

1 Sodium Valproate Extended-release 2 Tablets B

3 バルプロ酸ナトリウム徐放錠 B

5 Sodium Valproate Extended-release Tablets B
6 contain not less than 95.0% and not more than
7 105.0% of the labeled amount of sodium valproate
8 ($C_8H_{15}NaO_2$: 166.19).

9 **Method of preparation** Prepare as directed under Tab-
10 lets, with Sodium Valproate.

11 **Identification** To a quantity of the powdered Sodium
12 Valproate Extended-release Tablets B, equivalent to 1.0 g
13 of Sodium Valproate, add 10 mL of water, heat on a water
14 bath for 30 minutes, and filter. To 2.5 mL of the filtrate add
15 2.5 mL of water and 1 mL of a solution of cobalt (II) nitrate
16 hexahydrate (1 in 20), and heat on a water bath: a purple
17 precipitate is formed.

18 **Uniformity of dosage units** <6.02> Perform the Mass
19 variation test, or the Content uniformity test according to
20 the following method: it meets the requirement.

21 To 1 tablet of Sodium Valproate Extended-release Tab-
22 lets B add 150 mL of the mobile phase, allow to stand for
23 not less than 16 hours, shake until the film is disintegrated,
24 and add the mobile phase to make exactly 200 mL. Pipet V
25 mL of this solution, and add the mobile phase to make ex-
26 actly V' mL so that each mL contains about 1 mg of sodium
27 valproate ($C_8H_{15}NaO_2$). Centrifuge this solution, and filter
28 the supernatant liquid through a membrane filter with a
29 pore size not exceeding $0.45 \mu\text{m}$. Discard the first 5 mL of
30 the filtrate, pipet 20 mL of the subsequent filtrate, add ex-
31 actly 5 mL of the internal standard solution, and use this
32 solution as the sample solution. Then, proceed as directed
33 in the Assay.

$$34 \quad \text{Amount (mg) of sodium valproate (C}_8\text{H}_{15}\text{NaO}_2\text{)} \\ 35 \quad = M_S \times Q_T / Q_S \times V' / V \times 2$$

36 M_S : Amount (mg) of sodium valproate for assay taken

37 **Internal standard solution**—A solution of methyl parahy-
38 droxybenzoate in the mobile phase (1 in 50,000).

39 **Dissolution** <6.10> When the test is performed at 50 rev-
40 olutions per minute according to the Paddle method, using
41 900 mL of water as the dissolution medium, the dissolution
42 rates of a 200-mg tablet in 8 hours, in 11 hours and in 20
43 hours are 15 to 45%, 35 to 65%, and not less than 70%,
44 respectively, and those of a 400-mg tablet in 9 hours, in 12
45 hours and in 21 hours are 15 to 45%, 35 to 65%, and not
46 less than 70%, respectively.

47 Start the test with 1 tablet of Sodium Valproate Ex-
48 tended-release Tablets B, withdraw exactly 20 mL of the
49 medium at the specified minutes after starting the test and
50 supply exactly 20 mL of water warmed to $37 \pm 0.5^\circ\text{C}$ im-
51 mediately after withdrawing of the medium every time. Fil-
52 ter the media through a membrane filter with a pore size not
53 exceeding $0.45 \mu\text{m}$. Discard the first 2 mL of the filtrate,
54 pipet V mL of the subsequent filtrate, add water to make
55 exactly V' mL so that each mL contains about 0.22 mg of
56 sodium valproate ($C_8H_{15}NaO_2$), and use these solutions as
57 the sample solutions. Separately, weigh accurately about 55
58 mg of sodium valproate for assay, previously dried at
59 105°C for 3 hours, dissolve in water to make exactly 250
60 mL, and use this solution as the standard solution. Perform
61 the test with exactly $20 \mu\text{L}$ each of the sample solutions and
62 standard solution as directed under Liquid Chromatog-
63 raphy <2.01> according to the following conditions, and de-
64 termine the peak areas, $A_{T(n)}$ and A_S , of valproic acid in each
65 solution.

66 Dissolution rate (%) with respect to the labeled amount of
67 sodium valproate ($C_8H_{15}NaO_2$) on the n th medium with-
68 drawing ($n = 1, 2, 3$)

$$69 \quad = M_S \times \left\{ \frac{A_{T(n)}}{A_S} + \sum_{i=1}^{n-1} \left(\frac{A_{T(i)}}{A_S} \times \frac{1}{45} \right) \right\} \times \frac{V'}{V} \times \frac{1}{C} \times$$

70 360

71 M_S : Amount (mg) of sodium valproate for assay taken
72 C : Labeled amount (mg) of sodium valproate
73 ($C_8H_{15}NaO_2$) in 1 tablet

74 **Operating conditions**—

75 Perform as directed in the operating conditions in the
76 Assay.

77 **System suitability**—

78 **System performance**: When the procedure is run with 20
79 μL of the standard solution under the above operating
80 conditions, the number of theoretical plates and the
81 symmetry factor of the peak of valproic acid are not less
82 than 3000 and not more than 2.0, respectively.

83 **System repeatability**: When the test is repeated 6 times
84 with $20 \mu\text{L}$ of the standard solution under the above
85 operating conditions, the relative standard deviation of the
86 peak area of valproic acid is not more than 1.0%.

87 **Assay** To 20 Sodium Valproate Extended-release Tablets
88 B add 150 mL of the mobile phase, allow to stand for not
89 less than 16 hours, shake until the film is disintegrated, and
90 add the mobile phase to make exactly 200 mL. Pipet 5 mL
91 of this solution, add the mobile phase to make exactly V mL
92 so that each mL contains about 1 mg of sodium valproate
93 ($C_8H_{15}NaO_2$). Centrifuge this solution, and filter the super-
94 natant liquid through a membrane filter with a pore size not
95 exceeding $0.45 \mu\text{m}$. Discard the first 5 mL of the filtrate,

96 pipet 20 mL of the subsequent filtrate, add exactly 5 mL of
97 the internal standard solution, and use this solution as the
98 sample solution. Separately, weigh accurately about 0.1 g
99 of sodium valproate for assay, previously dried at 105°C
100 for 3 hours, dissolve in the mobile phase to make exactly
101 100 mL. Pipet 20 mL of this solution, add exactly 5 mL of
102 the internal standard solution, and use this solution as the
103 standard solution. Perform the test with 10 μL each of the
104 sample solution and standard solution as directed under
105 Liquid Chromatography <2.01> according to the following
106 conditions, and calculate the ratios, Q_T and Q_S , of the peak
107 area of valproic acid to that of the internal standard.

108 Amount (mg) of sodium valproate ($\text{C}_8\text{H}_{15}\text{NaO}_2$) in 1
109 tablet

$$110 = M_S \times Q_T / Q_S \times V / 50$$

111 M_S : Amount (mg) of sodium valproate for assay taken

112 *Internal standard solution*—A solution of methyl parahy-
113 droxybenzoate in the mobile phase (1 in 50,000).

114 *Operating conditions*—

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

117 Column: A stainless steel column 4.6 mm in inside
118 diameter and 15 cm in length, packed with
119 octadecylsilanized silica gel for liquid chromatography (5
120 μm in particle diameter).

121 Column temperature: A constant temperature of about
122 25°C.

123 Mobile phase: A mixture of 0.05 mol/L sodium
124 dihydrogen phosphate TS (pH 3.0) and acetonitrile for
125 liquid chromatography (1:1).

126 Flow rate: Adjust so that the retention time of valproic
127 acid is about 6 minutes.

128 *System suitability*—

129 System performance: When the procedure is run with 10
130 μL of the standard solution under the above operating
131 conditions, the internal standard and valproic acid are
132 eluted in this order with the resolution between these peaks
133 being not less than 7.

134 System repeatability: When the test is repeated 6 times
135 with 10 μL of the standard solution under the above
136 operating conditions, the relative standard deviation of the
137 ratio of the peak area of valproic acid to that of the internal
138 standard is not more than 1.0%.

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

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