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Mometasone Inhalation Powder, Pre-metered

General Notices

Mometasone Inhalation Powder, Pre-dispensed

Action and use

Glucocorticoid.

DEFINITION

Mometasone Inhalation Powder, pre-metered consists of Mometasone Furoate in microfine powder or aerodynamically equivalent, either alone or combined with a suitable carrier. It is administered by a dry-powder inhaler.

Content of mometasone furoate, $C_{27}H_{30}Cl_2O_6$

85.0 to 115.0% of the amount stated to be delivered by actuation of the valve.

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.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Discharge the container a sufficient number of times to obtain 1.2 mg of Mometasone Furoate and disperse in 10 mL of *methanol (80%)*. Shake vigorously, filter and use the filtrate.
(2) 0.0125% w/v of *mometasone furoate BPCRS* in methanol (80%).
(3) Equal volumes of solution (1) and solution (2).

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}* (Merck silica gel 60 F_{254} plates are suitable).
(b) Use the mobile phase as described below, allow the tank to saturate for 60 minutes.
(c) Apply 20 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

3 volumes of *acetonitrile*, 10 volumes of *methanol*, 26 volumes of *ethyl acetate* and 61 volumes of *toluene*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) exhibits a single compact spot the same size and shape as that obtained with solution (2).

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) is similar in position and size to that in the chromatogram obtained with solution (2).

B. In the Assay, the principal peak in the chromatogram obtained with solution (1) corresponds to the peak due to mometasone furoate 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. Carry out the procedure protected from light and prepare solutions immediately before use.

Solution A 0.1 volumes of *glacial acetic acid*, 50 volumes of *acetonitrile* and 50 volumes of *water*.
(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 a sufficient amount of mixture of 6 volumes of *acetonitrile* and 94 volumes of solution A to produce a solution expected to contain 0.0008% w/v of *mometasone furoate BPCRS* and filter.
(2) Dissolve 25 mg of *mometasone furoate BPCRS* in 6 mL of *acetonitrile* and dilute to 100 mL with solution A. Dilute 1.6 volumes of this solution to 50 volumes with solution a mixture of 6 volumes of *acetonitrile* and 94 volumes of solution A.
(3) Dissolve 5 mg of *mometasone furoate for system suitability EPCRS* in 4.5 mL of *acetonitrile* and add sufficient solution A to produce 10 mL.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Symmetry C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for 2.5 times the retention time of mometasone furoate.

MOBILE PHASE

Equal volumes of *acetonitrile* and *water*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to mometasone furoate (retention time about 25 minutes) are: impurity C, about 0.9 and impurity J, about 1.5.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between impurity C and mometasone furoate is at least 2.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{27}H_{30}Cl_2O_6$, per delivered dose from the chromatograms obtained and using the declared content of $C_{27}H_{30}Cl_2O_6$ in *mometasone furoate BPCRS*. Repeat the procedure as described for reservoir systems under Powders for Inhalation, Uniformity of delivered dose.

Related substances

Carry out the method for *liquid chromatography*, Appendix III A, using the following solutions. *Carry out the procedure protected from light and prepare solutions immediately before use.*

Solution A 50 volumes of *acetonitrile*, 50 volumes of *water* and 0.1 volumes of *acetic acid*.
(1) Discharge the container a sufficient number of times to obtain 1 mg of Mometasone Furoate, add 3 mL of *acetonitrile* and 2 mL of solution A. Mix with the aid of ultrasound, add sufficient solution A to produce 10 mL and centrifuge.
(2) Dilute 1 volume of solution (1) to 200 volumes with solution A.
(3) Dissolve 5 mg of *mometasone furoate for system suitability EPCRS* in 4.5 mL of *acetonitrile* and add sufficient solution A to produce 10 mL.
(4) Dilute 1 volume of solution (2) to 5 volumes with solution A.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Uniformity of delivered dose may be used.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to mometasone furoate (retention time about 24 minutes) are: impurity C, about 0.9; impurity J, about 1.5.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between impurity C and mometasone furoate is at least 2.5.

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 four times the principal peak in the chromatogram obtained with solution (2) (2%).

Disregard any peak with an area less than 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.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Mometasone Furoate.