Edition: BP 2025 (Ph. Eur. 11.6 update)

Fluticasone Inhalation Powder, pre-metered

General Notices

Fluticasone Powder for Inhalation, pre-dispensed

Action and use

Glucocorticoid.

DEFINITION

Fluticasone Inhalation Powder, pre-metered consists of Fluticasone Propionate in *microfine powder* either alone or combined with a suitable carrier. The blister is loaded into a dry-powder inhaler to generate an aerosol.

The inhalation powder, pre-metered complies with the requirements stated under Preparations for Inhalation and with the following requirements.

PRODUCTION

The size of aerosol particles to be inhaled is controlled so that a consistent portion is deposited in the lungs. The fine-particle characteristics of preparations for inhalation are determined using the method described in Appendix XII C7. Preparations for inhalation: Aerodynamic Assessment of Fine Particles. The test and limits should be agreed with the competent authority.

The water content is controlled to ensure the performance of the product as justified and authorised by the competent authority.

Content of fluticasone propionate, $C_{25}H_{31}F_3O_5S$

80.0 to 120.0% of the stated amount.

IDENTIFICATION

A. The *light absorption*, Appendix II B, in the range 210 to 300 nm of the final solution obtained in the test for Uniformity of delivered dose closely resembles that of a solution containing 0.0005% w/v of *fluticasone propionate BPCRS* in solvent A and exhibits a single maximum at 240 nm.
B. In the test for Uniformity of delivered dose, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Uniformity of delivered dose

Complies with the requirements stated under Inhalation Powders using the following method of analysis. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 35 volumes of *water* and 65

volumes of *methanol* (solvent A).

(1) Collect single doses of the preparation being examined using the procedure described under Inhalation Powders, Uniformity of delivered dose and dissolve the collected dose in sufficient of solvent A to produce a solution expected to contain 0.0005% w/v of Fluticasone Propionate.
(2) 0.0005% w/v of *fluticasone propionate BPCRS* in solvent A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS1 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 239 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

15 volumes of *acetonitrile*, 35 volumes of 0.01M *ammonium dihydrogen orthophosphate* and 50 volumes of *methanol* adjusted to pH 3.5 with *orthophosphoric acid* or *dilute ammonia*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *symmetry factor* of the principal peak is not greater than 2.5.

DETERMINATION OF CONTENT

Calculate the content of Fluticasone Propionate, $C_{25}H_{31}F_3O_5S$, per delivered dose using the declared content of $C_{25}H_{31}F_3O_5S$ in *fluticasone propionate BPCRS*. Repeat the procedure as described for pre-metered systems under Inhalation Powders, Uniformity of delivered dose.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Shake a quantity of the powder, containing 0.5 mg of Fluticasone Propionate in 10 mL of a mixture of 7 volumes of *acetonitrile*, 20 volumes of *water* and 23 volumes of *methanol* and filter.
(2) Dilute 1 volume of solution (1) to 200 volumes in equal volumes of *acetonitrile* and *water*.
(3) 0.0004% w/v of *fluticasone impurity D EPCRS* and 0.002% w/v of *fluticasone propionate BPCRS* in equal volumes of *acetonitrile* and *water*.
(4) Dilute 1 volume of solution (2) to 5 volumes in equal volumes of *acetonitrile* and *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS1 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 239 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 23 volumes of *acetonitrile* and 77 volumes of *methanol*.

Mobile phase B 0.01M *ammonium dihydrogen orthophosphate*, adjusted to pH 3.5 with *acetic acid* or *dilute ammonia*.

Equilibrate the column with a mobile phase ratio A:B of 60:40. Inject solutions (1) and (3) and start the elution isocratically with the chosen mobile phase. One minute after elution of the apex of the fluticasone propionate peak start a linear gradient elution to reach a mobile phase ratio A:B of 85:15 over a period of 10 minutes. Continue the chromatography for 10 minutes.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the peaks due to fluticasone propionate and fluticasone impurity D is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the sum of the areas of any *secondary peaks* is not greater than 5 times the principal peak in the chromatogram obtained with solution (2) (2.5%).

Disregard any peak with an area less than the area of the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

Use the average of the individual results determined in the test for Uniformity of delivered dose.