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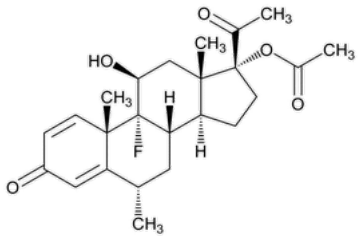
Fluorometholone Acetate



$C_{24}H_{31}FO_5$ 418.51

Pregna-1,4-diene-3,20-dione, 17-(acetyloxy)-9-fluoro-11-hydroxy-6-methyl-, (6α,11β)-;
9-Fluoro-11β,17-dihydroxy-6α-methylpregna-1,4-diene-3,20-dione, 17 acetate;
9-Fluoro-11β-hydroxy-6α-methyl-3,20-dioxopregna-1,4-dien-17-yl acetate. CAS RN®: 3801-06-7; UNII: 9I50C3I3OK.

Change to read:

DEFINITION

Fluorometholone Acetate contains NLT 98.0% and NMT ▲102.0%▲ (USP 1-Dec-2021) of fluorometholone acetate ($C_{24}H_{31}FO_5$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K ▲or 197A▲ (USP 1-Dec-2021)

Delete the following:

▲• **B. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*:** 197U

Sample solution: 10 µg/mL in methanol

Acceptance criteria: Meets the requirements▲ (USP 1-Dec-2021)

Add the following:

▲• **B.** The retention time of the fluorometholone acetate peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2021)

ASSAY

Change to read:

• **Procedure**

Mobile phase: Acetonitrile and water (40:60)

System suitability stock solution: 1.0 mg/mL of USP Fluorometholone RS prepared as follows. ▲Accurately weigh and transfer a portion of USP Fluorometholone RS to a suitable volumetric flask. Add methanol to 8% of the total volume and dilute with acetonitrile to volume.▲ (USP 1-Dec-2021)

Standard solution: 1.0 mg/mL of USP Fluorometholone Acetate RS in acetonitrile

System suitability solution: 0.03 mg/mL each of USP Fluorometholone RS and USP Fluorometholone Acetate RS from *System suitability stock solution* and *Standard solution*, respectively, in acetonitrile

Sample solution: 1.0 mg/mL of Fluorometholone Acetate in acetonitrile

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 10 µL

▲**Run time:** NLT 2.5 times the retention time of the fluorometholone acetate peak▲ (USP 1-Dec-2021)

System suitability

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

▲[NOTE—See *Table 1* for the relative retention times.]▲ (USP 1-DEC-2021)

Suitability requirements

Resolution: NLT 10 between fluorometholone and fluorometholone acetate, *System suitability solution*

▲▲ (USP 1-Dec-2021)

Tailing factor: NMT 2.0 for fluorometholone acetate, ▲*Standard solution*▲ (USP 1-Dec-2021)

Relative standard deviation: NMT ▲0.73%,▲ (USP 1-Dec-2021) *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of fluorometholone acetate ($C_{24}H_{31}FO_5$) in the portion of Fluorometholone Acetate taken:

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

r_U = peak response of fluorometholone acetate from the *Sample solution*

r_S = peak response of fluorometholone acetate from the *Standard solution*

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

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

Acceptance criteria: 98.0%–▲102.0%▲ (USP 1-Dec-2021) on the dried basis

IMPURITIES

Change to read:

• **ORGANIC IMPURITIES**

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

System suitability stock solution A: Prepare as directed for the *System suitability stock solution* in the *Assay*.

System suitability stock solution B: Prepare as directed for the *Standard solution* in the *Assay*.

System suitability solution: 0.03 mg/mL each of USP Fluorometholone RS and USP Fluorometholone Acetate RS, from *System suitability stock solution A* and *System suitability stock solution B*, respectively, in acetonitrile

▲**Sensitivity solution:** 0.5 µg/mL of USP Fluorometholone Acetate RS in acetonitrile▲ (USP 1-Dec-2021)

Standard solution: 0.03 mg/mL of USP Fluorometholone RS from *System suitability stock solution A* in acetonitrile

▲▲ (USP 1-Dec-2021)

Chromatographic system: Proceed as directed in the *Assay* except for the *Injection volume*.

Injection volume: 20 µL

System suitability

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

[NOTE—See *Table 1* for the relative retention times.]▲ (USP 1-DEC-2021)

Suitability requirements

Resolution: NLT 10 between fluorometholone and fluorometholone acetate, *System suitability solution*

▲▲ (USP 1-Dec-2021)

Relative standard deviation: ▲NMT 5.0% based on peak height response, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*▲ (USP 1-Dec-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

▲▲ (USP 1-Dec-2021)

Calculate the percentage of fluorometholone or fluorometholone diacetate in the portion of Fluorometholone Acetate taken:

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

r_U = peak height response of fluorometholone or fluorometholone diacetate from the *Sample solution*

r_S = peak height response of fluorometholone from the *Standard solution*

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

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

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

Calculate the percentage of all other fluorometholone acetate impurities in the portion of Fluorometholone Acetate taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

r_U = peak area response of each impurity (except the fluorometholone and fluorometholone diacetate peaks) from the *Sample solution*

r_T = sum of the peak area responses of all impurity peaks plus the fluorometholone acetate peak from the *Sample solution*

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

Acceptance criteria: See *Table 1*. ▲The reporting threshold is 0.05%.▲ (USP 1-Dec-2021)

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Fluorometholone	0.6	1.0[a]	1.0
▲Epoxymethyldeprodone▲ (USP 1-Dec-2021) [b]	0.89	1.0	0.5
Fluorometholone acetate	1.0	—	—
Fluorometholone diacetate ▲[c]▲ (USP 1-Dec-2021)	1.39	0.45[a]	1.0
▲Epoxyfluorometholone acetate▲ (USP 1-Dec-2021) [d]	1.58	1.0	0.5
▲Fluorometholone acetate diene▲ (USP 1-Dec-2021) [e]	1.77	1.8	0.3
▲Fluorometholone-9(11)-ene acetate▲ (USP 1-Dec-2021) [f]	1.82	1.0	0.2
Any unspecified impurity	—	1.0	0.1
Total impurities	—	—	1.5

[a] Relative to fluorometholone. ▲All other impurities relative to fluorometholone acetate unless otherwise marked.▲ (USP 1-Dec-2021)

[b] ▲9β,11β-Epoxy-17α-hydroxy-6α-methylpregna-1,4-diene-3,20-dione.

[c] 9-Fluoro-6α-methyl-3,20-dioxopregna-1,4-dien-11β,17-diyl diacetate.▲ (USP 1-Dec-2021)

[d] ▲9β,11β-Epoxy-6α-methyl-3,20-dioxapregna-1,4-dien-17-yl acetate.▲ (USP 1-Dec-2021)

[e] ▲6α-Methyl-3,20-dioxopregna-1,4,7,9(11)-tetraen-17-yl acetate.▲ (USP 1-Dec-2021)

[f] ▲6α-Methyl-3,20-dioxopregna-1,4,9(11)-trien-17-yl acetate.▲ (USP 1-Dec-2021)

SPECIFIC TESTS

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

  Sample solution: 20 mg/mL, in chloroform

  Acceptance criteria: +25.0° to +31.0°

- **Loss on Drying ⟨731⟩**

  Analysis: Dry under vacuum at 60° for 3 h.

  Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.

- **USP Reference Standards** (11)

USP Fluorometholone RS
USP Fluorometholone Acetate RS

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

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

Chromatographic Database Information: Chromatographic Database

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