1 Pregabalin Capsules

2 プレガバリンカプセル

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4 Pregabalin Capsules contain not less than 95.0% and 5 not more than 105.0% of the labeled amount of pregab-6 alin ($C_8H_{17}NO_2$: 159.23).

7 Method of preparation Prepare as directed under Cap-8 sules, with Pregabalin.

9 Identification Take out the contents of Pregabalin Cap-10 sules, and powder. To a portion of the powder, equivalent to 11 25 mg of Pregabalin, add 10 mL of methanol, shake thor-12 oughly, centrifuge, and use the supernatant liquid as the sam-13 ple solution. Separately, dissolve 10 mg of Pregabalin RS in 14 4 mL of methanol, and use this solution as the standard solu-15 tion. Perform the test with these solutions as directed under Thin-layer Chromatography $\langle 2.03 \rangle$. Spot 5 μ L each of the 16 sample solution and standard solution on a plate of silica gel 17 18 for thin-layer chromatography. Develop the plate with a mix-19 ture of methanol, acetonitrile and ammonia solution (28) 20 (65:34:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly a solution of ninhydrin in a mixture of 2-propa-21 22 nol and water (4:1) (1 in 1000) on the plate, and air-dry the 23 plate: the spots obtained from the sample solution and stand-24 ard solution show the same Rf value. 25 Purity Related Substances—Use the sample solution ob-

26 tained in the Assay as the sample solution. Perform the test 27 with 50 μ L of the sample solution as directed under Liquid 28 Chromatography <2.01> according to the following condi-29 tions. Determine each peak area by the automatic integration 30 method, and calculate their amounts by the area percentage method: the amount of the peak of related substance A having 31 32 the relative retention time of about 3.0 to pregabalin is not 33 more than 0.5%, the amount of the peak other than pregabalin 34 and the peak mentioned above is not more than 0.2%, and the 35 total amount of the peaks other than pregabalin is not more than 1.0%. For the area of the peak of related substance A 36 37 and the peaks having the relative retention time of about 1.4, 38 about 1.7, about 1.9 and about 2.1 to pregabalin, multiply the 39 correction factors, 0.05, 0.06, 0.05, 0.04 and 0.03, respec-40 tively.

41 Operating conditions—

42 Detector, column, column temperature, mobile phase, and43 flow rate: Proceed as directed in the operating conditions in44 the Assay.

Time span of measurement: For 15 minutes after injection,beginning after the solvent peak.

- 47 System suitability—
- 48 Test for required detectability: To 1 mL of the sample so-
- 49 lution, add the mobile phase to make 100 mL and use this

50 solution as the solution for system suitability test. Pipet 2 mL 51 of the solution for system suitability test, and add the mobile 52 phase to make exactly 20 mL. Confirm that the peak area of 53 pregabalin obtained with 50 μ L of this solution is equivalent 54 to 7 to 13% of that with 50 μ L of the solution for system 55 suitability test.

56 System performance: When the procedure is run with 50 57 μ L of the solution for system suitability test under the above 58 operating conditions, the number of theoretical plates and the 59 symmetry factor of the peak of pregabalin are not less than 60 1800 and not more than 2.0, respectively.

61 **Uniformity of dosage units** <*6.02>* Perform the Mass var-62 iation test, or the Content uniformity test according to the fol-63 lowing method: it meets the requirement.

64 Take out the contents of 1 capsule of Pregabalin Capsules, 65 and add the mobile phase. If necessary, wash the capsule shell with a small amount of the mobile phase, and add the 66 67 washing. Stir, and add the mobile phase to make exactly 50 68 mL. Filter this solution through a membrane filter with a pore 69 size not exceeding 0.45 μ m. Discard the first 10 mL of the 70 filtrate, pipet V mL of the subsequent filtrate, add the mobile 71 phase to make exactly V' mL so that each mL contains about 72 0.5 mg of pregabalin ($C_8H_{17}NO_2$), and use this solution as the 73 sample solution. Separately, weigh accurately about 25 mg 74 of Pregabalin RS (separately determine the water <2.48> in 75 the same manner as Pregabalin), and dissolve in the mobile phase to make exactly 50 mL, and use this solution as the 76 77 standard solution. Perform the test with exactly 50 μ L each 78 of the sample solution and standard solution as directed under 79 Liquid Chromatography <2.01> according to the following 80 conditions, and determine the peak areas, A_T and A_S , of 81 pregabalin in each solution.

Amount (mg) of pregabalin (C₈H₁₇NO₂)
=
$$M_{\rm S} \times A_{\rm T} / A_{\rm S} \times V' / V$$

 $M_{\rm S}$: Amount (mg) of Pregabalin RS taken, calculated on the anhydrous basis

86 Operating conditions—

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87 Proceed as directed in the operating conditions in the As-88 say.

89 System suitability—

90 System performance: When the procedure is run with 50 91 μ L of the standard solution under the above operating condi-92 tions, the number of theoretical plates and the symmetry fac-93 tor of the peak of pregabalin are not less than 1800 and not 94 more than 2.0, respectively.

95 System repeatability: When the test is repeated 6 times 96 with 50 μ L of the standard solution under the above operating 97 conditions, the relative standard deviation of the peak area of 98 pregabalin is not more than 1.0%. 99 Dissolution <6.10> When the test is performed at 50 revo100 lutions per minute according to the Paddle method using the
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101 sinker, using 900 mL of 1st fluid for dissolution test as the
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153 dissolution medium, the value Q in 30 minutes of Pregabalin
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103 Capsules is 80%. 104 Start the test with 1 capsule of Pregabalin Capsules, with-105 draw not less than 10 mL of the medium at the specified mi-106 nute after starting the test, and filter through a membrane fil-107 ter with a pore size not exceeding 0.45 μ m. Discard the first 108 3 mL of the filtrate, pipet V mL of the subsequent filtrate, add 109 the dissolution medium to make exactly V' mL so that each 110 mL contains about 28 μ g of pregabalin (C₈H₁₇NO₂), and use 111 this solution as the sample solution. Separately, weigh accu-112 rately about 28 mg of Pregabalin RS (separately determine 113 the water <2.48> in the same manner as Pregabalin), and dis-114 solve in dissolution medium to make exactly 100 mL. Pipet 5 mL of this solution, add the dissolution medium to make 115 exactly 50 mL, and use this solution as the standard solution. 116 117 Perform the test with exactly 50 μ L each of the sample solution and standard solution as directed under Liquid Chroma-118 119 tography <2.01> according to the following conditions, and 120 determine the peak areas, A_T and A_S , of pregabalin in each 121 solution.

122	Dissolution rate (%) with respect to the labeled amount
123	of pregabalin (C ₈ H ₁₇ NO ₂)
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$$124 \qquad = M_{\rm S} \times A_{\rm T} / A_{\rm S} \times V' / V \times 1 / C \times 90$$

- M_S: Amount (mg) of Pregabalin RS taken, calculated on
 the anhydrous basis
- 127C: Labeled amount (mg) of pregabalin (C₈H₁₇NO₂) in 1128capsule
- 129 Operating conditions—
- 130 Detector: An ultraviolet absorption photometer (wave-131 length: 210 nm).
- 132 Column: A stainless steel column 4.6 mm in inside diam-
- 183 133 eter and 15 cm in length, packed with cyanopropylsilanized 134 silica gel for liquid chromatography (5 μ m in particle diame-135 ter).
- Column temperature: A constant temperature of about35°C.
- Mobile phase: Dissolve 9.41 g of sodium 1-hexane sulfonate and 2 mL of triethylamine in 880 mL of water, and
 adjust to pH 3.1 with phosphoric acid. To this solution add
 130 mL of acetonitrile for liquid chromatography.
- 142 Flow rate: Adjust so that the retention time of pregabalin
- 143 is about 6 minutes.
- 144 System suitability—
- 145 System performance: When the procedure is run with 50
- 146 μ L of the standard solution under the above operating condi-
- 147 tions, the number of theoretical plates and the symmetry fac-
- 148 tor of the peak of pregabalin are not less than 5000 and not
- 149 more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 50 μ L of the standard solution under the above operating conditions, the relative standard deviation of the peak area of pregabalin is not more than 2.0%.

Assay Weigh accurately the mass of not less than 20 Pregabalin Capsules, take out the contents, and weigh accurately the mass of the emptied shells. Powder the contents, and weigh accurately a portion of the powder, equivalent to about 50 mg of pregabalin (C₈H₁₇NO₂), add the mobile phase, stir, and add the mobile phase to make exactly 50 mL. Filter this solution through a membrane filter with a pore size not exceeding 0.45 μ m. Discard the first 10 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 25 mg of Pregabalin RS (separately determine the water <2.48> in the same manner as Pregabalin), and dissolve in the mobile phase to make exactly 25 mL, and use this solution as the standard solution. Perform the test with exactly 50 μ L 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, $A_{\rm T}$ and $A_{\rm S}$, of pregabalin in each solution.

Amount (mg) of pregabalin (C₈H₁₇NO₂)
=
$$M_{\rm S} \times A_{\rm T} / A_{\rm S} \times 2$$

 $M_{\rm S}$: Amount (mg) of Pregabalin RS taken, calculated on the anhydrous basis

Operating conditions—

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

Column: A stainless steel column 3.9 mm in inside diameter and 30 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10 μ m in particle diameter).

Column temperature: A constant temperature of about 20°C.

Mobile phase: Dissolve 5.79 g of anhydrous disodium hydrogen phosphate and 3.52 g of potassium dihydrogen phosphate in 1000 mL of water, and adjust to pH 7.0 with phosphoric acid or potassium hydroxide TS. To 1 mL of this solution add 550 mL of water, 350 mL of methanol for liquid chromatography and 100 mL of acetonitrile for liquid chromatography.

Flow rate: Adjust so that the retention time of pregabalin is about 3.6 minutes.

193 System suitability—

194 System performance: When the procedure is run with 50 195 μ L of the standard solution under the above operating condi-196 tions, the number of theoretical plates and the symmetry fac-197 tor of the peak of pregabalin are not less than 1800 and not 198 more than 2.0, respectively.

- 199 System repeatability: When the test is repeated 6 times
- 200 with 50 μL of the standard solution under the above operating
- $201 \quad \text{conditions, the relative standard deviation of the peak area of} \\$
- 202 pregabalin is not more than 1.0%.
- 203 Containers and storage Containers—Tight containers.
- 204 Others
- 205 Related substance A: Refer to it described in Pregabalin.

206 Add the following to 9.01 Reference

- 207 Standards section (1).
- 208 Pregabalin RS