Dexamethasone Tablets

Type of Posting	Notice of Intent to Revise
Posting Date	30-Jul-2021
Targeted Official Date	To Be Determined, Revision Bulletin
Expert Committee	Small Molecules 5

In accordance with the Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Small Molecules 5 Expert Committee intends to revise the Dexamethasone Tablets monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to add *Dissolution Test 2* to accommodate drug products with different dissolution conditions and tolerances than the existing dissolution test. *Labeling* information has been incorporated to support the inclusion of *Dissolution Test 2*.

- *Dissolution Test 2* was validated using the X-bridge C18 brand of column with L1 packing. The typical retention time for dexamethasone is about 4.6 min.

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

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 Claire Chisolm, Senior Scientist II (301-230-3215 or cnc@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*.

Notice of Intent to Revise
Official: To Be Determined

Dexamethasone Tablets

DEFINITION

Dexamethasone Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of dexamethasone ($C_{22}H_{29}FO_5$).

IDENTIFICATION

- **A. Thin-Layer Chromatography**

Standard solution: 500 µg/mL of USP Dexamethasone RS in chloroform

Sample solution: Nominally, 1 mg/mL of dexamethasone prepared as follows. Evaporate 10 mL of the *Sample solution* as directed under the *Assay* on a steam bath just to dryness, and dissolve the residue in 1 mL of chloroform.

Chromatographic system

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

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume

Sample solution: 10 µL

Standard solution: 20 µL

Analysis

Samples: *Standard solution* and *Sample solution*

Develop the chromatogram in *Solvent A* as directed under *Single-Steroid Assay* ⟨511⟩. Mark the solvent front, and locate the spots on the plate by visualizing under short-wavelength UV light.

Acceptance criteria: The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard solution*.

ASSAY

- **Procedure**

Diluent: Methanol and water (50:50)

Mobile phase: Acetonitrile and water (33:66)

Standard solution: 0.1 mg/mL of USP Dexamethasone RS in *Diluent*

Sample solution: Nominally 0.1 mg/mL of dexamethasone prepared as follows. Transfer the equivalent of 5 mg of dexamethasone from finely powdered Tablets (NLT 10) to a 50-mL volumetric flask, and add 30 mL of *Diluent*. Sonicate the flask for 2 min, shake by mechanical means for 30 min, and dilute with *Diluent* to volume. Pass a portion of the mixture through a suitable filter to obtain a clear filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 30-cm; packing L1

Injection volume: 5–25 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 3.0%, for five replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of dexamethasone ($C_{22}H_{29}FO_5$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Dexamethasone RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of dexamethasone in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **Dissolution** ⟨711⟩

▲**Test 1**▲ (TBD)

Medium: Dilute 1 mL of hydrochloric acid with water to 100 mL; 500 mL

Apparatus 1: 100 rpm

Time: 45 min

Standard solution: Prepare as directed for *Standard Preparation* in *Assay for Steroids* ⟨351⟩, using USP Dexamethasone RS.

Sample solution: Extract a filtered aliquot of *Medium*, equivalent to 0.2 mg of dexamethasone, with three 15-mL portions of chloroform. Evaporate the combined chloroform extracts on a steam bath just to dryness, cool, and dissolve the residue in 20 mL of alcohol.

Analysis: Proceed as directed for *Procedure* in *Assay for Steroids* ⟨351⟩, except allow it to stand in the dark for 45 min.

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of dexamethasone ($C_{22}H_{29}FO_5$) dissolved:

$$\text{Result} = (A_U/A_S) \times 20 \times C_S \times (V/V_S) \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Dexamethasone RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 500 mL

V_S = volume of *Medium* extracted with chloroform (mL)

L = label claim (mg/Tablet)

Tolerances: NLT 70% (Q) of the labeled amount of dexamethasone ($C_{22}H_{29}FO_5$) is dissolved.

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

Medium: 0.1 N hydrochloric acid VS; 500 mL

Apparatus 1: 100 rpm

Time: 30 min

Solution A: 25% (v/v) phosphoric acid in water prepared as follows. Transfer 25 mL of phosphoric acid to a 100-mL volumetric flask containing about 50 mL of water. Cool and dilute with water to volume.

Buffer: 1.36 g/L of monobasic potassium phosphate in water. Add 1.0 mL of triethylamine to each liter of solution, and adjust with *Solution A* to a pH of 3.0.

Mobile phase: Methanol and *Buffer* (50:50)

Standard stock solution: 0.5 mg/mL of USP Dexamethasone RS in methanol. Sonicate to dissolve as needed.

Standard solution: (*L*/500) mg/mL of USP Dexamethasone RS from *Standard stock solution* in *Medium*, where *L* is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size and discard the first 5 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 5.0-cm; 3.5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: NLT 1.3 times the retention time of dexamethasone

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 dexamethasone ($C_{22}H_{29}FO_5$) dissolved:

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

r_U = peak response of dexamethasone from the *Sample solution*

r_S = peak response of dexamethasone from the *Standard solution*

C_S = concentration of USP Dexamethasone RS in the *Standard solution* (mg/mL)

V = volume of the *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of dexamethasone ($C_{22}H_{29}FO_5$) is dissolved. ▲ (TBD)

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

Procedure for content uniformity

Standard solution: Prepare as directed for *Standard Preparation* in *Assay for Steroids* ⟨351⟩, using USP Dexamethasone RS.

Sample solution: Place 1 Tablet in a separator with 15 mL of water, and swirl to disintegrate the Tablet completely. Extract with four 10-mL portions of chloroform, filtering each portion through chloroform-washed cotton into a 50-mL volumetric flask, and add chloroform to volume. Pipet a volume of this solution, equivalent to 200 µg of dexamethasone, into a glass-stoppered, 50-mL conical flask. Evaporate the chloroform on a steam bath just to dryness, cool, and dissolve the residue in 20.0 mL of alcohol. Use this where *Assay Preparation* is specified in *Assay for Steroids* ⟨351⟩*, Procedure*.

Analysis

Samples: *Standard solution* and *Sample solution*

Proceed as directed in *Assay for Steroids* ⟨351⟩*, Procedure*, except allow it to stand in the dark for 45 min.

Calculate the percentage of total steroids, as dexamethasone ($C_{22}H_{29}FO_5$), in the Tablet:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Dexamethasone RS in the *Standard solution* (mg/mL)

V = volume of the chloroform extract (mL) used to prepare the *Sample solution*

L = label claim (mg/Tablet)

Acceptance criteria: Meets 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 Dexamethasone RS

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Not Applicable

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