～*Information*～

[This monograph is applied to 2.5-mg tablet.]

Methotrexate Tablets

メトトレキサート錠

Methotrexate Tablets contain not less than 95.0% and not more than 105.0% of the labeled amount of methotrexate ($C_{20}H_{22}N_8O_5$: 454.44).

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

Identification To a quantity of powdered Methotrexate Tablets, equivalent to about 2.5 mg of Methotrexate, add 100 mL of diluted hydrochloric acid (1 in 100), shake, and filter or centrifuge. 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 between 305 nm and 309 nm.

Uniformity of dosage unit <*6.02*> Perform the test according to the following method: it meets the requirement of the Content uniformity test.

To 1 tablet of Methotrexate Tablets add the mobile phase, stir, and add the mobile phase to make exactly V mL so that each mL contains about 0.1 mg of methotrexate ($C_{20}H_{22}N_8O_5$). Centrifuge this solution, and use the supernatant liquid as the sample solution. Then, proceed as directed in the Assay.

Amount (mg) of methotrexate ($C_{20}H_{22}N_8O_5$)
$= M_S \times A_T / A_S \times V / 250$

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

Dissolution <*6.10*> When the test is performed at 50 revolutions per minute according to the Paddle method, using 900 mL of water as the dissolution medium, the dissolution rate in 45 minutes of Methotrexate Tablets is not less than 85% .

Start the test with 1 tablet of Methotrexate Tablets, withdraw not less than 20 mL of the medium at the specified minute after starting the test, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 10 mL of the filtrate, pipet V mL of the subsequent filtrate, add water to make exactly V' mL so that each mL contains about 2.8 μg of methotrexate ($C_{20}H_{22}N_8O_5$), and use this solution as the sample solution. Separately, weigh accurately about 25 mg of Methotrexate RS (separately determine the water <*2.48*> in the same manner as Methotrexate), and dissolve in the mobile phase to make exactly 100 mL. Pipet 1 mL of this solution, add water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 50 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*>, and determine the peak areas, A_T and A_S, of methotrexate in each solution.

Dissolution rate (%) with respect to the labeled amount of methotrexate ($C_{20}H_{22}N_8O_5$)
$= M_S \times A_T / A_S \times V' / V \times 1 / C \times 9$

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

C: Labeled amount (mg) of methotrexate ($C_{20}H_{22}N_8O_5$) in 1 tablet

Operating conditions —

Detector: An ultraviolet absorption photometer (wavelength: 302 nm).

Column: A stainless steel column 4 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25℃.

Mobile phase: To 250 mL of 0.2 mol/L of potassium dihydrogen phosphate TS add 29 mL of 0.2 mol/L sodium hydroxide TS and water to make 1000 mL. To 890 mL of this solution add 110 mL of acetonitrile.

Flow rate: Adjust so that the retention time of methotrexate is about 4 minutes.

System suitability —

System performance: When the procedure is run with 50 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of methotrexate are not less than 3000 and not more than 1.5, respectively.

System repeatability: When the test is repeated 6 times with 50 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%.

Assay Weigh accurately the mass of not less than 20 tablets of Methotrexate Tablets, and powder. Weigh accurately a portion of the powder, equivalent to about 10 mg of methotrexate ($C_{20}H_{22}N_8O_5$), add 50 mL of the mobile phase, shake, and add the mobile phase to make exactly 100 mL. Centrifuge this solution, and use the supernatant liquid as the sample solution. Separately, weigh accurately about 25 mg of Methotrexate RS (separately determine the water <*2.48*> in the same manner as Methotrexate), dissolve in the mobile phase to make exactly 250 mL, and use this solution as the standard solution. Perform the test with 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 ($C_{20}H_{22}N_8O_5$)
$= M_S \times A_T / A_S \times 2 / 5$

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 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 — Well-closed containers.

Storage — Light-resistant.