Voriconazole for Injection

注射用ボリコナゾール

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

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

Description Voriconazole for Injection is white masses or powder.

Identification To 5 mL of the sample solution obtained in the Assay add the mobile phase in the Assay to make 25 mL. Determine the absorption spectrum of this solution as directed under Ultraviolet-visible Spectrophotometry <*2.24*>: it exhibits a maximum between 254 nm and 258 nm.

pH Being specified separately when the drug is granted approval based on the Law.

Purity **(1)** Related substances－Dissolve the content of 1 container of Voriconazole for Injection in water so that each mL contains about 10 mg of voriconazole ($C_{16}H_{14}F_3N_5O$). To 5 mL of this solution add the mobile phase to make 100 mL, and use this solution as the sample solution. Pipet 5 mL of the sample solution, and add the mobile phase to make exactly 50 mL. Pipet 2 mL of this solution, add the mobile phase to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 20 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions. Determine each peak area by the automatic integration method: the area of the peak, having the relative retention time of about 0.26 to voriconazole, obtained from the sample solution is not larger than 2.5 times the peak area of voriconazole obtained from the standard solution, the area of the peak, having the relative retention time of about 0.32 to voriconazole, from the sample solution is not larger than the peak area of voriconazole from the standard solution, the area of the peak, having the relative retention time of about 0.5 to voriconazole, from the sample solution is not larger than 2 times the peak area of voriconazole from the standard solution, and the area of peak other than voriconazole, the peak having the relative retention time of about 0.61 to voriconazole and the peaks mentioned above from the sample solution is not larger than the peak area of voriconazole from the standard solution. Furthermore, the total area of the peaks other than voriconazole and the peak having the relative retention time of about 0.61 to voriconazole from the sample solution is not larger than 7 times the peak area of voriconazole from the standard solution. For the area of the peaks, having the relative retention times of about 0.26, about 0.32 and about 0.5 to voriconazole, multiply the relative response factor, 0.7, 0.7 and 1.2, respectively.

Operating conditions －

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

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

System suitability －

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

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

(2) Enantiomer － Dissolve the content of 1 container of Voriconazole for Injection in the mobile phase so that each mL contains about 1 mg of voriconazole ($C_{16}H_{14}F_3N_5O$). To 5 mL of this solution add the mobile phase to make 10 mL, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add the mobile phase to make exactly 100 mL. Pipet 1 mL of this solution, add the mobile phase to make exactly 10 mL, and use this solution as the standard solution. Perform the test with exactly 20 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions. Determine each peak area by the automatic integration method: the area of the peak, having the relative retention time of about 1.3 to voriconazole, from the sample solution is not larger than 4 times the peak area of voriconazole from the standard solution.

Operating conditions －

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

System suitability －

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

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

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

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

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

Sterility <*4.06*> Perform the test according to the Membrane filtration method: it meets the requirement.

Assay Take 10 containers of Voriconazole for Injection, dissolve the contents of each in the mobile phase, combine the solutions, and add the mobile phase to make exactly 1000 mL. Pipet 5

mL of this solution, add the mobile phase to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 50 mg of Voriconazole RS (separately determine the water *<2.48>* in the same manner as Voriconazole), and dissolve in the mobile phase to make exactly 50 mL. Pipet 5 mL of this solution, add the mobile phase to make exactly 50 mL, and use this solution as the standard solution. Perform the test with exactly 20 μL 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_T and A_S, of voriconazole in each solution.

Amount (mg) of voriconazole ($C_{16}H_{14}F_3N_5O$) in 1 container of Voriconazole for Injection

$= M_S \times A_T / A_S \times 4$

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

Operating conditions —

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

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

System suitability —

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

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of voriconazole are not less than 5000 and not more than 1.7, respectively.

Containers and storage Containers—Hermetic containers.

Add the following to 9.41 Reagents, Test Solutions:

Voriconazole $C_{16}H_{14}F_3N_5O$ [Same as the namesake monograph]