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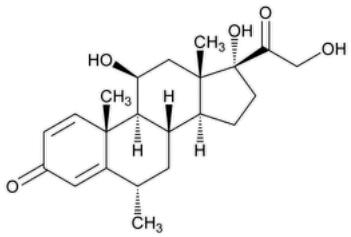
Methylprednisolone

Change to read:



$C_{22}H_{30}O_5$ ▲374.48▲ (USP 1-Dec-2023)

Pregna-1,4-diene-3,20-dione, 11,17,21-trihydroxy-6-methyl-, (6α,11β)-;

11β,17,21-Trihydroxy-6α-methylpregna-1,4-diene-3,20-dione CAS RN®: 83-43-2; UNII: X4W7ZR7023.

DEFINITION

Methylprednisolone contains NLT 97.0% and NMT 103.0% of methylprednisolone ($C_{22}H_{30}O_5$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K ▲or 197A▲ (USP 1-Dec-2023)

Delete the following:

▲• **B. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*:**▲ (USP 1-Dec-2023)

Add the following:

▲• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2023)

Delete the following:

▲• **C.**▲ (USP 1-Dec-2023)

ASSAY

Change to read:

• **Procedure**

▲**Solution A:** Acetonitrile, tetrahydrofuran, phosphoric acid, and water (10: 1.5: 0.1: 90)

Solution B: Acetonitrile, tetrahydrofuran, and phosphoric acid (100: 1.5: 0.1)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	83	17
14	83	17
30	52	48
30.1	83	17
35	83	17

Diluent: Acetonitrile, phosphoric acid, and water (50: 0.1: 50)

System suitability solution: 0.6 mg/mL of USP Methylprednisolone System Suitability Mixture RS in *Diluent*

Standard solution: 0.6 mg/mL of USP Methylprednisolone RS in *Diluent*

Sample solution: 0.6 mg/mL of Methylprednisolone in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 247 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for methylprednisolone related compound A and methylprednisolone are 0.93 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.7 between methylprednisolone related compound A and methylprednisolone, *System suitability solution*

Relative standard deviation: NMT 1.10%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of methylprednisolone ($C_{22}H_{30}O_5$) in the portion of Methylprednisolone taken:

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

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

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

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

C_U = concentration of Methylprednisolone in the *Sample solution* (mg/mL)▲ (USP 1-Dec-2023)

Acceptance criteria: 97.0%–103.0% on the dried basis

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.2%

Change to read:

• **ORGANIC IMPURITIES**

▲**Solution A, Solution B, Mobile phase, Diluent, System suitability solution, Sample solution,** and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 0.0003 mg/mL of USP Methylprednisolone RS in *Diluent*

Standard solution: 0.006 mg/mL of USP Methylprednisolone RS in *Diluent*

System suitability

Samples: *System suitability solution*, *Sensitivity solution*, and *Standard solution*

[NOTE—See *Table 2* for the relative retention times. The relative retention times in *Table 2* are provided for information that could aid in peak assignment.]

Table 2

Name	Relative Retention Time
Methylprednisolone related compound B	0.85
Methylprednisolone related compound H	0.88
Methylprednisolone related compound A	0.93
Methylprednisolone	1.0
Methylprednisolone related compound F	1.10
Methylprednisolone related compound G	1.56
Impurity I	1.60
Methylprednisolone related compound C	1.72

Name	Relative Retention Time
Methylprednisolone related compound E	2.01
Methylprednisolone related compound D (trans isomer)	2.21
Methylprednisolone related compound D (cis isomer)	2.34

Suitability requirements

Resolution: NLT 1.7 between methylprednisolone and methylprednisolone related compound A, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each impurity in the portion of Methylprednisolone taken:

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

r_U = peak response of each impurity from the *Sample solution*

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

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

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

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*. The reporting threshold is 0.05%.

Table 3

Name	Relative Response Factor	Acceptance Criteria, NMT (%)
Methylprednisolone related compound B	1.0	0.2
Methylprednisolone related compound H	1.0	0.2
Methylprednisolone related compound A	1.0	0.3
Methylprednisolone related compound F	1.0	0.15
Sum of methylprednisolone related compound G and Impurity I	1.0	0.3
Methylprednisolone related compound C	1.2	0.15
Methylprednisolone related compound E	1.0	0.15
Methylprednisolone related compound D[a]	1.0	0.5
Any unspecified impurity	1.0	0.10
Total impurities	—	2.0

[a] Sum of trans isomer and cis isomer.

▲ (USP 1-Dec-2023)

SPECIFIC TESTS

Change to read:

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: ▲10 mg/mL in alcohol▲ (USP 1-Dec-2023)

Acceptance criteria: ▲+97.0° to +103.0°, calculated on the dried basis▲ (USP 1-Dec-2023)

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight, light-resistant containers. ▲Store at controlled cold temperature.▲ (USP 1-Dec-2023)

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Methylprednisolone RS

▲ USP Methylprednisolone System Suitability Mixture RS

Contains a mixture of the following 10 compounds:

Methylprednisolone.

Methylprednisolone related compound A: 17,21-Dihydroxy-6α-methylpregna-1,4-diene-3,11,20-trione.

$C_{22}H_{28}O_5$ 372.46

Methylprednisolone related compound B: 11β,17,21,21-Tetrahydroxy-6α-methylpregna-1,4-diene-3,20-dione.

$C_{22}H_{30}O_6$ 390.48

Methylprednisolone related compound C: 11β-Hydroxy-6α-methylandrosta-1,4-diene-3,17-dione.

$C_{20}H_{26}O_3$ 314.43

Methylprednisolone related compound D: 11β,20-Dihydroxy-6α-methylpregna-1,4,17(20)-triene-3,21-dione.

$C_{22}H_{28}O_4$ 356.46

Methylprednisolone related compound E: 11β-Hydroxy-6α-methyl-3-oxoandrosta-1,4-diene-17β-carboxylic acid.

$C_{21}H_{28}O_4$ 344.45

Methylprednisolone related compound F: 11β,17,21-Trihydroxy-6α-methylpregn-4-ene-3,20-dione.

$C_{22}H_{32}O_5$ 376.49

Methylprednisolone related compound G: 17,21-Dihydroxy-6α-methylpregna-1,4,9(11)-triene-3,20-dione.

$C_{22}H_{28}O_4$ 356.46

Methylprednisolone related compound H: 11β,17,21-Trihydroxy-6β-methylpregna-1,4-diene-3,20-dione.

$C_{22}H_{30}O_5$ 374.48

Impurity I: Unknown structure.

▲ (USP 1-Dec-2023)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
METHYLPREDNISOLONE	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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