Prednisone Tablets

**Type of Posting**  Revision Bulletin
**Posting Date**  07–Jul–2020
**Official Date**  08–Jul–2020
**Expert Committee**  Chemical Medicines Monographs 5
**Reason for Revision**  Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 5 Expert Committee has revised the Prednisone Tablets monograph. The purpose for the 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(s).

- *Dissolution Test 2* was validated using an Inertsil ODS-3V brand of column with L1 packing. The typical retention time for Prednisone is about 4.1 min.

*Labeling* information has been incorporated to support the inclusion of *Dissolution Test 2*.

The Prednisone Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Ren-Hwa Yeh, Senior Scientific Liaison to the Chemical Medicines Monographs 5 Expert Committee (301-998-6818 or rhy@usp.org).
Prednisone Tablets

DEFINITION
Prednisone Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of prednisone (C₂₁H₂₆O₉).

IDENTIFICATION
• A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy; 197K
  Sample: Nominally 10 mg of prednisone from pulverized Tablets
  Analysis: Place the Sample in a 50-mL beaker, add 10 mL of water, and mix to form a slurry. Transfer the slurry to a 3-cm × 13-cm column packed with diatomaceous earth, and allow to absorb for 10 min. Elute the column with 60 mL of water-washed ether, and evaporate the eluate on a steam bath to dryness. Wash the residue with three 20-mL portions of n-heptane, and filter. Dry the residue at 105° for 30 min.
  Acceptance criteria: The crystals meet the requirements. If a difference appears, dissolve portions of both the crystals and the Reference Standard in methanol, evaporate the solutions to dryness, and repeat the tests.
• B.
  Analysis 1: Dissolve 6 mg of the crystals obtained in Identification test A in 2 mL of sulfuric acid, and allow to stand for 5 min.
  Acceptance criteria 1: An orange color is produced.
  Analysis 2: Pour the resulting solution from Analysis 1 into 10 mL of water.
  Acceptance criteria 2: The color changes first to yellow and then, gradually, to bluish green.

ASSAY
• PROCEDEURE
  Mobile phase: Peroxide-free tetrahydrofuran, methanol, and water (250:62:688). Prepare the Mobile phase such that, at a flow rate of 1.0 mL/min, the retention times of prednisone and acetanilide are about 8 and 6 min, respectively.
  Diluent: Methanol and water (1:1)
  Internal standard solution: 110 µg/mL of acetanilide in Diluent
  Standard stock solution: 0.2 mg/mL of USP Prednisone RS in Diluent
  Standard solution: 20 µg/mL of USP Prednisone RS and 11 µg/mL of acetanilide in Diluent from the Standard stock solution and the Internal standard solution, respectively. Prepare this solution fresh.
  Sample stock solution: Nominally 0.2 mg/mL of prednisone prepared as follows. Transfer an amount of powder equivalent to 20 mg of prednisone from NLT 20 powdered Tablets to a suitable volumetric flask. Add 5% of the flask volume of water, and sonicate for 1 min. Add 50% of the flask volume of methanol, and sonicate again for 1 min. Dilute with water to volume.
  Sample solution: Nominally 20 µg/mL of prednisone and 11 µg/mL of acetanilide in Diluent from the Sample stock solution and the Internal standard solution, respectively. Pass through a suitable filter of 5-µm pore size, discarding the first 20 mL of the filtrate.

Chromatographic system
(See Chromatography (621), System Suitability.)
  Model: LC
  Detector: UV 254 nm
  Column: 4-mm × 25-cm; packing L₁
  Injection volume: 10 µL

System suitability
  Sample: Standard solution
  Suitability requirements
    Resolution: NLT 3 between prednisone and acetanilide
    Relative standard deviation: NMT 2.0%

Analysis
  Samples: Standard solution and Sample solution
  Calculate the percentage of the labeled amount of prednisone (C₂₁H₂₆O₉) in the portion of Tablets taken:

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

where:
- \( R_J \) = peak response ratio of prednisone to acetanilide from the Sample solution
- \( R_S \) = peak response ratio of prednisone to acetanilide from the Standard solution
- \( C_S \) = concentration of USP Prednisone RS in the Standard solution (µg/mL)
- \( C_U \) = nominal concentration of prednisone in the Sample solution (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:
• DISSOLUTION (711).

Test 1\(^{(R8-8-Jul-2020)}\)
  Medium: Water; use 500 mL of the Medium for Tablets labeled to contain 10 mg of prednisone or less, and 900 mL for Tablets labeled to contain more than 10 mg of prednisone.
  Apparatus 2: 50 rpm
  Time: 30 min
  Standard solution: USP Prednisone RS in Medium. [Note—An amount of alcohol not to exceed 5% of the total volume of the Standard solution may be used to bring the prednisone Standard into solution before dilution with Medium.]
Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with Medium, if necessary, to a concentration that is similar to the Standard solution.

Instrumental conditions
- Mode: UV
- Analytical wavelength: Maximum at about 242 nm
- Tolerances: NLT 80% (Q) of the labeled amount of prednisone (C_{21}H_{26}O_{5}) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 2.

[Note—Protect solutions containing prednisone from light.]

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 75 rpm

Time: 30 min

Diluted phosphoric acid: Dilute 10 mL of phosphoric acid with water to 100 mL.

Buffer: Add 1.0 mL of triethylamine to 1000 mL of water and adjust with Diluted phosphoric acid to a pH of 5.2.

Mobile phase: Acetonitrile and Buffer (40:60)

Standard stock solution: 0.25 mg/mL of USP Prednisone RS prepared as follows. Transfer an appropriate amount of USP Prednisone RS to a suitable volumetric flask. Add 25% of the flask volume of acetonitrile and sonicate to dissolve. Dilute with water to volume.

Standard solution: \( (L/500) \) mg/mL of USP Prednisone RS from Standard stock solution in Medium, where \( L \) is the label claim in mg/Tablet. For Tablets of 20 mg strength, use \( (L/1000) \) mg/mL.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-μm pore size, discarding the first 2 mL of the filtrate. Dilute with Medium, if necessary.

Chromatographic system
- Mode: LC
- Detector: UV 242 nm
- Column: 4.6-mm × 25-cm; 5-µm packing L1
- Column temperature: 35°
- Flow rate: 1.5 mL/min
- Injection volume: 100 µL
- Run time: NLT 1.7 times the retention time of prednisone

System suitability
- Sample: Standard solution
- Suitability requirements
  - Tailing factor: NMT 2.0
  - Relative standard deviation: NMT 2.0%

Analysis
- Samples: Standard solution and Sample solution
  - Calculate the percentage of the labeled amount of prednisone (C_{21}H_{26}O_{5}) dissolved:
    \[
    \text{Result} = \left( \frac{r_U}{r_S} \right) \times \frac{C_S}{D} \times V \times \frac{1}{L} \times 100
    \]
    \( r_U \) = peak response of prednisone from the Sample solution
    \( r_S \) = peak response of prednisone from the Standard solution
    \( C_S \) = concentration of USP Prednisone RS in the Standard solution (mg/mL)
    \( D \) = dilution factor, if necessary
    \( V \) = volume of Medium, 500 mL
    \( L \) = label claim (mg/Tablet)
  - Tolerances: NLT 80% (Q) of the labeled amount of prednisone (C_{21}H_{26}O_{5}) is dissolved. 

Uniformity of Dosage Units (905)

Procedure for content uniformity
- Sample stock solution: Place 1 Tablet in a suitable volumetric flask that when the contents are diluted to volume, the resulting solution has a nominal concentration of 0.2 mg/mL of prednisone. Add 5 mL of water, swirl, sonicate for 1 min, add a volume of methanol equal to one-half the volume of the volumetric flask, and sonicate again for 1 min. Dilute with water to volume.
- Sample solution: Nominally 20 µg/mL of prednisone and 11 µg/mL of acetanilide in Diluent from the Sample stock solution and the Internal standard solution, respectively. Pass through a suitable filter of 5-µm pore size, discarding the first 20 mL of the filtrate.

Analysis
- Samples: Standard solution and Sample solution
  - Calculate the percentage of the labeled amount of prednisone (C_{21}H_{26}O_{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 prednisone to acetanilide from the Sample solution
    \( R_S \) = peak response ratio of prednisone to acetanilide from the Standard solution
    \( C_S \) = concentration of USP Prednisone RS in the Standard solution (µg/mL)
    \( C_U \) = nominal concentration of prednisone in the Sample solution (µg/mL)
**Acceptance criteria:** Meet the requirements

**ADDITIONAL REQUIREMENTS**

- **Packaging and Storage:** Preserve in well-closed containers.

**Add the following:**

- **Labeling:** When more than one Dissolution test is given, the labeling states the Dissolution test used only if Test 1 is not used. (RB 8-Jul-2020)

**USP Reference Standards**

USP Prednisone RS

---

**Page Information:**

Not Applicable

© 2020 The United States Pharmacopeial Convention All Rights Reserved.