Temozolomide for Injection

注射用テモゾロミド

Temozolomide for Injection is a preparation for injection which is dissolved before use.

It contains not less than 95.0% and not more than 105.0% of the labeled amount of temozolomide ($C_6H_6N_6O_2$: 194.15).

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

Description Temozolomide for Injection occurs as a white to pale red or light yellow-brown powder.

Identification Perform the test with 75 μL each of the sample solution and standard solution obtained in the Assay as directed under Liquid Chromatography <*2.01*> according to the following conditions: the retention times of the principal peaks in the chromatograms obtained from these solutions are the same, and the absorption spectra of these peaks exhibit similar intensities of absorption at the same wavelengths.

Operating conditions—

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

Detector: A photodiode array detector (wavelength: 270 nm, spectrum range of spectrum: 210 – 400 nm).

System suitability—

System performance: Proceed as directed in the system suitability in the Assay.

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

Purity Related substances—Use the sample solution obtained in the Assay as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 75 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions, and determine each peak area by the automatic integration method: the peak area of the related substance E, having the relative retention time of about 0.4 to temozolomide, obtained from the sample solution is not larger than 2/5 times the peak area of temozolomide from the standard solution, the peak area of the related substance IA, having the relative retention time of about 1.4, from the sample solution is not larger than the peak area of temozolomide from the standard solution, and the area of the peak other than temozolomide and the peaks mentioned above from the sample solution is not larger than 1/5 times the peak area of temozolomide from the standard solution. Furthermore, the total area of the peaks other than temozolomide from the sample solution is not larger than the peak area of temozolomide from the standard solution. For the peak areas of the related substances E and IA, multiply the relative response factors, 0.63 and 0.29, respectively.

Operating conditions—

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

Time span of measurement: About 3 times as long as the retention time of temozolomide.

System suitability—

System performance: Proceed as directed in the system suitability in the Assay.

Test for required detectability: Pipet 5 mL of the standard solution obtained in the Assay, and add the mobile phase to make exactly 200 mL. Pipet 2 mL of this solution, and add the mobile phase to make exactly 100 mL. When the procedure is run with 75 μL of this solution under the above operating conditions, the SN ratio of the peak of temozolomide is not less than 10.

System repeatability: When the test is repeated 6 times with 75 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of temozolomide is not more than 2.0%.

Water <*2.48*> To an amount of Temozolomide for Injection, equivalent to 100 mg of Temozolomide, add exactly 40 mL of methanol, dissolve the content, pipet 2 mL of the solution, and perform the test by coulometric titration: not more than 1.0%. Perform a blank determination in the same manner, and make any necessary correction.

Bacterial endotoxins <*4.01*> Less than 0.75 EU/mg.

Uniformity of dosage units <*6.02*> It meets the requirement of the Mass variation test (*T*: being specified separately when the drug is granted approval based on the Law.).

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 a number of Temozolomide for Injection, equivalent to 500 mg of temozolomide ($C_6H_6N_6O_2$), dissolve each content in water, wash each container with water, combine the washings with the former solution, and add water to the combined solution to make exactly *V* mL so that each mL contains about 2.5 mg of Temozolomide. Pi-

pet 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 31 mg of Temozolomide RS, and add the mobile phase to make exactly 50 mL. Pipet 10 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 75 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 temozolomide in each solution.

$$\text{Amount (mg) of temozolomide } (C_6H_6N_6O_2) = M_S \times A_T / A_S \times 16$$

M_S: Amount (mg) of Temozolomide RS taken

Operating conditions—

Proceed as directed in the operating conditions in the Assay under Temozolomide.

System suitability—

System performance: To 1 mg of temozolomide add a mixture of the mobile phase and 0.1 mol/L hydrochloric acid TS (1:1) to make 10 mL, heat at 80℃ for about 4 hours, and cool to about 4℃. To this solution add the mobile phase to make 25 mL. When the procedure is run with 75 μL of this solution under the above operating conditions, the resolution between the peaks of temozolomide and the related substance IA is not less than 2.5, and the symmetry factor of the peak of temozolomide is not more than 1.9.

System repeatability: When the test is repeated 6 times with 75 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of temozolomide is not more than 1.0%.

Containers and storage Containers—Hermetic containers.

Storage—At a temperature between 2℃ and 8℃.

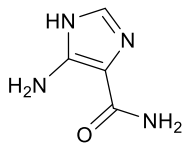
Others

Related substance E:

Refer to it described in Temozolomide.

Related substance IA:

5-Amino-1*H*-imidazole-4-carboxamide



Add the following to 9.01 Reference Standards (1):

Temozolomide RS

Add the following to 9.41 Reagents, Test Solutions:

Temozolomide $C_6H_6N_6O_2$ [Same as the namesake monograph]