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Fluticasone Propionate Inhalation Aerosol

DEFINITION

Fluticasone Propionate Inhalation Aerosol is a suspension of Fluticasone Propionate with suitable propellants in a pressurized container. The mean content per actuation contains NLT 85% and NMT 115% of the labeled amount of fluticasone propionate ($C_{25}H_{31}F_3O_5S$).

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197A

Spectral range: 4000 cm^{-1} to 600 cm^{-1}

Samples: Deposit between 5 and 20 actuations onto the zinc selenide plate of the HATR (Horizontal ATR) accessory. Dry the zinc selenide plate.

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

Change to read:

PROCEDURE

Buffer: 0.01 M [sodium dodecyl sulfate](#) containing 0.1% [glacial acetic acid](#)

Solution A: [Methanol](#) and *Buffer* (20:80)

Mobile phase: [Acetonitrile](#) and *Solution A* (1:1)

Standard solution: 50 $\mu g/mL$ of [USP Fluticasone Propionate RS](#) in [acetonitrile](#) and [water](#) (1:1)

Sample solution: Nominally 50 $\mu g/mL$ of fluticasone propionate prepared as follows. Shake the canister vigorously, and cool for 10 min in a dry ice–methanol bath. Remove the canister from the bath, and shake vigorously. Using a suitable device, carefully remove and keep the valve, and pour the contents into a suitable container. Allow the propellant to evaporate. Transfer the canister content to a suitable volumetric flask fitted with a suitable funnel using about 12% of the flask volume of [acetonitrile](#). Add 50% of the flask volume of [water](#). Swab the outer part of the valve with damp cotton wool soaked in [acetonitrile](#). Place the swab in the neck of the funnel in the volumetric flask. Allow the valve to dry, then dismantle, and wash the components and the canister wall with [acetonitrile](#). Collect the washings, and place in the same volumetric flask as the sample. Allow the flask to come to room temperature, and dilute with [acetonitrile](#) to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 239 nm

Column: 4.6-mm $\times$ 5-cm; 3.5- μm packing [L1](#)

Column temperature: 40°

Flow rate: 2 mL/min

Injection volume: 10 μL

System suitability

Sample: *Standard solution*

[NOTE—The retention time for the peak due to fluticasone propionate must be within the range of 1.0–1.6 min.]

Suitability requirements

Tailing factor: NMT 1.3 for the fluticasone propionate peak

Relative standard deviation: NMT 2.0%

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 the Inhalation Aerosol taken:

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

r_U = $\blacktriangle$ peak $\blacktriangle$ (IRA 1-Sep-2022) response from the *Sample solution*

r_S = $\blacktriangle$ peak $\blacktriangle$ (IRA 1-Sep-2022) response from the *Standard solution*

C_S = concentration of [USP Fluticasone Propionate RS](#) in the *Standard solution* ($\mu g/mL$)

C_U = nominal concentration of fluticasone propionate in the *Sample solution* (µg/mL)

Acceptance criteria: 85%–115%

Delete the following:

▲PERFORMANCE TESTS▲ (IRA 1-Sep-2022)

IMPURITIES

Change to read:

• **ORGANIC IMPURITIES:** Protect the *Sample solution*▲ (IRA 1-Sep-2022) from light.

Solution A: Prepare a solution of 0.05% v/v [phosphoric acid](#) in [acetonitrile](#).

Solution B: Prepare a solution of 0.05% v/v [phosphoric acid](#) in [methanol](#).

Solution C: Prepare a solution of 0.05% v/v [phosphoric acid](#) in [water](#).

Mobile phase: See ▲[Table 1](#).

Table 1▲ (IRA 1-Sep-2022)

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

System suitability solution: Dissolve 2 mg of [USP Fluticasone Propionate System Suitability Mixture RS](#) in 5 mL of *Solution A*. Add 5 mL of *Solution C*, and mix.

Sample solution: Nominally 200 µg/mL of fluticasone propionate in *Solution A* prepared as follows. Place a canister into a freezing mixture of dry ice and [methanol](#), and cool for approximately 5 min. Carefully remove the valve from the canister, and pass the contents through a filter of 0.22-µm pore size. When the filter bed is dry, wash it with two 5-mL aliquots of [cyclohexane](#). Allow the paper to dry, then carefully transfer to an appropriate container. Dissolve the drug present on the filter paper in 50% of the final required volume of *Solution A*. Dilute with *Solution C* to volume to obtain the nominal concentration.

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

Sample: *System suitability solution*

[NOTE—See ▲[Table 2](#)▲ (IRA 1-Sep-2022) for relative retention times.]

Suitability requirements

Resolution: NLT 0.6 between the fluticasone propionate related compound B and fluticasone propionate related compound C peaks and NLT 1.5 between the fluticasone propionate related compound D and fluticasone propionate peaks

Tailing factor: NMT 1.1 for the fluticasone propionate peak

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Inhalation Aerosol taken:

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

r_U = ▲peak▲ (IRA 1-Sep-2022) response of each impurity from the *Sample solution*

r_T = total peak area for all peaks ≥0.05% by area of the peak due to fluticasone propionate from the *Sample solution*

Acceptance criteria: See ▲[Table 2](#).

Table 2▲ (IRA 1-Sep-2022)