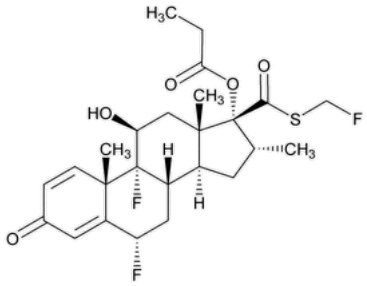
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Dec-2022
Document Type: USP Monographs
DocId: GUID-9697738B-8121-425D-900C-DB916F090110_5_en-US
DOI: https://doi.org/10.31003/USPNF_M34220_05_01
DOI Ref: 633rb

Fluticasone Propionate

Change to read:



$C_{25}H_{31}F_3O_5S$ 500.57

Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6α,11β,16α,17α)-*S*-(fluoromethyl) ester; *S*-Fluoromethyl 6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxyandrosta-1,4-diene-17β-carbothioate;

▲6α,9-Difluoro-17-{[(fluoromethyl)sulfanyl]carbonyl}-11β-hydroxy-16α-methyl-3-oxoandrosta-1,4-dien-17α-yl propanoate▲ (USP 1-Dec-2022) CAS RN®: 80474-14-2; UNII: O2GMZ0LF5W.

Change to read:

DEFINITION

Fluticasone Propionate contains NLT 98.0% and NMT ▲102.0%▲ (USP 1-Dec-2022) of ▲fluticasone propionate▲ (USP 1-Dec-2022) ($C_{25}H_{31}F_3O_5S$), calculated on the anhydrous, solvent-free basis.

IDENTIFICATION

Change to read:

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** ▲197A, 197K, or▲ (USP 1-Dec-2022) 197M
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

- **Procedure**

Buffer: 1.15 g/L of monobasic ammonium phosphate, adjusted with phosphoric acid to a pH of 3.5 ▲▲ (USP 1-Dec-2022)

Mobile phase: Methanol, acetonitrile, and *Buffer* (50:15:35)

System suitability solution: ▲0.04 mg/mL of USP Fluticasone Propionate RS and 0.008 mg/mL of USP Fluticasone Propionate Related Compound D RS▲ (USP 1-Dec-2022) in *Mobile phase*

Standard solution: 0.04 mg/mL of USP Fluticasone Propionate RS in *Mobile phase*

Sample solution: 0.04 mg/mL of Fluticasone Propionate in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 239 nm

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

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for fluticasone propionate and fluticasone propionate related compound D are about 1.0 and 1.10, respectively.]

Suitability requirements

Resolution: NLT 1.5 between fluticasone propionate and fluticasone propionate related compound D, *System suitability solution*

Relative standard deviation: NMT ▲0.73%▲ (USP 1-Dec-2022) *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of fluticasone propionate ($C_{25}H_{31}F_3O_5S$) in the portion of Fluticasone Propionate taken:

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

r_U = peak response of fluticasone propionate from the *Sample solution*

r_S = peak response of fluticasone propionate from the *Standard solution*

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

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

Acceptance criteria: 98.0%–▲102.0%▲ (USP 1-Dec-2022) on the anhydrous, solvent-free basis

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A: 0.5 mL of phosphoric acid in 1000 mL of acetonitrile

Solution B: 0.5 mL of phosphoric acid in 1000 mL of methanol

Solution C: 0.5 mL of phosphoric acid in 1000 mL of water

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)	Solution C (%)
0	42	3	55
40	53	3	44
60	87	3	10
70	87	3	10
75	42	3	55

System suitability solution: ▲0.2 mg/mL of USP Fluticasone Propionate System Suitability Mixture RS prepared as follows. Transfer a suitable amount of USP Fluticasone Propionate System Suitability Mixture RS to an appropriate volumetric flask and dissolve in 50% of the flask volume of *Solution A*. Sonication may be used to aid dissolution. Dilute with *Solution C* to volume.

Sensitivity stock solution: 0.1 mg/mL of USP Fluticasone Propionate RS prepared as follows. Transfer a suitable amount of USP Fluticasone Propionate RS to an appropriate volumetric flask and dissolve in 50% of the flask volume of *Solution A*. Sonication may be used to aid dissolution. Dilute with *Solution C* to volume.

Sensitivity solution: 0.1 µg/mL of USP Fluticasone Propionate RS from *Sensitivity stock solution* in *Solution C*▲ (USP 1-Dec-2022)

Sample solution: 0.2 mg/mL ▲of Fluticasone Propionate▲ (USP 1-Dec-2022) prepared as follows. ▲Transfer a suitable amount of Fluticasone Propionate to an appropriate volumetric flask and dissolve in 50% of the flask volume of *Solution A*. Sonication may be used to aid dissolution. Dilute with *Solution C* to volume.▲ (USP 1-Dec-2022)

Chromatographic system

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

Mode: LC

Detector: UV 239 nm

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

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Samples: *System suitability solution* ▲and *Sensitivity solution*▲ (USP 1-Dec-2022)

Suitability requirements

Resolution: NLT 0.6 between fluticasone propionate related compound B and fluticasone propionate related compound C; NLT 1.5 between fluticasone propionate related compound D and fluticasone propionate, *System suitability solution*

▲**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*▲ (USP 1-Dec-2022)

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Fluticasone Propionate taken:

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

r_U = peak response for each impurity

r_T = sum of the responses of all the peaks

Acceptance criteria: See *Table 2*. ▲The reporting threshold is 0.05%.▲ (USP 1-Dec-2022)

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
▲Fluticasone sulfenic acid[a]▲ (USP 1-Dec-2022)	0.5	0.2
Fluticasone propionate related compound B	0.75	0.1
Fluticasone propionate related compound C	0.8	0.1
Fluticasone propionate related compound D	0.95	0.3
Fluticasone propionate	1.0	—
▲Fluticasone dimer[b]▲ (USP 1-Dec-2022)	1.3	0.3
Any ▲▲ (USP 1-Dec-2022) unspecified impurity	—	0.1
Total impurities ▲▲ (USP 1-Dec-2022)	—	1.0

[a] 6α,9-Difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxyandrosta-1,4-diene-17β-carbonylsulfenic acid.

[b] 6α,9-Difluoro-17-{[(fluoromethyl)sulfanyl]carbonyl}-11β-hydroxy-16α-methyl-3-oxoandrosta-1,4-dien-17α-yl 6α,9-difluoro-11β,17-dihydroxy-16α-methyl-3-oxoandrosta-1,4-diene-17β-carboxylate.

Change to read:

• **Limit of Acetone**

Internal standard solution: 0.05% (v/v) solution of tetrahydrofuran in dimethylformamide

Standard solution: 0.05% (v/v) acetone in *Internal standard solution*

Sample solution: 50 mg/mL of Fluticasone Propionate in the *Internal standard solution*

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 25-m; 2-µm film of phase G16

Carrier gas: Nitrogen or helium

Temperatures

Detector: 250°

Splitless injector: 150°

Column: See *Table 3*.

Table 3

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
60	0	60	3.5
60	30	180	3.0

Flow rate: 5.5 mL/min

Injection volume: 0.1 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of acetone ▲▲ (USP 1-Dec-2022) in the portion of Fluticasone Propionate taken:

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

R_U = peak response ratio of acetone to tetrahydrofuran from the *Sample solution*

R_S = peak response ratio of acetone to tetrahydrofuran from the *Standard solution*

D = density of acetone at 20° (g/mL)

C_S = concentration of acetone in the *Standard solution* (% v/v)

C_U = concentration of Fluticasone Propionate in the *Sample solution* (g/mL)

Acceptance criteria: NMT 1.0% ▲▲ (USP 1-Dec-2022)

SPECIFIC TESTS

Change to read:

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

Sample solution: ▲0.5 g/100 mL▲ (USP 1-Dec-2022) of Fluticasone Propionate in dichloromethane▲▲ (USP 1-Dec-2022)

Acceptance criteria: +32° to +36° at 20°, calculated on the anhydrous, solvent-free basis

Change to read:

• **Water Determination** ⟨921⟩, *Method I*: NMT 0.2% ▲▲ (USP 1-Dec-2022)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at a temperature not exceeding 30°.

Delete the following:

▲• **Labeling** ▲ (USP 1-Dec-2022)

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Fluticasone Propionate RS

▲ USP Fluticasone Propionate Related Compound D RS

6α,9-Difluoro-11β-hydroxy-16α-methyl-17-[(methylsulfanyl)carbonyl]-3-oxoandrosta-1,4-dien-17α-yl propanoate;
Also known as *S*-methyl 6α, 9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxyandrosta-1,4-diene-17β-carbothioate.

$C_{25}H_{32}F_2O_5S$ 482.58▲ (USP 1-Dec-2022)

USP Fluticasone Propionate System Suitability Mixture RS

▲Contains a mixture of the following 4 compounds:

Fluticasone propionate.

Fluticasone propionate related compound B: 6α,9-Difluoro-11β-hydroxy-16α-methyl-2',3,4'-trioxo-17α-spiro[androsta-1,4-diene-17,5'-(1,3)oxathiolane].

$C_{22}H_{24}F_2O_5S$ 438.49

Fluticasone propionate related compound C: 6α,9-Difluoro-17-{[(fluoromethyl)sulfanyl]carbonyl}-11β-hydroxy-16α-methyl-3-oxoandrosta-1,4-dien-17α-yl acetate;
Also known as *S*-Fluoromethyl 17α-acetyloxy-6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxoandrosta-1,4-diene-17β-carbothioate.

$C_{24}H_{29}F_3O_5S$ 486.55

Fluticasone propionate related compound D.▲ (USP 1-Dec-2022)

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 47(3)

Current DocID: GUID-9697738B-8121-425D-900C-DB916F090110_5_en-US

DOI: https://doi.org/10.31003/USPNF_M34220_05_01

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