In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 5 Expert Committee has revised the Methylprednisolone Tablets monograph. The purpose of this revision is to add Dissolution Test 2 to accommodate FDA-approved drug products with different dissolution conditions and/or tolerances than the existing dissolution test. Labeling information has been incorporated to support the inclusion of Dissolution Test 2.

Additionally, minor editorial changes have been made to update the monograph to current USP style.

The Methylprednisolone Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Robyn Fales, Senior Scientist I (240-221-2047 or rnp@usp.org).
Methylprednisolone Tablets

DEFINITION
Methylprednisolone Tablets contain NLT 92.5% and NMT 107.5% of the labeled amount of methylprednisolone (C22H30O5).

IDENTIFICATION
• A. Spectroscopic Identification Tests (197), Infrared Spectroscopy: 197K
  Sample: Digest an amount nominally equivalent to about 40 mg of methylprednisolone from powdered Tablets with 25 mL of solvent hexane for 15 min. Filter, and discard the filtrate. Digest the residue with 25 mL of chloroform for 15 min. Filter, evaporate the filtrate to dryness, and dry at 105° for 2 h.
  Acceptance criteria: Meets the requirements

• B.
  Sample: Use the Sample from Identification A.
  Analysis: Dissolve about 5 mg of Sample in 2 mL of sulfuric acid.
  Acceptance criteria: A red color is produced

ASSAY
• Procedure
  Mobile phase: Butyl chloride, water-saturated butyl chloride, tetrahydrofuran, methanol, and glacial acetic acid (95:95:14:7:6)
  Solution A: 3% Glacial acetic acid in chloroform
  Internal standard solution: 0.2 mg/mL of prednisone in Solution A
  Standard solution: 0.2 mg/mL of USP Methylprednisolone RS in the Internal standard solution
  Sample solution: Nominally 0.19 mg/mL of methylprednisolone prepared as follows. Transfer an amount nominally equivalent to about 10 mg of methylprednisolone, from 20 finely powdered Tablets in a mortar and pestle, to a suitable container. Add 2.5 mL of water and swirl to form a fine slurry. Add 50.0 mL of Internal standard solution and shake for 15 min. If necessary, pass a portion of the solution through a suitable filter or centrifuge a portion of the solution and analyze the clear supernatant.

Chromatographic system
(See Chromatography (621), System Suitability.)
  Mode: LC
  Detector: UV 254 nm
  Column: 4.0-mm × 25.0-cm; packing L3
  Flow rate: 1 mL/min
  Injection volume: 10 µL

System suitability
  Sample: Standard solution
  [Note—The relative retention times for prednisone and methylprednisolone are about 0.7 and 1.0, respectively.]
  Suitability requirements
Resolution: NLT 4.0 between prednisone and methylprednisolone
Relative standard deviation: NMT 2.0%

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of the labeled amount of methylprednisolone (C_{22}H_{30}O_{5}) in the portion of Tablets taken:

\[ \text{Result} = \left( \frac{R_U}{R_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100 \]

- \( R_U \) = peak response ratio of methylprednisolone to prednisone from the Sample solution
- \( R_S \) = peak response ratio of methylprednisolone to prednisone from the Standard solution
- \( C_S \) = concentration of USP Methylprednisolone RS in the Standard solution (mg/mL)
- \( C_U \) = nominal concentration of methylprednisolone in the Sample solution (mg/mL)

Acceptance criteria: 92.5%–107.5%

PERFORMANCE TESTS

Change to read:

- **Dissolution** (711)

Test 1 (RB 1-Jun-2022)
- Medium: Water; 900 mL
- Apparatus 2: 50 rpm
- Time: 30 min
- Standard solutions: 20 µg/mL of USP Methylprednisolone RS prepared as follows. Dissolve a suitable quantity of USP Methylprednisolone RS in 0.1% of the flask volume of alcohol and dilute with water to volume. Prepare quantitative dilutions of this solution for the development of a standard curve.
- Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with Medium, if necessary

Instrumental conditions
- Mode: UV
- Analytical wavelength: 246 nm
- Cell: 1 cm
- Blank: Water

Analysis
- Samples: Standard solutions, Sample solution, and Blank
  Using a standard curve, representing the absorbance versus concentration of the Standard solutions, determine the labeled amount of methylprednisolone (C_{22}H_{30}O_{5}) dissolved.

Tolerances: NLT 70% (Q) of the labeled amount of methylprednisolone (C_{22}H_{30}O_{5}) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 2.
- Medium: Water; 500 mL
- Apparatus 2: 50 rpm
- Time: 20 min
- Standard stock solution: 0.2 mg/mL of USP Methylprednisolone RS prepared as follows. Transfer a suitable amount of USP Methylprednisolone RS to an appropriate volumetric flask. Add 2% of the
flask volume of ethyl alcohol and sonicate to dissolve. Dilute with water to volume.

**Standard solution A:** 0.002 mg/mL of USP Methylprednisolone RS from *Standard stock solution* in water

**Standard solution B:** 0.004 mg/mL of USP Methylprednisolone RS from *Standard stock solution* in water

**Standard solution C:** 0.008 mg/mL of USP Methylprednisolone RS from *Standard stock solution* in water

**Standard solution D:** 0.010 mg/mL of USP Methylprednisolone RS from *Standard stock solution* in water

**Standard solution E:** 0.012 mg/mL of USP Methylprednisolone RS from *Standard stock solution* in water

**Sample solution:** Pass a portion of the solution under test through a suitable filter of 0.45-μm pore size.

**Instrumental conditions**

*Mode:* UV

*Analytical wavelength:* 246 nm

*Cell:* 1 cm

*Blank:* Water

**System suitability**

**Samples:** Standard solution A, Standard solution B, Standard solution C, Standard solution D, and Standard solution E

**Suitability requirements**

*Correlation coefficient:* NLT 0.99, as determined from the linear calibration constructed in the Analysis

**Analysis**

**Samples:** Standard solution A, Standard solution B, Standard solution C, Standard solution D, Standard solution E, Sample solution, and Blank

Determine the responses for Standard solution A, Standard solution B, Standard solution C, Standard solution D, and Standard solution E. Construct a linear calibration curve by plotting response values of Standard solution A, Standard solution B, Standard solution C, Standard solution D, and Standard solution E versus their corresponding concentrations in mg/mL. Determine the concentration (C) in mg/mL of methylprednisolone (C\(_{22}\)H\(_{30}\)O\(_5\)) in the portion of Tablets taken from the calibration curve. Calculate the percentage of the labeled amount of methylprednisolone (C\(_{22}\)H\(_{30}\)O\(_5\)) dissolved:

\[
\text{Result} = C \times V \times (1/L) \times 100
\]

\(C\) = concentration of methylprednisolone in the Sample solution (mg/mL), as determined from the calibration curve

\(V\) = volume of Medium, 500 mL

\(L\) = label claim (mg/Tablet)

**Tolerances:** NLT 80% (Q) of the labeled amount of methylprednisolone (C\(_{22}\)H\(_{30}\)O\(_5\)) is dissolved.

(RB 1-Jun-2022)

• **Uniformity of Dosage Units** (905): Meet the requirements

Sample solution: Place 1 Tablet in a suitable container. For tablet-labeled strengths of 10 mg or less, add 0.5 mL of water. For tablet-labeled strengths greater than 10 mg, add 1.0 mL of water. Allow the Tablet to stand for about 2 min, then swirl the container to disperse the Tablet. Add 5.0 mL of Internal standard solution for each milligram of labeled Tablet strength, shake for 15 min, and pass a portion of solution through a suitable filter or centrifuge a portion of the solution and analyze the clear supernatant.

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of the labeled amount of methylprednisolone (C\textsubscript{22}H\textsubscript{30}O\textsubscript{5}) in the Tablet taken:

\[
\text{Result} = \left( \frac{R_U}{R_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100
\]

- \( R_U \) = peak response ratio of methylprednisolone to prednisone from the Sample solution
- \( R_S \) = peak response ratio of methylprednisolone to prednisone from the Standard solution
- \( C_S \) = concentration of USP Methylprednisolone RS in the Standard solution (mg/mL)
- \( C_U \) = nominal concentration of methylprednisolone in the Sample solution (mg/mL)

ADDITIONAL REQUIREMENTS

- Packaging and Storage: Preserve in tight containers.

Add the following:

- **Labeling:** When more than one Dissolution Test is given, the labeling states the test used only if Test 1 is not used.▲ (RB 1-Jun-2022)

- **USP Reference Standards** (11),
  USP Methylprednisolone RS

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