

1 Voriconazole for Injection

2 注射用ポリコナゾール

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4 Voriconazole for Injection is a preparation for injection
5 which is dissolved before use. It contains not less than
6 93.0% and not more than 105.0% of the labeled amount of
7 voriconazole ($C_{16}H_{14}F_3N_5O$: 349.31). Correct the amount
8 obtained in the Assay with T value.

9 **Method of preparation** Prepare as directed under Injections,
10 with Voriconazole.

11 **Description** Voriconazole for Injection is white masses or pow-
12 der.

13 **Identification** To 5 mL of the sample solution obtained in the
14 Assay add the mobile phase in the Assay to make 25 mL. Deter-
15 mine the absorption spectrum of this solution as directed under
16 Ultraviolet-visible Spectrophotometry <2.24>: it exhibits a maxi-
17 mum between 254 nm and 258 nm.

18 **pH** Being specified separately when the drug is granted ap-
19 proval based on the Law.

20 **Purity (1)** Related substances—Dissolve the content of 1 con-
21 tainer of Voriconazole for Injection in water so that each mL con-
22 tains about 10 mg of voriconazole ($C_{16}H_{14}F_3N_5O$). To 5 mL of this
23 solution add the mobile phase to make 100 mL, and use this solu-
24 tion as the sample solution. Pipet 5 mL of the sample solution, and
25 add the mobile phase to make exactly 50 mL. Pipet 2 mL of this
26 solution, add the mobile phase to make exactly 100 mL, and use
27 this solution as the standard solution. Perform the test with exactly
28 20 μ L each of the sample solution and standard solution as di-
29 rected under Liquid Chromatography <2.01> according to the fol-
30 lowing conditions. Determine each peak area by the automatic in-
31 tegration method: the area of the peak, having the relative reten-
32 tion time of about 0.26 to voriconazole, obtained from the sample
33 solution is not larger than 2.5 times the peak area of voriconazole
34 obtained from the standard solution, the area of the peak, having
35 the relative retention time of about 0.32 to voriconazole, from the
36 sample solution is not larger than the peak area of voriconazole
37 from the standard solution, the area of the peak, having the relative
38 retention time of about 0.5 to voriconazole, from the sample solu-
39 tion is not larger than 2 times the peak area of voriconazole from
40 the standard solution, and the area of peak other than voriconazole,
41 the peak having the relative retention time of about 0.61 to
42 voriconazole and the peaks mentioned above from the sample so-
43 lution is not larger than the peak area of voriconazole from the
44 standard solution. Furthermore, the total area of the peaks other
45 than voriconazole and the peak having the relative retention time
46 of about 0.61 to voriconazole from the sample solution is not
47 larger than 7 times the peak area of voriconazole from the standard
48 solution. For the area of the peaks, having the relative retention
49 times of about 0.26, about 0.32 and about 0.5 to voriconazole, mul-
50 tiple the relative response factor, 0.7, 0.7 and 1.2, respectively.

51 *Operating conditions* —

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

54 Time span of measurement: About 1.3 times as long as the
55 retention time of voriconazole.

56 *System suitability* —

57 System performance: Suspend 0.1 g of voriconazole in 10 mL
58 of a solution of sodium hydroxide (1 in 25), add the mobile phase
59 to make 20 mL, and allow to stand for 30 minutes. To 1 mL of this
60 solution add the mobile phase to make 100 mL. When the
61 procedure is run with 20 μ L of this solution, the resolution
62 between the peaks, having the relative retention times about 0.26
63 and about 0.32 to voriconazole, is not less than 1.5.

64 System repeatability: To 5 mL of the standard solution add the
65 mobile phase to make 10 mL. When the test is repeated 6 times
66 with 20 μ L of this solution under the above operating conditions,
67 the relative standard deviation of the peak area of voriconazole is
68 not more than 5.0%.

69 **(2) Enantiomer** — Dissolve the content of 1 container of
70 Voriconazole for Injection in the mobile phase so that each mL
71 contains about 1 mg of voriconazole ($C_{16}H_{14}F_3N_5O$). To 5 mL of
72 this solution add the mobile phase to make 10 mL, and use this
73 solution as the sample solution. Pipet 1 mL of the sample solution,
74 and add the mobile phase to make exactly 100 mL. Pipet 1 mL of
75 this solution, add the mobile phase to make exactly 10 mL, and
76 use this solution as the standard solution. Perform the test with
77 exactly 20 μ L each of the sample solution and standard solution
78 as directed under Liquid Chromatography <2.01> according to the
79 following conditions. Determine each peak area by the automatic
80 integration method: the area of the peak, having the relative reten-
81 tion time of about 1.3 to voriconazole, from the sample solution is
82 not larger than 4 times the peak area of voriconazole from the
83 standard solution.

84 *Operating conditions* —

85 Proceed as directed in the operating conditions in the Purity (3)
86 under Voriconazole.

87 *System suitability* —

88 Proceed as directed in the system suitability in the Purity (3)
89 under Voriconazole.

90 **Bacterial endotoxins** <4.01> Less than 1.5 EU/mg.

91 **Uniformity of dosage units** <6.02> It meets the requirement of
92 the Mass variation test. (T : 106.0%)

93 **Foreign insoluble matter** <6.06> Perform the test according to
94 Method 2: it meets the requirement.

95 **Insoluble particulate matter** <6.07> It meets the requirement.

96 **Sterility** <4.06> Perform the test according to the Membrane fil-
97 tration method: it meets the requirement.

98 **Assay** Take 10 containers of Voriconazole for Injection, dis-
99 solve the contents of each in the mobile phase, combine the solu-
100 tions, and add the mobile phase to make exactly 1000 mL. Pipet 5

101 mL of this solution, add the mobile phase to make exactly 100 mL,
102 and use this solution as the sample solution. Separately, weigh ac-
103 curately about 50 mg of Voriconazole RS (separately determine
104 the water <2.48> in the same manner as Voriconazole), and dis-
105 solve in the mobile phase to make exactly 50 mL. Pipet 5 mL of
106 this solution, add the mobile phase to make exactly 50 mL, and
107 use this solution as the standard solution. Perform the test with
108 exactly 20 μ L each of the sample solution and standard solution
109 as directed under Liquid Chromatography <2.01> according to the
110 following conditions, and determine the peak areas, A_T and A_S , of
111 voriconazole in each solution.

112 Amount (mg) of voriconazole ($C_{16}H_{14}F_3N_5O$) in 1 container of
113 Voriconazole for Injection
114 $= M_S \times A_T / A_S \times 4$

115 M_S : Amount (mg) of Voriconazole RS taken, calculated on the
116 anhydrous basis

117 *Operating conditions* —

118 Detector, column, column temperature and mobile phase:
119 Proceed as directed in the operating conditions in the Assay under
120 Voriconazole.

121 Flow rate: Adjust so that the retention time of voriconazole is
122 about 9 minutes.

123 *System suitability* —

124 System repeatability: Proceed as directed in the system
125 suitability in the Assay under Voriconazole.

126 System performance: When the procedure is run with 20 μ L of
127 the standard solution under the above operating conditions, the
128 number of theoretical plates and the symmetry factor of the peak
129 of voriconazole are not less than 5000 and not more than 1.7, re-
130 spectively.

131 **Containers and storage** Containers—Hermetic containers.

132 **Add the following to 9.41 Reagents, Test**
133 **Solutions:**

134 **Voriconazole** $C_{16}H_{14}F_3N_5O$ [Same as the namesake mono-
135 graph]

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