Methylprednisolone Tablets

Type of Posting	Revision Bulletin
Posting Date	27-May-2022
Official Date	1-Jun-2022
Expert Committee	Small Molecules 5

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).

Revision Bulletin
Official: June 1, 2022

Methylprednisolone Tablets

DEFINITION

Methylprednisolone Tablets contain NLT 92.5% and NMT 107.5% of the labeled amount of methylprednisolone ($C_{22}H_{30}O_5$).

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:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

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

Procedure for content uniformity

Mobile phase, Solution A, Internal Standard solution, Standard solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

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 ($C_{22}H_{30}O_5$) in the Tablet taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

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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