

Prednisone Tablets

Type of Posting	Notice of Intent to Revise
Posting Date	30–Aug–2019
Targeted Official Date	To Be Determined, Revision Bulletin
Expert Committee	Chemical Medicines Monographs 5

In accordance with section 7.04 (c) of the 2015–2020 Rules and Procedures of the Council of Experts and the [Pending Monograph Guideline](#), this is to provide notice that the Chemical Medicines Monographs 5 Expert Committee intends to revise the Prednisone Tablets monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to add *Dissolution Test 2* to the monograph.

- *Dissolution Test 2* was validated using an Inertsil ODS 3V brand of L1 column. 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 proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.¹

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).

¹ This text is not the official version of a *USP–NF* monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the *USP–NF* for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product's final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the *Pharmacopeial Forum* must also meet the requirements outlined in the [USP Guideline on Use of Accelerated Processes for Revisions to the USP–NF](#).

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. INFRARED ABSORPTION <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▲ (TBD)

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,

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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 (C₂₁H₂₆O₅) 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 (C₂₁H₂₆O₅) is dissolved. ▲ (TBD)

• 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 (C₂₁H₂₆O₅) 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. ▲ (TBD)
- **USP REFERENCE STANDARDS** <11>
USP Prednisone RS