Rosuvastatin Calcium Tablets

ロスバスタチンカルシウム錠

Rosuvastatin Calcium Tablets contain not less than 95.0% and not more than 105.0% of the labeled amount of rosuvastatin ($C_{22}H_{28}FN_3O_6S$: 481.54).

Method of preparation Prepare as directed under Tablets, with Rosuvastatin Calcium.

Identification Perform the test with 10 μL each of the sample solution and standard solution obtained in the Assay, as directed under Liquid Chromatography <*2.01*> according to the following conditions: the principal peaks in the chromatograms obtained from the sample solution and the standard solution show the same retention time, and both spectra of these peaks in the chromatograms exhibit similar intensities of absorption at the same wavelengths.

Operating conditions—

Column, column temperature, mobile phase, and flow rate: Proceed as directed in the operating conditions in the Assay. Detector: A photodiode array detector (wavelength: 242 nm; spectrum range of measurement: 220 – 400 nm).

System suitability—

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

Purity Related substances—To a number of Rosuvastatin Calcium Tablets, equivalent to 0.1 g of rosuvastatin ($C_{22}H_{28}FN_3O_6S$), add 50 mL of water, shake for 30 minutes, then add 25 mL of acetonitrile, and shake for 30 minutes. To this solution add water to make exactly 100 mL, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 5 mL of the filtrate, and use the subsequent filtrate as the sample solution. Pipet 1 mL of this solution, add a mixture of water and acetonitrile (3:1) 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 peak area of the related substance C, having the relative retention time of about 1.6 to rosuvastatin, obtained from the sample solution is not larger than 1.4 times the peak area of rosuvastatin from the standard solution, the peak area of the related substance D, having the relative retention time of about 2.3, from the sample solution is not larger than 7/10 times the peak area of rosuvastatin from the standard solution, and the area of the peak other than rosuvastatin and the peaks mentioned above from the sample solution is not larger than 1/5 times the peak area of rosuvastatin from the standard solution. Furthermore, the total area of the peaks other than rosuvastatin from the sample solution is not larger than 2.1 times the peak area of rosuvastatin from the standard solution. For the area of the peak of the related substance C, multiply the response factor 1.4.

Operating conditions—

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

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

System suitability—

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

Test for required detectability: Pipet 5 mL of the standard solution, add a mixture of water and acetonitrile (3:1) to make exactly 100 mL. Confirm that the peak area of rosuvastatin obtained with 10 μL of this solution is equivalent to 3.5 to 6.5% of that with 10 μL of the standard solution.

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 area of rosuvastatin is not more than 2.0%.

Uniformity of dosage units <*6.02*> Perform the test according to the following method: it meets the requirement of the Content uniformity test.

To 1 tablet of Rosuvastatin Calcium Tablets add 3*V*/4 mL of 0.1 mol/L phosphate buffer solution (pH 7), and shake for 45 minutes. To 1 mL of this solution add 0.1 mol/L phosphate buffer solution (pH 7) to make exactly *V* mL so that each mL contains about 25 μg of rosuvastatin ($C_{22}H_{28}FN_3O_6S$), and filter through a membrane filter with a pore size not exceeding 0.2 μm. Discard the first 5 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.1 g of Rosuvastatin Calcium RS (separately determine the water <*2.48*> in the same manner as Rosuvastatin Calcium), add 0.1 mol/L phosphate buffer solution (pH 7) to make exactly 250 mL. Pipet 15 mL of this solution, add 0.1 mol/L phosphate buffer solution (pH 7) to make exactly 250 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S, of the sample solution and standard solution at 241 nm as directed under Ultraviolet-visible Spectrophotometry <*2.24*>.

$$\text{Amount (mg) of rosuvastatin } (C_{22}H_{28}FN_3O_6S) = M_S \times A_T / A_S \times 3V / 12{,}500 \times 0.962$$

M_S: Amount (mg) of Rosuvastatin Calcium RS taken, calculated on the anhydrous basis

Dissolution *<6.10>* When the test is performed at 50 revolutions per minute according to the Paddle method, using 900 mL of 0.05 mol/L citrate buffer solution (pH 6.6) as the dissolution medium, the dissolution rate in 30 minutes of Rosuvastatin Calcium Tablets is not less than 80%.

Start the test with 1 tablet of Rosuvastatin Calcium Tablets, 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 5 mL or more of the filtrate, pipet V mL of the subsequent filtrate, add the dissolution medium to make exactly V'mL so that each mL contains about 2.8 μg of rosuvastatin ($C_{22}H_{28}FN_3O_6S$), and use this solution as the sample solution. Separately, weigh accurately about 0.1 g of Rosuvastatin Calcium RS (separately determine the water *<2.48>* in the same manner as Rosuvastatin Calcium), add 50 mL of water, sonicate, add 25 mL of acetonitrile to dissolve, and add water to make exactly 100 mL. Pipet 10 mL of this solution, add the dissolution medium to make exactly 200 mL. Pipet 10 mL of this solution, and add the dissolution medium to make exactly 200 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 rosuvastatin in each solution.

Dissolution rate (%) with respect to the labeled amount of rosuvastatin ($C_{22}H_{28}FN_3O_6S$)

$$= M_S \times A_T / A_S \times V' / V \times 1 / C \times 9 / 4 \times 0.962$$

M_S: Amount (mg) of Rosuvastatin Calcium RS taken, calculated on the anhydrous basis

C: Labeled amount (mg) of rosuvastatin ($C_{22}H_{28}FN_3O_6S$) in 1 tablet

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 242 nm).

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

Column temperature: A constant temperature of about 25℃.

Mobile phase: A mixture of water, acetonitrile and phosphoric acid (600:400:1).

Flow rate: Adjust so that the retention time of rosuvastatin is about 2 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 rosuvastatin are not less than 1900 and 1.0 – 1.4, 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 rosuvastatin is not more than 1.5%.

Assay To 10 tablets of Rosuvastatin Calcium Tablets add exactly 300 mL of water, and shake for 30 minutes. To this solution add 125 mL of acetonitrile, shake for 15 minutes, and add water to make exactly 500 mL. Pipet 5 mL of this solution, add a mixture of water and acetonitrile (3:1) to make exactly V mL so that each mL contains about 25 μg of rosuvastatin ($C_{22}H_{28}FN_3O_6S$), and filter this solution through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 5 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.1 g of Rosuvastatin Calcium RS (separately determine the water *<2.48>* in the same manner as Rosuvastatin Calcium), add 50 mL of water, sonicate, add 25 mL of acetonitrile, cool to room temperature, and add water to make exactly 100 mL. Pipet 5 mL of this solution, add a mixture of water and acetonitrile (3:1) to make exactly 200 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 the peak areas, A_T and A_S, of rosuvastatin in each solution.

Amount (mg) of rosuvastatin ($C_{22}H_{28}FN_3O_6S$) in 1 tablet of Rosuvastatin Calcium Tablets

$$= M_S \times A_T / A_S \times V / 400 \times 0.962$$

M_S: Amount (mg) of Rosuvastatin Calcium RS taken, calculated on the anhydrous basis

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 242 nm).

Column: A stainless steel column 3.2 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 40℃.

Mobile phase: A mixture of water, acetonitrile and diluted trifluoroacetic acid (1 in 100) (62:37:1).

Flow rate: Adjust so that the retention time of rosuvastatin is about 13 minutes.

System suitability—

System performance: To 10 mg of rosuvastatin calcium add 100 mL of water and 20 mL of 1 mol/L hydrochloric acid TS, heat on a water bath of 60℃ for 2 hours, and neutralize with sodium hydroxide TS. After cooling, add 50

mL of acetonitrile and water to make 200 mL. To 10 mL of this solution add 10 mL of a mixture of water and acetonitrile (3:1). When the procedure is run with 10 μL of this solution under the above operating conditions, the resolution between rosuvastatin and the related substance B (diastereomer) having the relative retention time of about 1.1 to rosuvastatin is not less than 1.5.

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 area of rosuvastatin is not more than 1.5%.

Containers and storage Containers—Tight containers.

Others

Related substances B (diastereomer), C, and D: Refer to those described in Rosuvastatin Calcium.

Add the following to 9.01 Reference Standards (1):

Rosuvastatin Calcium RS

Add the following to 9.41 Reagents, Test Solutions:

0.1 mol/L Citric acid TS Dissolve 21 g of citric acid monohydrate in water to make 1000 mL.

0.05 mol/L Citrate buffer solution (pH 6.6) Dissolve 147 g of trisodium citrate dihydrate in 2000 mL of water, add 3.6 g of citric acid monohydrate to dissolve, and add water to make 10 L. To this solution add 0.1 mol/L sodium citrate TS or 0.1 mol/L citric acid TS to adjust the pH to 6.6.

0.1 mol/L Phosphate buffer solution (pH 7) Dissolve 13.6 g of potassium dihydrogen phosphate in 800 mL of water, adjust the pH to 7 ± 0.4 with sodium hydroxide TS, and add water to make 1000 mL.

Rosuvastatin calcium $(C_{22}H_{27}FN_3O_6S)_2Ca$ [Same as the namesake monograph]

0.1 mol/L Sodium citrate TS Dissolve 29.4 g of trisodium citrate dihydrate in water to make 1000mL