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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 NLT 95.0% and NMT 115.0% of the labeled amount of fluticasone propionate ($C_{25}H_{31}F_3O_5S$).

IDENTIFICATION

• A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 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 about 3500 rpm for about 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 about 3500 rpm for about 10 min, and discard the supernatant. Add 10 mL of [water](#) to each tube, insert the stopper, and shake vigorously for about 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 about 3500 rpm for about 10 min. Decant the supernatant into an agate mortar. Evaporate the methanol either by carefully blowing dry 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.

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

System suitability solution: 50 µg/mL of [USP Phenylethyl Alcohol RS](#), 10 µg/mL of [USP Fluticasone Propionate RS](#), and 1 µg/mL of [USP Fluticasone Propionate Related Compound D RS](#) in *Diluent*

Standard solution: 10 µg/mL of [USP Fluticasone Propionate RS](#) in *Diluent*

Sample solution: Nominally 10 µg/mL of fluticasone propionate 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](#).)

Mode: LC

Detector: UV 210 and 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*

Record the chromatogram at 210 nm for 5 min and then change the wavelength to 239 nm.

[NOTE—The relative retention times for phenylethyl alcohol, fluticasone propionate, and fluticasone propionate related compound D are about 0.42, 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 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fluticasone propionate ($C_{25}H_{31}F_3O_5S$) in the portion of Nasal Spray taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response 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: 95.0%–115.0%

OTHER COMPONENTS

• CONTENT OF PHENYLETHYL ALCOHOL

Diluent, Mobile phase, System suitability solution, Chromatographic system, and System suitability: Proceed as directed in the Assay.

Standard solution: 0.05 mg/mL of [USP Phenylethyl Alcohol RS](#) in *Diluent*

Sample solution: Transfer 1.0 g of the Nasal Spray to a 50-mL volumetric flask. Add about 40 mL of *Diluent*, and sonicate for 10 min. Dilute with *Diluent* to volume, and shake. Allow to stand for 10 min until the supernatant is clear. Use the clear supernatant for analysis.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity, in mg/g, of phenylethyl alcohol in the portion of Nasal Spray taken:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/W)$$

r_U = peak response of phenylethyl alcohol from the *Sample solution*

r_S = peak response of phenylethyl alcohol from the *Standard solution*

C_S = concentration of [USP Phenylethyl Alcohol RS](#) in the *Standard solution* (mg/mL)

V = volume of the *Sample solution*, 50 mL

W = weight of the Nasal Spray in the *Sample solution* (g)

Acceptance criteria

For 50 sprays: 1.75–2.63 mg/g

For 120 sprays: 1.88–2.63 mg/g

• CONTENT OF BENZALKONIUM CHLORIDE

Buffer: Dissolve 10.8 g of [monobasic sodium phosphate dihydrate](#) in 90 mL of [water](#), and adjust with [phosphoric acid](#) to a pH of 2.5. Dilute with [water](#) to 100 mL.

Solution A: Mix 50 mL of *Buffer*, 750 mL of [water](#), and 200 mL of methanol. Add 5 mL of [triethylamine](#). Mix and adjust with [phosphoric acid](#) to a pH of 2.5.

Solution B: Mix 1 L of methanol with 50 mL of [phosphoric acid](#).

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	55	45
3.0	5	95
3.2	55	45
5.0	55	45

Diluent: Methanol, [water](#), and [hydrochloric acid](#) (693:297:10)

System suitability solution: 0.04 mg/mL of [USP Benzalkonium Chloride RS](#) in *Diluent* prepared as follows. Transfer a suitable volume of [USP Benzalkonium Chloride RS](#) to a suitable volumetric flask and dilute to volume with *Diluent*.

Standard stock solution: 200 µg/mL of [USP Benzalkonium Bromide RS](#) in [water](#). [NOTE—Sonication for about 2 min may be used to ensure complete dissolution. A few drops of methanol may be used to resolve the formation of foam prior to dilution.]

Standard solution: 20 µg/mL of [USP Benzalkonium Bromide RS](#). Transfer an aliquot of *Standard stock solution* to a suitable volumetric flask. Dilute with *Diluent* to volume.

Sample solution: Transfer 1.0 g of the Nasal Spray to a 10-mL volumetric flask. Dilute with *Diluent* to volume. Centrifuge if necessary. [NOTE—Centrifuging at about 4000 rpm for about 15 min may be suitable. Supernatant may be passed through a suitable filter with a pore size of NMT 0.2 µm with a glass syringe.]

Chromatographic system(See [Chromatography \(621\), System Suitability](#).)**Mode:** LC**Detector:** UV 210 nm**Column:** 4.6-mm × 3.0-cm; 2.6-μm packing [L1](#)**Column temperature:** 50°**Flow rate:** 2 mL/min**Injection volume:** 100 μL**System suitability****Samples:** *System suitability solution* and *Standard solution*[NOTE—See [Table 2](#) for relative retention times. The C₁₀ benzalkonium homolog may not be present.]**Suitability requirements****Resolution:** NLT 2.5 between the pairs of C₁₂ and C₁₄ benzalkonium homologs and the C₁₄ and C₁₆ benzalkonium homologs, *System suitability solution***Tailing factor:** NMT 2.0, *Standard solution***Relative standard deviation:** NMT 2%, *Standard solution***Analysis****Samples:** *Standard solution* and *Sample solution*Calculate the sum of the corrected benzalkonium peak responses (r_{cu}) in the portion of *Sample solution* taken:

$$\text{Result} = \Sigma[r_u \times (1/F)]$$

 r_u = peak response of each C₁₀, C₁₂, C₁₄, and C₁₆ benzalkonium homolog from the *Sample solution* F = relative response factor for the corresponding benzalkonium homolog relative to benzalkonium bromide (see [Table 2](#))**Table 2**

Benzalkonium Chloride Homolog	Relative Retention Time	Relative Response Factor
C ₁₀	0.65	1.2
C ₁₂	1.0	1.1
C ₁₄	1.35	1.0
C ₁₆	1.59	0.98

Calculate the amount of benzalkonium chloride in the portion of Nasal Spray taken:

$$\text{Result} = (r_{cu}/r_s) \times C_s \times (V/W)$$

 r_{cu} = sum of the corrected peak responses of the benzalkonium homologs from the *Sample solution* r_s = peak response of benzalkonium from the *Standard solution* C_s = concentration of [USP Benzalkonium Bromide RS](#) in the *Standard solution* (μg/mL) V = volume of the *Sample solution* (mL) W = weight of Nasal Spray in the *Sample solution* (g)**Acceptance criteria:** 140–220 μg/g**PERFORMANCE TESTS**• **DELIVERED DOSE UNIFORMITY** (within container)**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.**Mobile phase:** [Methanol](#), [acetonitrile](#), and *Buffer* (50:15:35)**System suitability solution:** 5 μg/mL of [USP Fluticasone Propionate RS](#) and 0.5 μg/mL of [USP Fluticasone Propionate Related Compound D RS](#) in *Diluent***Standard solution:** 4 μg/mL of [USP Fluticasone Propionate RS](#) in *Diluent*