**Mode:** GC
**Detector:** Flame ionization
**Column:** 0.53-mm × 25-m; 2-µm film of phase G16
**Carrier gas:** Nitrogen or helium
**Temperature**
**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 size:** 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 (w/w) 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% (w/w)

## SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation* ⟨**781S**⟩**:** +32° to +36° at 20°, calculated on the anhydrous, solvent-free basis
**Sample solution:** 0.5% (w/v) of Fluticasone Propionate in dichloromethane (0.5 g in 100 mL)
- **Water Determination,** *Method I* ⟨**921**⟩**:** NMT 0.2% (w/w)

## ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at a temperature not exceeding 30 °.
- **Labeling:** Fluticasone Propionate in the form of microcrystals is so labeled.
- **USP Reference Standards** ⟨**11**⟩
USP Fluticasone Propionate RS
USP Fluticasone Propionate Resolution Mixture RS
USP Fluticasone Propionate System Suitability Mixture RS
It is a mixture of USP Fluticasone Propionate RS and fluticasone propionate related compounds B, C, and D.
*Fluticasone propionate related compound A:* 6α,9α-Difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxyandrosta-1,4-diene-17β-carbonylsulfenic acid.
*Fluticasone propionate related compound B:* 6α,9α-Difluoro-11β-hydroxy-16α-methyl-2′,3,4′-trioxo-17α-spiro(androsta-1,4-diene-17,5′-(1,3)oxathiolane).
*Fluticasone propionate related compound C: S*-Fluoromethyl 17α-acetyloxy-6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothioate.
*Fluticasone propionate related compound D: S*-Methyl 6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxy-androsta-1,4-diene-17β-carbothioate.
*Fluticasone propionate related compound E:* 6α,9α-Difluoro-11β,17α-dihydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carboxylic acid 6α,9α-difluoro-17β-(fluoromethylthio) carbonyl-11β-hydroxy-16α-methyl-3-oxo-androsta-1,4-dien-17α-yl ester.

# Fluticasone Propionate Cream

## DEFINITION

Fluticasone Propionate Cream contains NLT 90.0% and NMT 110.0% of the labeled amount of fluticasone propionate ($C_{25}H_{31}F_3O_5S$).

## IDENTIFICATION

- **A. Thin-Layer Chromatographic Identification Test** ⟨**201**⟩
**Standard solution:** 0.4 mg/mL of USP Fluticasone Propionate RS in acetonitrile
**Test solution:** Transfer a quantity of Cream, equivalent to 1000 µg of fluticasone propionate, to a 125-mL separatory funnel. Add 25 mL of acetonitrile and 25 mL of hexane to the separatory funnel. Stopper and shake the funnel until the Cream is completely dispersed. Shake the separatory funnel for an additional 3 min, and allow the phases to separate. Filter the lower layer through a 20-mL syringe containing a cotton plug into a 50-mL volumetric flask. Repeat the extraction with one 7-mL aliquot of acetonitrile, and filter the lower layer into the volumetric flask. Wash the cotton plug with 2 mL of acetonitrile, and collect the washings into the volumetric flask. Dilute the sample extract with acetonitrile to volume. Transfer 12 mL of the sample extract to a glass tube suitable for evaporation, and evaporate to dryness at about 40°. Dissolve the residue in 0.6 mL of acetonitrile. [NOTE—The *Test solution* may be cloudy because of the presence of undissolved excipients.]
**Chromatographic system**
(See *Chromatography* ⟨621⟩*, Thin-Layer Chromatography*.)
**Adsorbent:** 0.2-mm layer of chromatographic silica gel mixture on a high-performance thin-layer chromatographic plate, 5-µm particle size
**Application volume:** 40 µL
**Developing solvent system:** Dichloromethane, ethyl acetate, and glacial acetic acid (30:8:1)
**Analysis**
**Samples:** *Standard solution* and *Test solution*
Separately apply the *Standard solution* and the *Test solution* to the plate. On the same plate, apply 20 µL of the *Standard solution,* allow the application to dry, and apply 20 µL of the *Test solution* on top of the dried 20- µL *Standard solution* spot. Allow each of the applications to dry thoroughly. Place the plate in a tank equilibrated with the developing solvent, and allow the developing solvent to travel about 8 cm from the point of application. Remove the plate and allow to air-dry. Examine the plate under ultraviolet light at 254 nm.
**Acceptance criteria:** The $R_F$ value of the principal spot from the *Test solution* corresponds to that of the *Standard solution*. [NOTE—If the excipients in the Cream interfere with the appearance of the principal spot obtained for the *Test solution*, use the *Standard solution* and the *Test solution* overspot to confirm identity.]
- **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

- **Procedure**
[NOTE—Protect the *Standard solution* and the *Sample solution* from direct light by using a light-protective volumetric flask and autosampler vials.]
**Buffer:** 1.2 g/L of monobasic ammonium phosphate. Adjust with phosphoric acid to a pH of 3.50 ± 0.03.
**Mobile phase:** Methanol, acetonitrile, and *Buffer* (46:14:40)
**Diluent:** Alcohol and water (65:35)
**System suitability stock solution:** 0.5 mg/mL of USP Fluticasone Propionate Nasal Spray Resolution Mixture RS in

methanol. [NOTE—USP Fluticasone Propionate Nasal Spray Resolution Mixture RS is a mixture of fluticasone propionate and fluticasone propionate related compound D.]
**System suitability solution:** 10 µg/mL of USP Fluticasone Propionate Nasal Spray Resolution Mixture RS in *Diluent* from *System suitability stock solution*
**Standard stock solution:** 0.5 mg/mL USP Fluticasone Propionate RS. Dissolve the standard first in a volume of methanol, equivalent to 80% of the final volume, and dilute with water to volume.
**Standard solution:** 20 µg/mL USP Fluticasone Propionate RS in *Diluent,* from *Standard stock solution*
**Sample solution:** Equivalent to 20 µg/mL of fluticasone propionate. Transfer a quantity of Cream, equivalent to 1000 µg of fluticasone propionate, to a 125-mL separator y funnel. Add to the separator y funnel 25 mL of *Diluent*. Stopper and shake vigorously until the Cream is completely dispersed. Add 25 mL of hexane, shake for an additional 3 min, and allow the phases to separate. Filter the lower layer through a 20-mL syringe containing a cotton plug into a 50-mL volumetric flask. Repeat the extraction with one 5-mL and one 2-mL aliquot of *Diluent*, filtering the lower layers into the volumetric flask. Wash the cotton plug with 1 mL of *Diluent*, and collect the washings into the volumetric flask. Dilute the sample with *Diluent* to volume.
**Chromatographic system**
(See *Chromatography* ⟨621⟩*, System Suitability*.)
**Mode:** LC
**Detector:** 240 nm
**Column:** 4.6-mm × 25-cm; 5-µm packing L1
**Column temperature:** 50°
**Flow rate:** 1.5 mL/min
**Injection size:** 20 µL
**System suitability**
**Samples:** *System suitability solution* and *Standard solution*
**Suitability requirements**
**Resolution:** NLT 1.4 between fluticasone propionate and fluticasone propionate related compound D, *System suitability solution*
**Tailing factor:** NMT 1.4, *Standard solution* (calculated using the width of the peak at 10% of the height)
**Relative standard deviation:** NMT 2.0%, *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 Cream 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* (µg/mL)
$C_U$ = nominal concentration of fluticasone propionate in the *Sample solution* (µg/mL)
**Acceptance criteria:** 90.0%–110.0%

**PERFORMANCE TESTS**
• **MINIMUM FILL** ⟨755⟩**:** Meets the requirements

**SPECIFIC TESTS**
• **pH** ⟨791⟩**:** 4.5–6.5
• **MICROBIAL ENUMERATION TESTS** ⟨61⟩ and **TESTS FOR SPECIFIED MICROORGANISMS** ⟨62⟩**:** Meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The total aerobic microbial count is NMT 100 cfu/g, and the total combined molds and yeasts count is NMT 10 cfu/g.

**ADDITIONAL REQUIREMENTS**
• **PACKAGING AND STORAGE:** Preserve in collapsible tubes or tight containers, protected from light. Store between 2 ° and 30°.

• **USP REFERENCE STANDARDS** ⟨11⟩
USP Fluticasone Propionate RS
USP Fluticasone Propionate Nasal Spray Resolution Mixture RS
This Reference Standard is a mixture of fluticasone propionate and fluticasone propionate related compound D, and the chemical names for both are given below:
*Fluticasone propionate: S*-Fluoromethyl 6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxyandrosta-1,4-diene-17β-carbothioate.
*Fluticasone propionate related compound D: S*-Methyl-6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxyandrosta-1,4-diene-17β-carbothioate.

## Fluticasone Propionate Nasal Spray

**DEFINITION**
Fluticasone Propionate Nasal Spray is a white, opaque suspension of Fluticasone Propionate in water. It is supplied in a form suitable for nasal administration. It contains NL T 95.0% and NMT 115.0% of the labeled amount of fluticasone propionate ($C_{25}H_{31}F_3O_5S$).

**IDENTIFICATION**
• **A. INFRARED ABSORPTION** ⟨197M⟩
**Sample:** Transfer 30 g of Nasal Spray equally into two 50-mL centrifuge tubes. Add 10 mL of water to each tube, insert the stopper, and shake vigorously for 2 min. Centrifuge at 3500 rpm for 10 min, and discard the supernatant. Add 10 mL of water to each tube, insert the stopper, and shake vigorously for 2 min. Centrifuge at 3500 rpm for 10 min, and discard the supernatant. Add 10 mL of water to each tube, insert the stopper, and shake vigorously for 2 min. Centrifuge at 3500 rpm for 10 min, and discard the supernatant. To one tube add 10 mL of methanol. Shake to disperse the residue, and transfer to the other tube. Shake the other tube for 1 min. Centrifuge at 3500 rpm for 10 min. Decant the supernatant into an agate mortar. Evaporate the methanol either by carefully blowing dr y with compressed air or nitrogen, or by allowing the methanol to evaporate naturally. If using an air or nitrogen line, use a suitable in-line filter to avoid contamination. Allow the residue to dry overnight in a desiccator over silica gel.
**Acceptance criteria:** Meets the requirements
• **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**
• **PROCEDURE**
**Diluent:** Acetonitrile and 0.001 M hydrochloric acid (60:40)
**Buffer:** 1.2 g/L of monobasic ammonium phosphate. Adjust with phosphoric acid to a pH of 3.5 ± 0.05.
**Mobile phase:** Methanol, acetonitrile, and *Buffer* (50:15:35)
**System suitability solution:** 50 µg/mL of USP Phenylethyl Alcohol RS and 10 µg/mL of USP Fluticasone Propionate Nasal Spray Resolution Mixture RS in *Diluent*
**Standard solution:** 10 µg/mL of USP Fluticasone Propionate RS in *Diluent*
**Sample solution:** Nominally 10 µg/mL prepared as follows: Transfer an amount of the Nasal Spray containing 0.5 mg of fluticasone propionate to a 50-mL volumetric flask. Add about 40 mL of *Diluent*, and sonicate the flask for 10 min. Dilute with *Diluent* to volume, and shake. Allow to stand for 10 min until the supernatant is a clear solution. Inject the clear supernatant into the chromatograph.
**Chromatographic system**
(See *Chromatography* ⟨621⟩*, System Suitability*.)