Methylprednisolone Sodium Succinate for Injection

Type of Posting	Notice of Intent to Revise
Posting Date	28-May-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 Methylprednisolone Sodium Succinate for Injection monograph.

Based on the supporting documentation received from a manufacturer awaiting FDA approval, the Expert Committee proposes to revise the drug product description to include Sodium Bicarbonate as a salt forming reagent in the *Definition* section.

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 Michael Chang, Staff Scientist (301-230-3217 or mxc@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

Methylprednisolone Sodium Succinate for Injection

Change to read:

DEFINITION

Methylprednisolone Sodium Succinate for Injection is a sterile mixture of Methylprednisolone Sodium Succinate with suitable buffers. It may be prepared from Methylprednisolone Sodium Succinate or from Methylprednisolone Hemisuccinate with the aid of Sodium Hydroxide, ▲Sodium Bicarbonate,▲ (TBD) or Sodium Carbonate. It contains the equivalent of NLT 90.0% and NMT 110.0% of the labeled amount of methylprednisolone ($C_{22}H_{30}O_5$) in the volume of constituted solution designated on the label.

IDENTIFICATION

- **A. Infrared Absorption**

Sample: Nominally 100 mg of methylprednisolone sodium succinate from Methylprednisolone Sodium Succinate for Injection

Analysis: Transfer the *Sample* to a separator, dissolve in 10 mL of water, add 1 mL of 3 N hydrochloric acid, and extract immediately with 50 mL of chloroform. Filter the chloroform extract through cotton, evaporate on a steam bath to dryness, and dry under vacuum at 60° for 3 h.

Acceptance criteria: The IR absorption spectrum of a mineral oil dispersion of the residue so obtained exhibits maxima only at the same wavelengths as those of a similar preparation of USP Methylprednisolone Hemisuccinate RS.

ASSAY

- **Procedure**

Diluent: Chloroform and glacial acetic acid (97:3)

Mobile phase: Butyl chloride, water-saturated butyl chloride, tetrahydrofuran, methanol, and glacial acetic acid (95:95:14:7:6)

Standard stock solution: 0.30 mg/mL of USP Methylprednisolone RS in *Diluent*

Internal standard solution: 3 mg/mL of USP Fluorometholone RS in tetrahydrofuran

Standard solution: 0.65 mg/mL of USP Methylprednisolone Hemisuccinate RS prepared as follows. Transfer an appropriate amount of USP Methylprednisolone Hemisuccinate RS to a suitable volumetric flask. Pipet 10% of the flask volume of the *Internal standard solution* and 10% of the flask volume of the *Standard stock solution*. Dilute with *Diluent* to volume.

Sample solution: Transfer a suitable quantity of constituted solutions (mix the constituted solutions prepared from the contents of 10 vials of Methylprednisolone Sodium Succinate for Injection) equivalent to 50 mg of methylprednisolone to a suitable flask containing 10.0 mL of the *Internal standard solution*, and dilute with *Diluent* to 100.0 mL. Shake thoroughly for 5 min, then allow the phases to separate, discarding the upper phase.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing L3

Flow rate: 1 mL/min

Injection volume: 6 µL

[NOTE—The order of elution of peaks in the *Standard solution* is as follows. Internal standard peak, methylprednisolone hemisuccinate peak, and successive smaller peaks of free methylprednisolone and methylprednisolone 17-hemisuccinate.]

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 constituted Methylprednisolone Sodium Succinate for Injection taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

R_U = ratio of the sum of the peak areas for methylprednisolone hemisuccinate and methylprednisolone 17-hemisuccinate to the peak area of the internal standard from the *Sample solution*

R_S = ratio of the sum of the peak areas for methylprednisolone hemisuccinate and methylprednisolone 17-hemisuccinate to the peak area of the internal standard from the *Standard solution*

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

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

M_{r1} = molecular weight of methylprednisolone, 374.47

M_{r2} = molecular weight of methylprednisolone hemisuccinate, 474.54

To this calculated amount, add the percentage of free methylprednisolone found in the test for *Free Methylprednisolone*.

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

- **FREE METHYLPREDNISOLONE**

Analysis

Samples: *Standard solution* and *Sample solution*

Using the chromatograms obtained in the *Assay*, measure the areas of the peaks from the internal standard and free methylprednisolone.

Calculate the percentage of free methylprednisolone in the portion of *Sample solution* taken:

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

R_U = peak area ratio of the free methylprednisolone to the internal standard from the *Sample solution*

R_S = peak area ratio of the free methylprednisolone to the internal standard 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: The amount of free methylprednisolone is NMT 6.6% of the labeled amount of methylprednisolone ($C_{22}H_{30}O_5$).

PERFORMANCE TESTS

- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meets the requirements

SPECIFIC TESTS

- **pH** ⟨791⟩

  Sample solution: 50 mg/mL of methylprednisolone sodium succinate

  Acceptance criteria: 7.0–8.0

- **Sterility Tests** ⟨71⟩**:** Meets the requirements
- **Bacterial Endotoxins Test** ⟨85⟩**:** NMT 0.17 USP Endotoxin Units/mg of methylprednisolone
- **Loss on Drying** ⟨731⟩

  Analysis: Dry at 105° for 3 h.

  Acceptance criteria: NMT 2.0%

- **Constituted Solution:** At the time of use, it meets the requirements for *Injections and Implanted Drug Products* ⟨1⟩*, Specific Tests, Completeness and Clarity of Solutions*.
- **Particulate Matter in Injections** ⟨788⟩**:** Meets the requirements for small-volume injections
- **Other Requirements:** Meets the requirements in *Labeling* ⟨7⟩*, Labels and Labeling for Injectable Products*

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements* ⟨659⟩*, Injection Packaging, Packaging for Constitution*.
- **USP Reference Standards** ⟨11⟩

  USP Fluorometholone RS

  USP Methylprednisolone RS

  USP Methylprednisolone Hemisuccinate RS

Page Information:

Not Applicable

Current DocID: