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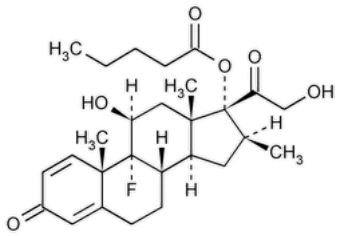
Betamethasone Valerate

Change to read:



$C_{27}H_{37}FO_6$ ▲476.59▲ (USP 1-Aug-2024)

Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16-methyl-17-[(1-oxopentyl)oxy]-, (11β,16β)-;

9-Fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17-valerate CAS RN®: 2152-44-5; UNII: 9IFA5XM7R2.

DEFINITION

Betamethasone Valerate contains NLT 97.0% and NMT 103.0% of betamethasone valerate ($C_{27}H_{37}FO_6$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197M ▲or 197A▲ (USP 1-Aug-2024)

Change to read:

• **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-Aug-2024)

ASSAY

Change to read:

• **Procedure**

▲**Mobile phase:** Acetonitrile and water (50:50). [Note—The mobile phase composition should be tightly controlled (±2%) to maintain the elution order and resolution between specified and unspecified impurities.]

System suitability solution: 250 µg/mL of USP Betamethasone Valerate System Suitability Mixture RS and 2.5 µg/mL of USP Betamethasone Valerate Related Compound D RS in *Mobile phase*. Sonicate to dissolve.

Standard solution: 250 µg/mL of USP Betamethasone Valerate RS in *Mobile phase*. Sonicate to dissolve.

Sample solution: 250 µg/mL of Betamethasone Valerate in *Mobile phase*. Sonicate to dissolve.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Temperatures

Autosampler: 4°

Column: 30°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of betamethasone valerate

System suitability

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

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 5.0 between betamethasone valerate and betamethasone valerate related compound H; NLT 1.5 between betamethasone valerate related compound H and betamethasone valerate related compound D, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of betamethasone valerate ($C_{27}H_{37}FO_6$) in the portion of Betamethasone Valerate taken:

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

r_U = peak response of betamethasone valerate from the *Sample solution*

r_S = peak response of betamethasone valerate from the *Standard solution*

C_S = concentration of USP Betamethasone Valerate RS in the *Standard solution* (µg/mL)

C_U = concentration of Betamethasone Valerate in the *Sample solution* (µg/mL)

▲ (USP 1-Aug-2024)

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

IMPURITIES

• **Residue on Ignition ⟨281⟩**

Analysis: Use a platinum crucible.

Acceptance criteria: NMT 0.2%

Add the following:

▲• **Limit of Betamethasone Valerate Related Compound H**

Mobile phase: Acetonitrile and water (40:60)

Diluent: Acetonitrile and water (50:50)

System suitability solution: 250 µg/mL of USP Betamethasone Valerate System Suitability Mixture RS in *Diluent*. Sonicate to dissolve.

Standard solution: 0.375 µg/mL of USP Betamethasone Valerate RS in *Diluent*

Sample solution: 250 µg/mL of Betamethasone Valerate in *Diluent*. Sonicate to dissolve.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Temperatures

Autosampler: 4°

Column: 30°

Flow rate: 1.4 mL/min

Injection volume: 75 µL

Run time: NLT 3 times the retention time of betamethasone valerate

System suitability

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

[Note—The relative retention times for betamethasone valerate and betamethasone valerate related compound H are 1.0 and 1.36, respectively.]

Suitability requirements

Resolution: NLT 7.5 between betamethasone valerate and betamethasone valerate related compound H, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of betamethasone valerate related compound H in the portion of Betamethasone Valerate taken:

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

r_U = peak response of betamethasone valerate related compound H from the *Sample solution*

r_S = peak response of betamethasone valerate from the *Standard solution*

C_S = concentration of USP Betamethasone Valerate RS in the *Standard solution* (µg/mL)

C_U = concentration of Betamethasone Valerate in the *Sample solution* (µg/mL)

F = relative response factor, 0.95

Acceptance criteria: NMT 0.15%▲ (USP 1-Aug-2024)

Change to read:

• **Organic Impurities**

▲[Note—Solutions containing betamethasone valerate should be prepared fresh and injected within 4 h.]

Mobile phase and **System suitability solution:** Prepare as directed in the *Assay*.

Sensitivity solution: 0.12 µg/mL of USP Betamethasone Valerate RS in *Mobile phase*

Standard solution: 1.75 µg/mL of USP Betamethasone RS, 0.25 µg/mL of USP Betamethasone Valerate RS, and 0.75 µg/mL of USP Betamethasone Valerate Related Compound A RS in *Mobile phase*

Sample solution: 250 µg/mL of Betamethasone Valerate in *Mobile phase*. Sonicate to dissolve.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Temperatures

Autosampler: 4°

Column: 30°

Flow rate: 1.2 mL/min

Injection volume: 35 µL

Run time: NLT 2 times the retention time of betamethasone valerate

System suitability

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

Suitability requirements

Resolution: NLT 5.0 between betamethasone valerate and betamethasone valerate related compound H; NLT 1.5 between betamethasone valerate related compound H and betamethasone valerate related compound D, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of betamethasone and betamethasone valerate related compound A in the portion of Betamethasone Valerate taken:

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

r_U = peak response of betamethasone or betamethasone valerate related compound A from the *Sample solution*

r_S = peak response of betamethasone or betamethasone valerate related compound A from the *Standard solution*

C_S = concentration of USP Betamethasone RS or USP Betamethasone Valerate Related Compound A RS in the *Standard solution* (µg/mL)

C_U = concentration of Betamethasone Valerate in the *Sample solution* (µg/mL)

Calculate the percentage of 9-fluoroprednisolone 17-valerate, betamethasone valerate related compound C, betamethasone valerate related compound D, 6α-bromobetamethasone 17-valerate, and any unspecified impurity in the portion of Betamethasone Valerate taken:

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

r_U = peak response of 9-fluoroprednisolone 17-valerate, betamethasone valerate related compound C, betamethasone valerate related compound D, 6α-bromobetamethasone 17-valerate, or any unspecified impurity from the *Sample solution*

r_S = peak response of betamethasone valerate from the *Standard solution*

C_S = concentration of USP Betamethasone Valerate RS in the *Standard solution* (µg/mL)

C_U = concentration of Betamethasone Valerate in the *Sample solution* (µg/mL)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Betamethasone	0.27	—	0.7
9-Fluoroprednisolone 17-valerate[a]	0.59	0.95	0.15
Betamethasone valerate related compound C[b]	0.82	—	0.15
Betamethasone valerate	1.0	—	—
Betamethasone valerate related compound H[c,d]	1.3	—	—
Betamethasone valerate related compound D[e]	1.4	1.0	0.10
Betamethasone valerate related compound A[f]	1.6	—	0.5
6α-Bromobetamethasone 17-valerate[g]	1.9	0.83	0.3
Any unspecified impurity	—	1.0	0.1
Total impurities[h]	—	—	1.5

[a] 9-Fluoro-11β,21-dihydroxy-3,20-dioxopregna-1,4-diene-17-yl valerate.

[b] 9-Fluoro-11β,21-dihydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-17-yl valerate; also known as dexamethasone 17-valerate.

[c] Also known as beclomethasone 17-valerate.

[d] This impurity is quantified using the *Limit of Betamethasone Valerate Related Compound H* test.

[e] Also known as 9α-bromobetamethasone 17-valerate.

[f] Also known as betamethasone 21-valerate.

[g] 6α-Bromo-9-fluoro-11β,21-dihydroxy-16β-methyl-3,20-dioxopregna-1,4-diene-17-yl valerate.

[h] The sum of all impurities from the *Organic Impurities* and the *Limit of Betamethasone Valerate Related Compound H* tests.

▲ (USP 1-Aug-2024)

SPECIFIC TESTS

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

Sample solution: 10 mg/mL in dioxane

Acceptance criteria: +75° to +82°

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

Change to read:

• **USP Reference Standards** ⟨11⟩

▲USP Betamethasone RS▲ (USP 1-Aug-2024)

USP Betamethasone Valerate RS

▲USP Betamethasone Valerate Related Compound A RS

9-Fluoro-11β,17-dihydroxy-16β-methyl-3,20-dioxopregna-1,4-diene-21-yl valerate.

$C_{27}H_{37}FO_6$ 476.59

USP Betamethasone Valerate Related Compound D RS

9-Bromo-11β,21-dihydroxy-16β-methyl-3,20-dioxopregna-1,4-dien-17-yl valerate.

$C_{27}H_{37}BrO_6$ 537.49

USP Betamethasone Valerate System Suitability Mixture RS

It contains a mixture of the following 2 compounds:

Betamethasone valerate.

Betamethasone valerate related compound H: 9-Chloro-11β,21-dihydroxy-16β-methyl-3,20-dioxopregna-1,4-diene-17-yl valerate.

$C_{27}H_{37}ClO_6$ 493.04▲ (USP 1-Aug-2024)

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

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

Chromatographic Database Information: Chromatographic Database

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