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Budesonide Inhalation Powder

General Notices

Budesonide Powder for Inhalation, metered dose powder inhaler
Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	Medicinal Chemicals 3
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Target Publication Date (subject to change)	BP 2028
Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. Related substances Threshold amended.

Action and use

Glucocorticoid.

DEFINITION

Budesonide Inhalation Powder consists of Budesonide in [microfine powder](#) or aerodynamically equivalent, either alone or combined with a suitable carrier. It is administered by a dry-powder inhaler.

The inhalation powder 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 budesonide, $C_{25}H_{34}O_6$

80.0 to 120.0% of the stated amount.

IDENTIFICATION

- A. Dilute a quantity of the inhalation powder with sufficient [water](#) to produce a solution containing 0.002% w/v of Budesonide and filter. The [light absorption](#) of the resulting solution, [Appendix II B](#), in the range 200 nm to 350 nm exhibits a maximum only at 247 nm.
- B. In the Assay, 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).
- C. *For products containing [lactose](#)* disperse 0.25 g of the inhalation powder 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, protected from light.

Solvent A 34 volumes of [acetonitrile](#) and 66 volumes of [phosphate buffer solution pH 3.2](#).

- (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 solvent A to produce a solution containing 0.001% w/v of Budesonide.
- (2) 0.001% w/v of [budesonide BPCRS](#) in solvent A.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (15 cm × 4.6 mm) packed with [end-capped octadecylsilyl silica gel for chromatography](#) (3 µm) (Spherisorb ODS2 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 240 nm.
- (f) Inject 200 µL of each solution.

MOBILE PHASE

2 volumes of [ethanol](#), 34 volumes of [acetonitrile](#) and 66 volumes of [phosphate buffer solution pH 3.2](#).

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the [resolution](#) between the peaks due to epimer B and epimer A is at least 1.5.

DETERMINATION OF CONTENT

Calculate the amount of budesonide, $C_{25}H_{34}O_6$, per delivered dose using the declared content of $C_{25}H_{34}O_6$ in [budesonide BPCRS](#). Repeat the procedure as described for reservoir systems under Inhalation Powders, Uniformity of delivered dose.

Related substances

Carry out the method for [liquid chromatography](#), [Appendix III D](#), using the following solutions, protected from light.

Prepare a mixture of 34 volumes of [acetonitrile](#) and 66 volumes of [phosphate buffer solution pH 3.2](#) (solvent A).

- (1) Dissolve a quantity of the inhalation powder containing 2 mg of Budesonide in 3.4 mL of [acetonitrile](#). Mix with the aid of ultrasound, add sufficient [phosphate buffer solution pH 3.2](#) to produce 10 mL and filter.
- (2) Dilute 1 volume of solution (1) to 200 volumes with solvent A.
- (3) Dilute 1 volume of solution (2) to 5 volumes with solvent A.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (15 cm × 4.6 mm) packed with [end-capped octadecylsilyl silica gel for chromatography](#) (3 µm) (Spherisorb ODS2 is suitable).
- (b) Use gradient elution and the mobile phase described below.
- (c) Use a flow rate of 1 mL per minute.
- (d) Use a column temperature of 50°.
- (e) Use a detection wavelength of 240 nm.
- (f) Inject 100 µL of each solution.

MOBILE PHASE

Mobile phase A 2 volumes of [ethanol](#), 34 volumes of [acetonitrile](#) and 66 volumes of [phosphate buffer solution pH 3.2](#).

Mobile phase B Equal volumes of [acetonitrile](#) and [phosphate buffer solution pH 3.2](#).

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-38	100	0	isocratic
38-50	100→0	0→100	linear gradient
50-60	0	100	isocratic
60-61	0→100	100→0	linear gradient
61-70	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions the retention time relative to budesonide epimer B (retention time about 17 minutes) is epimer A, about 1.1.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (2), the [resolution](#) between the peaks due to epimer B and epimer A is at least 1.5;

in the chromatogram obtained with solution (3), the [signal-to-noise ratio](#) of each of the peaks due to epimer A and epimer B is at least 10.

LIMITS

In the chromatogram obtained with solution (1):

the area of any [secondary peak](#) is not greater than the sum of the areas of the epimer peaks in the chromatogram obtained with solution (2) (0.5%);

the sum of the areas of any [secondary peaks](#) is not greater than 3 times the sum of the areas of the epimer peaks in the chromatogram obtained with solution (2) (1.5%).

Disregard any peak with an area less than the sum of the areas of the epimer peaks in the chromatogram obtained with solution (3) (0.1%).

Epimer A

In the chromatogram obtained with solution (1), as described under Uniformity of delivered dose, the content of epimer A (second peak) is 40.0% to 51.0% of the sum of the areas of the two epimer peaks of budesonide.

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 Budesonide.

DRAFT MONOGRAPH
SUBJECT TO CHANGE