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

Beclometasone Pressurised Inhalation

General Notices

Beclometasone Pressurised Inhalations from different manufacturers, whilst complying with the requirements of the monograph, are not necessarily interchangeable.

Action and use

Glucocorticoid.

DEFINITION

Beclometasone Pressurised Inhalation is a solution or suspension of Beclometasone Dipropionate in a suitable liquid in a pressurised container fitted with a metering dose valve.

The pressurised inhalation 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, $C_{28}H_{37}ClO_7$

85.0 to 115.0% of the stated amount.

IDENTIFICATION

The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of beclometasone dipropionate (2) (*RS 379*). Examine the substance as a dispersion in *potassium bromide* prepared in the following manner. Discharge the container a sufficient number of times, under conditions of very low relative humidity (less than 5%), into a mortar to obtain 2 mg of Beclometasone Dipropionate. Heat at 110° for 2 hours at a pressure of 2 kPa, cool, grind the residue thoroughly with 0.1 g of *potassium bromide*, add a further 0.2 g of *potassium bromide* and mix thoroughly.

TESTS

Uniformity of delivered dose

Complies with the requirements stated under Pressurised Metered-dose Preparations for Inhalation using the following method of analysis. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

Solution A 0.272% w/v of *potassium dihydrogen orthophosphate*.
(1) Collect single doses of the preparation being examined using the procedure described under *Pressurised Metered-dose Preparations for Inhalation*, Uniformity of delivered dose and dissolve the collected dose in sufficient *methanol (70%)* to produce a solution containing 0.00025% w/v of Beclometasone Dipropionate.
(2) 0.00025% w/v of *Beclometasone Dipropionate BPCRS* in *methanol (70%)*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (50 mm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (3.5 µm) (Waters Sunfire C18 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 50°.
(e) Use a detection wavelength of 239 nm.
(f) Inject 100 µL of each solution.

MOBILE PHASE

52 volumes of *tetrahydrofuran*, 240 volumes of *acetonitrile*, 260 volumes of *methanol* and 450 volumes of Solution A. Adjust the final pH to 3.25 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions the retention time of the peak due to beclometasone is about 8 minutes.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the column efficiency of the peak due to beclometasone dipropionate is at least 2000 theoretical plates.

DETERMINATION OF CONTENT

Calculate the content of beclometasone dipropionate, $C_{28}H_{37}ClO_7$, per delivered dose from the chromatograms obtained and using the declared content of $C_{28}H_{37}ClO_7$, in *beclometasone dipropionate BPCRS*. Repeat the procedure as described under Pressurised Metered-dose Preparations for Inhalation.

Related substances

Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions in *acetone*.

(1) Discharge the container into a small, dry flask a sufficient number of times to obtain 0.5 mg of Beclometasone Dipropionate and dissolve the residue in 2 mL of *acetone*. Evaporate the solution to a volume such that the whole solution can be applied to the plate.
(2) 0.1% w/v of *beclometasone dipropionate BPCRS*.
(3) Dilute 1 volume of solution (2) to 2 volumes.
(4) Dilute 1 volume of solution (2) to 4 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel*.
(b) Use the mobile phase described below.
(c) Apply separately to the plate the whole of solution (1) and 10 µL of each of solutions (2), (3) and (4).
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow it to dry in air, spray with *alkaline tetrazolium blue solution* and heat at 50° for 5 minutes. Cool and spray again with *alkaline tetrazolium blue solution*.

MOBILE PHASE

3 volumes of *methanol* and 97 volumes of *1,2-dichloroethane*.

LIMITS

In the chromatogram obtained with solution (1):

any *secondary spot* is not more intense than the spot in the chromatogram obtained with solution (2) (2%);

not more than one such spot is more intense than the spot in the chromatogram obtained with solution (3) (1%);

not more than two such spots are more intense than the spot in the chromatogram obtained with solution (4) (0.5%).

Disregard any spot with an Rf value of more than 0.85.

ASSAY

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

LABELLING

The label states the content of active ingredient in terms of the equivalent delivered dose.