

1 Rosuvastatin Calcium Tablets

2 ロスバスタチンカルシウム錠

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4 Rosuvastatin Calcium Tablets contain not less than
5 95.0% and not more than 105.0% of the labeled
6 amount of rosuvastatin ($C_{22}H_{28}FN_3O_6S$: 481.54).

7 **Method of preparation** Prepare as directed under Tab-
8 lets, with Rosuvastatin Calcium.

9 **Identification** Perform the test with 10 μ L each of the
10 sample solution and standard solution obtained in the Assay,
11 as directed under Liquid Chromatography <2.01> according
12 to the following conditions: the principal peaks in the chro-
13 matograms obtained from the sample solution and the
14 standard solution show the same retention time, and both
15 spectra of these peaks in the chromatograms exhibit similar
16 intensities of absorption at the same wavelengths.

17 *Operating conditions*—

18 Column, column temperature, mobile phase, and flow
19 rate: Proceed as directed in the operating conditions in the
20 Assay. Detector: A photodiode array detector (wavelength:
21 242 nm; spectrum range of measurement: 220 – 400 nm).

22 *System suitability*—

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

25 **Purity** Related substances— To a number of Rosuvastatin
26 Calcium Tablets, equivalent to 0.1 g of rosuvastatin
27 ($C_{22}H_{28}FN_3O_6S$), add 50 mL of water, shake for 30 minutes,
28 then add 25 mL of acetonitrile, and shake for 30 minutes.
29 To this solution add water to make exactly 100 mL, and fil-
30 ter through a membrane filter with a pore size not exceeding
31 0.45 μ m. Discard the first 5 mL of the filtrate, and use the
32 subsequent filtrate as the sample solution. Pipet 1 mL of this
33 solution, add a mixture of water and acetonitrile (3:1) to
34 make exactly 100 mL, and use this solution as the standard
35 solution. Perform the test with exactly 10 μ L each of the
36 sample solution and standard solution as directed under Liq-
37 uid Chromatography <2.01> according to the following con-
38 ditions, and determine each peak area by the automatic in-
39 tegration method: the peak area of the related substance C,
40 having the relative retention time of about 1.6 to rosuvas-
41 tatin, obtained from the sample solution is not larger than
42 1.4 times the peak area of rosuvastatin from the standard
43 solution, the peak area of the related substance D, having
44 the relative retention time of about 2.3, from the sample so-
45 lution is not larger than 7/10 times the peak area of rosuvas-
46 tatin from the standard solution, and the area of the peak
47 other than rosuvastatin and the peaks mentioned above from
48 the sample solution is not larger than 1/5 times the peak area
49 of rosuvastatin from the standard solution. Furthermore, the

50 total area of the peaks other than rosuvastatin from the sam-
51 ple solution is not larger than 2.1 times the peak area of
52 rosuvastatin from the standard solution. For the area of the
53 peak of the related substance C, multiply the response factor
54 1.4.

55 *Operating conditions*—

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

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

62 *System suitability*—

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

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

71 System repeatability: When the test is repeated 6 times
72 with 10 μ L of the standard solution under the above
73 operating conditions, the relative standard deviation of the
74 peak area of rosuvastatin is not more than 2.0%.

75 **Uniformity of dosage units** <6.02> Perform the test ac-
76 cording to the following method: it meets the requirement
77 of the Content uniformity test.

78 To 1 tablet of Rosuvastatin Calcium Tablets add 3V/4 mL
79 of 0.1 mol/L phosphate buffer solution (pH 7), and shake
80 for 45 minutes. To 1 mL of this solution add 0.1 mol/L
81 phosphate buffer solution (pH 7) to make exactly V mL so
82 that each mL contains about 25 μ g of rosuvastatin
83 ($C_{22}H_{28}FN_3O_6S$), and filter through a membrane filter with
84 a pore size not exceeding 0.2 μ m. Discard the first 5 mL of
85 the filtrate, and use the subsequent filtrate as the sample so-
86 lution. Separately, weigh accurately about 0.1 g of Rosu-
87 vastatin Calcium RS (separately determine the water <2.48>
88 in the same manner as Rosuvastatin Calcium), add 0.1
89 mol/L phosphate buffer solution (pH 7) to make exactly 250
90 mL. Pipet 15 mL of this solution, add 0.1 mol/L phosphate
91 buffer solution (pH 7) to make exactly 250 mL, and use this
92 solution as the standard solution. Determine the absorb-
93 ances, A_T and A_S , of the sample solution and standard solu-
94 tion at 241 nm as directed under Ultraviolet-visible Spec-
95 trophotometry <2.24>.

$$96 \quad \text{Amount (mg) of rosuvastatin } (C_{22}H_{28}FN_3O_6S) \\ 97 \quad = M_S \times A_T / A_S \times 3V / 12,500 \times 0.962$$

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

100 **Dissolution** <6.10> When the test is performed at 50 rev-
 101 olutions per minute according to the Paddle method, using
 102 900 mL of 0.05 mol/L citrate buffer solution (pH 6.6) as the
 103 dissolution medium, the dissolution rate in 30 minutes of
 104 Rosuvastatin Calcium Tablets is not less than 80%.

105 Start the test with 1 tablet of Rosuvastatin Calcium Tab-
 106 lets, withdraw not less than 20 mL of the medium at the
 107 specified minute after starting the test, and filter through a
 108 membrane filter with a pore size not exceeding 0.45 μm .
 109 Discard the first 5 mL or more of the filtrate, pipet V mL of
 110 the subsequent filtrate, add the dissolution medium to make
 111 exactly V mL so that each mL contains about 2.8 μg of rosu-
 112 vastatin ($\text{C}_{22}\text{H}_{28}\text{FN}_3\text{O}_6\text{S}$), and use this solution as the sam-
 113 ple solution. Separately, weigh accurately about 0.1 g of
 114 Rosuvastatin Calcium RS (separately determine the water
 115 <2.48> in the same manner as Rosuvastatin Calcium), add
 116 50 mL of water, sonicate, add 25 mL of acetonitrile to dis-
 117 solve, and add water to make exactly 100 mL. Pipet 10 mL
 118 of this solution, add the dissolution medium to make exactly
 119 200 mL. Pipet 10 mL of this solution, and add the dissolu-
 120 tion medium to make exactly 200 mL, and use this solution
 121 as the standard solution. Perform the test with exactly 20 μL
 122 each of the sample solution and standard solution as di-
 123 rected under Liquid Chromatography <2.01> according to
 124 the following conditions, and determine the peak areas, A_T
 125 and A_S , of rosuvastatin in each solution.

126 Dissolution rate (%) with respect to the labeled amount of
 127 rosuvastatin ($\text{C}_{22}\text{H}_{28}\text{FN}_3\text{O}_6\text{S}$)

$$128 = M_S \times A_T / A_S \times V' / V \times 1 / C \times 9 / 4 \times$$

$$129 0.962$$

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

132 C : Labeled amount (mg) of rosuvastatin ($\text{C}_{22}\text{H}_{28}\text{FN}_3\text{O}_6\text{S}$)
 133 in 1 tablet

134 *Operating conditions*—

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

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

141 Column temperature: A constant temperature of about
 142 25°C.

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

145 Flow rate: Adjust so that the retention time of
 146 rosuvastatin is about 2 minutes.

147 *System suitability*—

148 System performance: When the procedure is run with 20
 149 μL of the standard solution under the above operating
 150 conditions, the number of theoretical plates and the

151 symmetry factor of the peak of rosuvastatin are not less than
 152 1900 and 1.0 – 1.4, respectively.

153 System repeatability: When the test is repeated 6 times
 154 with 20 μL of the standard solution under the above
 155 operating conditions, the relative standard deviation of the
 156 peak area of rosuvastatin is not more than 1.5%.

157 **Assay** To 10 tablets of Rosuvastatin Calcium Tablets add
 158 exactly 300 mL of water, and shake for 30 minutes. To this
 159 solution add 125 mL of acetonitrile, shake for 15 minutes,
 160 and add water to make exactly 500 mL. Pipet 5 mL of this
 161 solution, add a mixture of water and acetonitrile (3:1) to
 162 make exactly V mL so that each mL contains about 25 μg
 163 of rosuvastatin ($\text{C}_{22}\text{H}_{28}\text{FN}_3\text{O}_6\text{S}$), and filter this solution
 164 through a membrane filter with a pore size not exceeding
 165 0.45 μm . Discard the first 5 mL of the filtrate, and use the
 166 subsequent filtrate as the sample solution. Separately,
 167 weigh accurately about 0.1 g of Rosuvastatin Calcium RS
 168 (separately determine the water <2.48> in the same manner
 169 as Rosuvastatin Calcium), add 50 mL of water, sonicate,
 170 add 25 mL of acetonitrile, cool to room temperature, and
 171 add water to make exactly 100 mL. Pipet 5 mL of this solu-
 172 tion, add a mixture of water and acetonitrile (3:1) to make
 173 exactly 200 mL, and use this solution as the standard solu-
 174 tion. Perform the test with exactly 10 μL each of the sample
 175 solution and standard solution as directed under Liquid
 176 Chromatography <2.01> according to the following condi-
 177 tions, and determine the peak areas, A_T and A_S , of rosuvas-
 178 tatin in each solution.

179 Amount (mg) of rosuvastatin ($\text{C}_{22}\text{H}_{28}\text{FN}_3\text{O}_6\text{S}$) in 1 tablet of
 180 Rosuvastatin Calcium Tablets

$$181 = M_S \times A_T / A_S \times V / 400 \times 0.962$$

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

184 *Operating conditions*—

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

187 Column: A stainless steel column 3.2 mm in inside
 188 diameter and 25 cm in length, packed with
 189 octadecylsilanized silica gel for liquid chromatography (5
 190 μm in particle diameter).

191 Column temperature: A constant temperature of about
 192 40°C.

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

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

197 *System suitability*—

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

202 mL of acetonitrile and water to make 200 mL. To 10 mL of
203 this solution add 10 mL of a mixture of water and
204 acetonitrile (3:1). When the procedure is run with 10 μ L of
205 this solution under the above operating conditions, the
206 resolution between rosuvastatin and the related substance B
207 (diastereomer) having the relative retention time of about
208 1.1 to rosuvastatin is not less than 1.5.

209 System repeatability: When the test is repeated 6 times
210 with 10 μ L of the standard solution under the above
211 operating conditions, the relative standard deviation of the
212 peak area of rosuvastatin is not more than 1.5%.

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

214 **Others**

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

217 **Add the following to 9.01 Reference**

218 **Standards (1):**

219 **Rosuvastatin Calcium RS**

220 **Add the following to 9.41 Reagents,**

221 **Test Solutions:**

222 **0.1 mol/L Citric acid TS** Dissolve 21 g of citric acid
223 monohydrate in water to make 1000 mL.

224 **0.05 mol/L Citrate buffer solution (pH 6.6)** Dissolve
225 147 g of trisodium citrate dihydrate in 2000 mL of water,
226 add 3.6 g of citric acid monohydrate to dissolve, and add
227 water to make 10 L. To this solution add 0.1 mol/L sodium
228 citrate TS or 0.1 mol/L citric acid TS to adjust the pH to 6.6.

229 **0.1 mol/L Phosphate buffer solution (pH 7)** Dissolve
230 13.6 g of potassium dihydrogen phosphate in 800 mL of
231 water, adjust the pH to 7 ± 0.4 with sodium hydroxide TS,
232 and add water to make 1000 mL.

233 **Rosuvastatin calcium** ($C_{22}H_{27}FN_3O_6S$)₂Ca [Same as
234 the namesake monograph]

235 **0.1 mol/L Sodium citrate TS** Dissolve 29.4 g of triso-
236 dium citrate dihydrate in water to make 1000mL

237