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Fluticasone Propionate and Salmeterol Inhalation Powder

DEFINITION

Fluticasone Propionate and Salmeterol Inhalation Powder is a mixture of fluticasone propionate and salmeterol xinafoate for use in dry powder inhalers. The Inhalation Powder contains NLT 90% and NMT 110% of the labeled amount of fluticasone propionate ($C_{25}H_{31}F_3O_5S$) and NLT 90% and NMT 110% of the labeled amount of salmeterol ($C_{25}H_{37}NO_4$) as salmeterol xinafoate.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Ultraviolet-Visible Spectroscopy:** 197U

Diluent: [Methanol](#) and [water](#) (70:30)

Standard solution: A mixture of [USP Fluticasone Propionate RS](#) and [USP Salmeterol Xinafoate RS](#) according to the individual product strengths in the Inhalation Powder under test in *Diluent*

Sample solution: Dissolve a suitable number of unit doses of the Inhalation Powder under test in a suitable volume of *Diluent*.

Acceptance criteria: Meets the requirements

Change to read:

- **B.** 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: To each liter of 2.9 g/L of [sodium dodecyl sulfate](#) in [water](#), add 1 mL of [glacial acetic acid](#).

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

Mobile phase: [Acetonitrile](#) and *Solution A* (50:50)

Diluent: [Methanol](#) and [water](#) (70:30)

Standard solution: 10 µg/mL of [USP Fluticasone Propionate RS](#) and 3 µg/mL of [USP Salmeterol Xinafoate RS](#) in *Diluent*

Sample solution: Nominally 5–25 µg/mL of fluticasone propionate and 2.4 µg/mL of salmeterol from NLT 12 unit doses in *Diluent*

Chromatographic system

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

Mode: LC

Detectors

Fluticasone propionate: UV 239 nm

Salmeterol: Fluorescence with excitation at 225 nm and emission at 305 nm. Use emission response for quantification.

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

Column temperature: 40°

Flow rate: 2 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention time of salmeterol

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for fluticasone propionate and salmeterol are 0.6 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.5 between salmeterol and fluticasone propionate

Tailing factor: NMT 1.5 for salmeterol and fluticasone propionate

Relative standard deviation: NMT 2.0% for salmeterol and fluticasone propionate

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 Inhalation Powder 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)

Calculate the percentage of the labeled amount of salmeterol ($C_{25}H_{37}NO_4$) in the portion of ▲Inhalation Powder▲ (IRA 1-Sep-2022) taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times (M_{r1}/M_{r2}) \times 100$$

r_u = peak response of salmeterol from the *Sample solution*

r_s = peak response of salmeterol from the *Standard solution*

C_s = concentration of [USP Salmeterol Xinafoate RS](#) in the *Standard solution* (µg/mL)

C_u = nominal concentration of salmeterol free base in the *Sample solution* (µg/mL)

M_{r1} = molecular weight of salmeterol free base, 415.57

M_{r2} = molecular weight of salmeterol xinafoate, 603.75

Acceptance criteria: 90%–110% each for fluticasone propionate and salmeterol

Delete the following:

▲PERFORMANCE TESTS▲ (IRA 1-Sep-2022)

IMPURITIES

Change to read:

• ORGANIC IMPURITIES

[NOTE—Protect all solutions containing fluticasone propionate or salmeterol from light.]

Solution A: 5.7 g/L of [monobasic ammonium phosphate](#) in [water](#) adjusted with [10% phosphoric acid TS](#) to a pH of 2.9

Solution B: [Acetonitrile](#)

Mobile phase: See ▲[Table 1](#).

Table 1▲ (IRA 1-Sep-2022)

Time (min)	Solution A (%)	Solution B (%)
0	70	30
60	22	78
61	70	30
70	70	30

Diluent: [Methanol](#), [water](#), and [phosphoric acid](#) (70: 30: 0.05)

Acidified methanol: To each liter of [methanol](#), add 0.5 mL of [phosphoric acid](#).

System suitability solution: 0.15 mg/mL of [USP Salmeterol Xinafoate RS](#), 0.05 mg/mL of [USP Fluticasone Propionate RS](#), and 0.4 µg/mL each of [USP Fluticasone Propionate Related Compound D RS](#) and [USP Fluticasone Propionate Related Compound J RS](#) in *Diluent*

Standard solution: 2 µg/mL of [USP Salmeterol Related Compound H RS](#) and 4 µg/mL of [USP Fluticasone Propionate RS](#) in *Diluent*

Sensitivity solution: 0.05 µg/mL of [USP Salmeterol Related Compound H RS](#) and 0.1 µg/mL of [USP Fluticasone Propionate RS](#) from the *Standard solution* in *Diluent*

Sample solution: Nominally 200–500 µg/mL of fluticasone propionate prepared as follows. Transfer the contents of NLT 10 unit doses to a 10-mL volumetric flask. Add 6 mL of acidified [methanol](#) and sonicate for 10 min. Add 3 mL of [water](#), mix, and allow the solution to equilibrate. Dilute with acidified [methanol](#) to volume.

Chromatographic system

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

Mode: LC

Detector: UV 228 nm

Column: 4.6-mm × 25-cm; 5-µm packing [L1](#)

Column temperature: 35°

Flow rate: 1 mL/min