Prednisone Tablets

Type of Posting	Revision Bulletin
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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).

Revision Bulletin
Official: July 8, 2020

Prednisone Tablets

DEFINITION
Prednisone Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of prednisone ($C_{21}H_{26}O_5$).

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

- **Procedure**

  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*.)

  Mode: 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 ($C_{21}H_{26}O_5$) 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 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▲ (RB 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

(See *Chromatography ⟨621⟩, System Suitability*.)

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:

$$\text{Result} = (r_U/r_S) \times C_S \times D \times V \times (1/L) \times 100$$

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.▲ (RB 8-Jul-2020)

• **Uniformity of Dosage Units ⟨905⟩**

Procedure for content uniformity

Mobile phase, Diluent, Internal standard solution, Standard stock solution, Standard solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

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:

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

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** ⟨11⟩

USP Prednisone RS

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