Methylprednisolone Sodium Succinate for Injection

Type of Posting	Revision Bulletin
Posting Date	4-May-2022
Official Date	5-May-2022
Expert Committee	Small Molecules 5

In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 5 Expert Committee has revised the Methylprednisolone Sodium Succinate for Injection monograph. The purpose of this revision is to revise the drug product description to include Sodium Bicarbonate as a salt forming reagent in the *Definition* section based on a manufacturer's approved specifications.

The Methylprednisolone Sodium Succinate for Injection Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Robyn Fales, Senior Scientist I (240-221-2047 or rnp@usp.org).

Revision Bulletin
Official: May 5, 2022

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,▲ (RB 5-May-2022) 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: