

1 **Doripenem for Injection**

2 注射用ドリペネム

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4 Doripenem for Injection is a preparation for
5 injection, which is dissolved before use.

6 It contains not less than 95.0% and not more than
7 105.0% of the labeled potency of doripenem
8 ($C_{15}H_{24}N_4O_6S_2$: 420.50).

9 **Method of preparation** Prepare as directed under Injec-
10 tions, with Doripenem Hydrate.

11 **Description** Doripenem for Injection occurs as a white to
12 pale yellow-brown-white crystalline powder.

13 **Identification** Proceed as directed in the Identification
14 (2) under Doripenem Hydrate.

15 **pH** <2.54> Dissolve an amount of Doripenem for Injec-
16 tion, equivalent to 0.3 g (potency) of Doripenem Hydrate,
17 in 30 mL of water: the pH of the solution is between 4.5
18 and 6.0.

19 **Purity** (1) Clarity and color of solution—Dissolve an
20 amount of Doripenem for Injection, equivalent to 0.2 g (po-
21 tency) of Doripenem Hydrate in 20 mL of water, and per-
22 form the test with this solution as directed in the Purity (1)
23 under Doripenem Hydrate.

24 (2) Related substances—(i) Dissolve an amount of
25 Doripenem for Injection, equivalent to 20 mg (potency) of
26 Doripenem Hydrate, in 10 mL of water, and use this solu-
27 tion as the sample solution. Pipet 1 mL of the sample solu-
28 tion, add water to make exactly 100 mL, and use this solu-
29 tion as the standard solution. Perform the test with exactly
30 20 μ L each of the sample solution and standard solution as
31 directed under Liquid Chromatography <2.01> according to
32 the following conditions, and determine each peak area by
33 the automatic integration method: the area of the peak other
34 than doripenem and the peak, having the relative retention
35 time of about 2.1 to doripenem, related substance A having
36 the relative retention time of about 2.2, related substance B
37 having the relative retention time of about 2.5 and related
38 substance C having the relative retention time of about 3.2,
39 obtained from the sample solution is not larger than 1/10
40 times the peak area of doripenem from the standard solu-
41 tion, and the total area of the peaks, other than doripenem
42 and the peaks mentioned above, from the sample solution
43 is not larger than 1/2 times the peak area of doripenem from
44 the standard solution.

45 **Operating conditions**—

46 Proceed as directed in the operating conditions in the Pu-
47 rity (3) (i) under Doripenem Hydrate.

48 **System suitability**—

49 Test for required detectability: Pipet 2.5 mL of the
50 standard solution, and add water to make exactly 50 mL.
51 Confirm that the peak area of doripenem obtained with 20
52 μ L of this solution is equivalent to 3.5 to 6.5% of that with
53 20 μ L of the standard solution.

54 **System performance**: When the procedure is run with 20
55 μ L of the standard solution under the above operating
56 conditions, the number of theoretical plates and the
57 symmetry factor of the peak of doripenem are not less than
58 5000 and not more than 1.3, respectively.

59 **System repeatability**: When the test is repeated 3 times
60 with 20 μ L of the standard solution under the above
61 operating conditions, the relative standard deviation of the
62 peak area of doripenem is not more than 0.95%.

63 (ii) Dissolve an amount of Doripenem for Injection,
64 equivalent to about 20 mg (potency) of Doripenem Hydrate,
65 in 10 mL of water, and use this solution as the sample so-
66 lution. Pipet 1 mL of the sample solution, add water to
67 make exactly 100 mL, and use this solution as the standard
68 solution. Perform the test with exactly 20 μ L each of the
69 sample solution and standard solution as directed under
70 Liquid Chromatography <2.01> according to the following
71 conditions. Determine each peak area by the automatic in-
72 tegration method: the peak area of related substance D, hav-
73 ing the relative retention time of about 0.5 to doripenem,
74 obtained from the sample solution is not larger than the
75 peak area of doripenem from the standard solution.

76 **Operating conditions**—

77 Proceed as directed in the operating conditions in the
78 Purity (3) (ii) under Doripenem Hydrate.

79 **System performance**: To 1 mL of the sample solution
80 add 1 mL of 0.1 mol/L hydrochloric acid TS, allow to stand
81 at $25 \pm 5^\circ\text{C}$ for 15 minutes, and add water to make 100 mL.
82 When the procedure is run with 20 μ L of this solution under
83 the above operating conditions, related substance D and
84 doripenem are eluted in this order with the resolution
85 between these peaks being not less than 5. The number of
86 theoretical plates and the symmetry factor of the peak of
87 related substance D are not less than 300 and 0.7 to 1.3,
88 respectively, and those of the peak of doripenem are not
89 less than 5000 and 0.7 to 1.3, respectively.

90 **System repeatability**: When the test is repeated 6 times
91 with 20 μ L of the standard solution under the above
92 operating conditions, the relative standard deviation of the
93 peak area of doripenem is not more than 2.0%.

94 **Water** <2.48> 4.0 – 5.0% (0.3 g, volumetric titration,
95 back titration).

96 **Bacterial endotoxins** <4.01> Less than 0.25 EU/mg (po-
97 tency).

98 **Uniformity of dosage units** <6.02> It meets the require-
99 ment of the Mass variation test.

100 **Foreign insoluble matter** <6.06> Perform the test ac-
101 cording to Method 2: it meets the requirement.

102 **Insoluble particulate matter** <6.07> It meets the require-
103 ment.

104 **Sterility** <4.06> Perform the test according to the Mem-
105 brane filtration method: it meets the requirement.

106 **Assay** Weigh accurately the mass of the contents of not
107 less than 10 containers of Doripenem for Injection. Weigh
108 accurately an amount of the contents, equivalent to about
109 25 mg (potency) of Doripenem Hydrate, dissolve in water
110 to make exactly 200 mL, and use this solution as the sample
111 solution. Separately, weigh accurately about 25 mg (po-
112 tency) of Doripenem RS (separately determine the water
113 <2.48> in the same manner as Doripenem Hydrate), dis-
114 solve in water to make exactly 200 mL, and use this solu-
115 tion as the standard solution. Then, proceed as directed in
116 the Assay under Doripenem Hydrate.

117 Amount [μg (potency)] of doripenem ($\text{C}_{15}\text{H}_{24}\text{N}_4\text{O}_6\text{S}_2$)
118 $= M_S \times A_T / A_S \times 1000$

119 M_S : Amount [mg (potency)] of Doripenem RS taken, cal-
120 culated on the anhydrous basis

121 **Containers and storage** Containers—Hermetic contain-
122 ers. Plastic containers for aqueous injections may be used.

123 **Others**

124 Related substances A, B, C and D: Refer to them de-
125 scribed in Doripenem Hydrate.

126 **Add the following to 9.01 Reference**
127 **Standards (1):**

128 **Doripenem RS**

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