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Fluticasone Propionate Inhalation Powder

DEFINITION
Fluticasone Propionate Inhalation Powder contains NLT 90% and NMT 110% of the labeled amount of fluticasone propionate ($C_{25}H_{31}F_3O_5S$).

IDENTIFICATION
Change to read:

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the ▲*Assay*.▲

(IRA 1-Sep-2022)

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* (49:51)

Diluent: Methanol and water (70:30)

Standard solution: 6–12 µg/mL of USP Fluticasone Propionate RS in *Diluent*

Sample solution: Nominally 6–12 µg/mL of fluticasone propionate from NLT 12 unit doses in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 239 nm

Column: 4.6-mm × 5-cm; 3.5-µm packing L1

Flow rate: 2 mL/min

Column temperature: 40°

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

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

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

r_S = ▲peak▲ (IRA 1-Sep-2022) 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: 90%–110%

Delete the following:

▲PERFORMANCE TESTS▲ (IRA 1-Sep-2022)

IMPURITIES
Change to read:

• **Organic Impurities**

[Note—Protect sample and standard solutions 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
70.1	42	3	55
90	42	3	55

System suitability solution: Dissolve 2 mg of USP Fluticasone Propionate System Suitability Mixture RS in 12 mL of *Solution A*. Add 8 mL of *Solution C*, and mix.

Sensitivity solution: 0.5 µg/mL of USP Fluticasone Propionate RS in *Solution A*

Sample solution: Nominally 100 µg/mL of fluticasone propionate from NLT 10 unit doses prepared as follows. Transfer the contents of the appropriate number of unit doses into a suitable volumetric flask. Add 60% of the flask volume of ▲*Solution A*,▲ (IRA 1-Sep-2022) and sonicate for 2 min. Add 40% of the flask volume of ▲*Solution C*,▲ (IRA 1-Sep-2022) mix, and allow the solution to equilibrate. Dilute with ▲*Solution C*▲ (IRA 1-Sep-2022) to volume if necessary. Mix, allow any undissolved excipient material to settle, and inject the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 239 nm

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

Flow rate: 1 mL/min

Column temperature: 40°

Injection volume: 100 µL

System suitability

Samples: *System suitability solution* and *Sensitivity solution*

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*

Tailing factor: NMT 1.3 for fluticasone propionate, *System suitability solution*

Signal-to-noise ratio: NLT 10 for fluticasone propionate, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of each fluticasone propionate related impurity in the portion of sample taken:

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

r_U = peak response of each impurity from the *Sample solution*

r_T = total peak response 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)

Name	Relative Retention Time	Acceptance Criteria, (%)
Fluticasone sulfenic acid[a]	0.47	<0.2
Fluticasone propionate related compound B[b]	0.75	—
Fluticasone propionate related compound C[b]	0.77	—
Fluticasone propionate related compound D	0.95	<0.3
Fluticasone propionate	1.0	—
Fluticasone propionate dimer[c]	1.31	<0.3
Any unspecified degradation product	—	<0.1
Total[d]	—	NMT 1.1

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

[b] These are process impurities that are included in the table for identification only. These impurities are controlled in the drug substance. They are not to be reported for the drug product and are not included in the total impurities.

[c] 6α,9α-Difluoro-11β,17α-dihydroxy-16α-methyl-3-oxoandrosta-1,4-diene-17β-carboxylic acid 6α,9α-difluoro-17β-(fluoromethylthio)carbonyl-11β-dihydroxy-16α-methyl-3-oxoandrosta-1,4-diene-17β-yl ester.

[d] Sum of all impurity peaks ≥0.05%.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^1 cfu/g of bulked powder, the total aerobic yeasts and molds count does not exceed 10^1 cfu/g of bulked powder. It meets the requirements of the tests for absence of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella* species, and Enterobacteriaceae in 1 g of bulked powder.

Change to read:

• **Particulate Matter in Injections ⟨788⟩**

The test described below and the specification are applicable only to a microscopic particle count test methodology. *Particulate Matter in Injections ⟨788⟩* describes details of the test apparatus to be used for the determination of particulate matter using a microscopic particle count test methodology. Samples should be carefully prepared to avoid environmental contamination and testing should be performed with suitable controls, including the appropriate use of blank determinations.

Diluent: Methanol and water (65:35) filtered through a filter of 0.45-µm pore size

Filter: Mixed cellulose and ester; 25-mm diameter and 0.45-µm pore size

Sample solution: Transfer the contents of 4 unit doses from each of two inhalers into a suitable receptacle, and dissolve the drug and excipient particles in about 75 mL of *Diluent*.

Analysis

Sample: *Sample solution*

Pass the *Sample solution* through the *Filter* and allow the *Filter* to dry under conditions that will limit particulate contamination. Using a microscopic particle count test method, enumerate the number of particles present in the *Sample solution*.

Calculate the number of particles per dose:

$$\text{Number of particles/dose} = (N_{<10} + N_{10-100} + N_{>100})/8$$

$N_{<10}$ = total number of particles <10 µm in the *Sample solution*

N_{10-100} = total number of particles between 10 and 100 µm in the *Sample solution*

$N_{>100}$ = total number of particles >100 µm present in the *Sample solution*

Acceptance criteria: See ▲*Table 3*.

Table 3▲ (IRA 1-Sep-2022)

Particle Size Range (µm)	Number of Particles/Dose (NMT)
<10	200
10–100	100
>100	10
Total	300

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature, in a dry place away from direct heat or sunlight.

• **USP Reference Standards** ⟨11⟩

USP Fluticasone Propionate RS

USP Fluticasone Propionate System Suitability Mixture RS

It is a mixture of:

Fluticasone propionate;

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-oxoandrosta-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].

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

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

Chromatographic Database Information: Chromatographic Database

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