the internal standard solution, sonicate for 30

minutes with occasional vigorous shaking, and add ethanol (99.5) to make 100 mL. Centrifuge this solution, and filter the supernatant liquid through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 3 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately an amount of Clarithromycin RS, equivalent about 50 mg (potency), and dissolve in ethanol (99.5) to make exactly 50 mL. Pipet 10 mL of this solution, add exactly 2 mL of the internal standard solution, add ethanol (99.5) to make 20 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 calculate the ratios, Q_T and Q_S, of the peak area of clarithromycin to that of the internal standard.

Amount [mg (potency)] of clarithromycin ($C_{38}H_{69}NO_{13}$)
$= M_S \times Q_T / Q_S$

M_S: Amount [mg (potency)] of Clarithromycin RS taken

Internal standard solution—A solution of butyl parahydroxybenzoate in ethanol (99.5) (1 in 12,500).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 210 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 50℃.

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

Flow rate: Adjust 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 ratio of the peak area of clarithromycin to that of the internal standard is not more than 2.0%.

Containers and storage Containers—Tight containers.

Storage—Light-resistant.