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Fluticasone Propionate and Salmeterol Inhalation Aerosol

DEFINITION

Fluticasone Propionate and Salmeterol Inhalation Aerosol is a suspension of Fluticasone Propionate and Salmeterol with suitable propellants in a pressurized container. The mean content per actuation contains NLT 88% and NMT 112% of the labeled amount of fluticasone propionate (C₂₅H₃₁F₃O₅S). The mean content per actuation contains NLT 88% and NMT 112% of the labeled amount of salmeterol (C₂₅H₃₇NO₄) as salmeterol xinafoate.

IDENTIFICATION

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

Wavenumber range: 4000 –600 cm⁻¹

Sample: Discharge an appropriate number of actuations from two containers into an agate mortar. Allow the propellant to evaporate and dry if necessary. Transfer the residue to the sample window.

Acceptance criteria: Meets the requirements. In addition, the ratio of the fluticasone propionate band at 833 cm⁻¹ to that of the salmeterol band at 744 cm⁻¹ meets the requirements in [Table 1](#).

Table 1

Fluticasone Propionate/Salmeterol (µg/µg for each dose)	Ratio (band at 833 cm ⁻¹ /band at 744 cm ⁻¹)
45/21	NMT 2.5
115/21	2.5–4.0
230/21	NLT 4.0

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

• **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* (50:50)

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

Standard solution: 50 µg/mL of [USP Fluticasone Propionate RS](#) and 15 µg/mL of [USP Salmeterol Xinafoate RS](#) in *Diluent*

Sample solution: Nominally 20–110 µg/mL of fluticasone propionate and 10 µg/mL of salmeterol 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. Dissolve the canister contents in a minimum amount of [methanol](#) and quantitatively transfer to a suitable volumetric flask containing 30% of the flask volume of [water](#). Rinse the canister and valve with [methanol](#) into the same volumetric flask. Allow the flask to come to room temperature and dilute with [methanol](#) to volume.

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:** 5 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 fluticasone propionate and salmeterol**Tailing factor:** NMT 1.5 for fluticasone propionate and salmeterol**Relative standard deviation:** NMT 2.0% for fluticasone propionate and salmeterol**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 Aerosol 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 Aerosol 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:** 88%–112% 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.]

Buffer: 0.05 M [monobasic ammonium phosphate](#) adjusted with 10% (v/v) of [phosphoric acid](#) to a pH of 2.9**Solution A:** [Acetonitrile](#) and *Buffer* (30:70)**Solution B:** [Acetonitrile](#) and *Buffer* (78:22)**Mobile phase:** See ▲[Table 2](#).**Table 2▲** (IRA 1-Sep-2022)

Time (min)	Solution A (%)	Solution B (%)
0	100	0
60	0	100
61	100	

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