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Methotrexate Tablets

DEFINITION

Methotrexate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of methotrexate ($C_{20}H_{22}N_8O_5$).

IDENTIFICATION

Change to read:

- **A.** ▲ [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), *Ultraviolet-Visible Spectroscopy*: **197U** ▲ (CN 1-MAY-2020)

Standard solution: 25 µg/mL of [USP Methotrexate RS](#) in dilute hydrochloric acid (1 in 100)

Sample solution: Dissolve 1 Tablet in 100 mL of dilute hydrochloric acid (1 in 100), and filter the solution.

Acceptance criteria: The UV absorption spectrum of the *Sample solution* exhibits maxima and minima at the same wavelengths as that of the *Standard solution*.

ASSAY

• PROCEDURE

Buffer: 0.2 M dibasic sodium phosphate and 0.1 M citric acid (63:37), adjusted if necessary with 0.1 M citric acid or 0.2 M dibasic sodium phosphate to a pH of 6.0

Mobile phase: Acetonitrile and *Buffer* (10:90)

System suitability solution: 0.1 mg/mL each of [USP Methotrexate RS](#) and folic acid in *Mobile phase*

Standard solution: 100 µg/mL of [USP Methotrexate RS](#) in *Mobile phase*

Sample solution: Equivalent to 100 µg/mL of methotrexate from powdered Tablets (NLT 20 Tablets) in *Mobile phase*. Dissolve the methotrexate using a mechanical shaker or ultrasonic bath.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 302 nm

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for folic acid and methotrexate are 0.35 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 8.0 between the folic acid and methotrexate peaks

Relative standard deviation: NMT 2.5% for the methotrexate peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of methotrexate ($C_{20}H_{22}N_8O_5$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Methotrexate RS](#) in the *Standard solution* (µg/mL)

C_U = nominal concentration of methotrexate in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- [DISSOLUTION \(711\)](#)

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm
Time: 45 min

Standard solution: [USP Methotrexate RS](#) in *Medium*

Detector: UV 306 nm (maximum absorbance)

Analysis: Determine the amount of $C_{20}H_{22}N_8O_5$ dissolved from UV absorbances on filtered portions of the solution under test, suitably diluted with *Medium*, in comparison with a *Standard solution*.

Tolerances: NLT 75% (Q) of the labeled amount of methotrexate ($C_{20}H_{22}N_8O_5$) is dissolved.

- [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meet the requirements

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. A unit-of-use container contains a quantity of Tablets sufficient to provide one week's therapy as indicated in the labeling.
- **LABELING:** When packaged in a unit-of-use container, the label indicates the total amount of methotrexate present as one week's supply.
- [USP REFERENCE STANDARDS \(11\)](#).
[USP Methotrexate RS](#)

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
METHOTREXATE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: [Chromatographic Database](#)

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