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Beclometasone Inhalation Powder, pre-metered

General Notices

Beclometasone Powder for Inhalation, pre-dispensed

Action and use

Glucocorticoid.

DEFINITION

Beclometasone Inhalation Powder, pre-metered consists of Beclometasone Dipropionate or Beclometasone Dipropionate Monohydrate in *microfine powder* either alone or combined with a suitable carrier. The pre-metered unit 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 beclometasone dipropionate, $C_{28}H_{37}ClO_7$

When supplied as disks, 90.0 to 110.0% of the stated amount per pre-metered unit. When supplied as capsules, 80.0 to 120.0% of the stated amount per pre-metered unit.

IDENTIFICATION

A. In the Assay, the principal peak in the chromatogram obtained with solution (1) has the same retention time as the principal peak in the chromatogram obtained with solution (2).
B. Disperse a quantity of powder, containing the equivalent of 200 µg of beclometasone dipropionate in 5 mL of 1M *sodium hydroxide* in a 25 mL conical flask. Add three drops of *copper sulfate solution* and shake. A precipitate may form which dissolves to give a clear blue solution. Heat the solution to boiling; a red precipitate is produced.
C. *For products containing lactose* disperse 0.25 g of the powder for inhalation in 5 mL of *water*. Add 5 mL of 6M *ammonia* and heat in a water-bath at 80° for 10 minutes. An orange-red colour is produced.

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.

(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 a mixture of 45 volumes of *water* and 55 volumes of *acetonitrile* to produce a solution containing the equivalent of 0.00005% w/v of beclometasone dipropionate.
(2) Dilute 10 mL of a solution containing 0.0005% w/v of *beclometasone dipropionate BPCRS* in *methanol* to 100 mL with a mixture of 45 volumes of *water* and 55 volumes of *acetonitrile*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *base-deactivated end-capped octylsilyl silica gel for chromatography* (5 µm) (Lichrospher 60 RP-select B is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.3 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 240 nm.
(f) Inject 100 µL of each solution.

MOBILE PHASE

25 volumes of *water* and 75 volumes of *methanol*.

DETERMINATION OF CONTENT

Calculate the content of beclometasone dipropionate, $C_{28}H_{37}ClO_7$, per delivered dose using the declared content of $C_{28}H_{37}ClO_7$ in *beclometasone dipropionate 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) Dissolve a quantity of the mixed contents of 20 units containing the equivalent of 1.2 mg of beclometasone dipropionate in the mobile phase and dilute to 5 mL with the mobile phase.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase.
(3) 0.0040% w/v each of *beclometasone 17-propionate BPCRS* and *beclometasone 21-propionate BPCRS* in the mobile phase.
(4) Dilute 1 volume of solution (2) to 20 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Lichrosorb RP18 or Lichrospher RP18 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 column temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 100 µL of each solution.
(g) For solutions (1) and (2) allow the chromatography to proceed for twice the retention time of the principal peak.

MOBILE PHASE

Dilute 60 volumes of *acetonitrile* to 100 volumes with *water*.

When the chromatograms are recorded under the prescribed conditions, the retention time for beclometasone 17-propionate is about 6 minutes, for beclometasone 21-propionate, about 7 minutes and for beclometasone dipropionate, about 13 minutes.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to beclometasone 17-propionate and beclometasone 21-propionate is at least 1.4. If necessary adjust the concentration of *acetonitrile* in the mobile phase.

LIMITS

In the chromatogram obtained with solution (1):

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

not more than one such *secondary peak* has an area greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

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

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.05%).

ASSAY

Weigh and powder the contents of 20 pre-dispensed units. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dissolve a quantity of the mixed contents of the pre-dispensed unit in sufficient of the mobile phase to produce a solution containing the equivalent of 0.001% w/v of beclometasone dipropionate.
(2) 0.001% w/v of *beclometasone dipropionate BPCRS* in the mobile phase.
(3) 0.001% w/v each of *beclometasone 17-propionate BPCRS* and *beclometasone 21-propionate BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to beclometasone 17-propionate and beclometasone 21-propionate is at least 1.4. If necessary adjust the concentration of *acetonitrile* in the mobile phase.

DETERMINATION OF CONTENT

Calculate the content of $C_{28}H_{37}ClO_7$ using the declared content of $C_{28}H_{37}ClO_7$ in *beclometasone dipropionate BPCRS*.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of beclometasone dipropionate.