Methotrexate for Injection

注射用メトトレキサート

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

It contains not less than 95.0% and not more than 115.0% of the labeled amount of methotrexate ($C_{20}H_{22}N_8O_5$: 454.44).

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

Description Methotrexate for Injection occurs as a light yellow to reddish yellow crystalline powder or mass.

Identification To 1 mL of a solution of Methotrexate for Injection (1 in 400) add 0.1 mol/L hydrochloric acid TS to make 250 mL. Determine the absorption spectrum of this solution as directed under Ultraviolet-visible Spectrophotometry <*2.24*>: it exhibits maxima between 241 nm and 245 nm, and 305 nm and 309 nm.

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

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

Bacterial endotoxins <*4.01*> Less than 0.1 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 Dissolve the contents of 20 containers of Methotrexate for Injection in the mobile phase, wash the containers with the mobile phase, combine the solution of the content and washings, and add the mobile phase to make exactly 1000 mL. Pipet *V* mL of this solution, add the mobile phase to make exactly *V'* mL so that each mL contains about 0.1 mg of methotrexate ($C_{20}H_{22}N_8O_5$), and use this solution as the sample solution. Separately, weigh accurately about 10 mg of Methotrexate RS (separately determine the water <*2.48*> in the same manner as Methotrexate), 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, and determine the peak areas, A_T and A_S, of methotrexate in each solution.

Amount (mg) of methotrexate ($C_{20}H_{22}N_8O_5$) in 1 container of Methotrexate for Injection

$$= M_S \times A_T / A_S \times V' / V \times 1 / 2$$

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

Operating conditions—

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

Column: A stainless steel column of 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

System suitability—

System performance: Dissolve 10 mg each of methotrexate and folic acid in 100 mL of the mobile phase. When the procedure is run with 20 μL of this solution under the above operating conditions, folic acid and methotrexate are eluted in this order with the resolution between these peaks being not less than 8.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of methotrexate is not more than 1.0%.

Containers and storage Containers—Hermetic containers. Storage—Light-resistant.