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Budesonide Nebuliser Suspension

General Notices

Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	Medicinal Chemicals 3
Contact Details	michael.whaley@mhra.gov.uk maryna.dmitriieva@mhra.gov.uk sophie.cherrington@mhra.gov.uk bpcom@mhra.gov.uk
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Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. Related substances Test solution concentration amended, threshold amended.

Action and use

Glucocorticoid.

DEFINITION

Budesonide Nebuliser Suspension is a suspension of Budesonide in a suitable vehicle, intended to be converted into aerosols by a nebuliser.

The nebuliser suspension complies with the requirements stated under Preparations for Inhalation and with the following requirements.

PRODUCTION

The active substance delivery rate and the total active substance delivered are determined using the methods described in [Appendix XII C. 8](#). Preparations for Nebulisation: Characterisation. Where justified and authorised, a different apparatus and procedure may be used.

The particle-size distribution is determined using an apparatus and procedure described in [Appendix XII C. 8](#). Preparations for Nebulisation: Characterisation. Where justified and authorised, a different

apparatus and procedure may be used.

Content of budesonide, $C_{25}H_{34}O_6$

92.5 to 105.0% of the stated amount.

IDENTIFICATION

- A. Dilute a quantity of the nebuliser suspension being examined 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).

TESTS

Acidity

pH, 4.0 to 5.0, [Appendix V L](#).

Related substances

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) To a quantity of the nebuliser suspension containing 1 mg of Budesonide add 3.4 mL of [acetonitrile](#). Mix with the aid of ultrasound, add sufficient [phosphate buffer solution pH 3.2](#) to produce 10 mL, centrifuge and use the supernatant liquid.
- (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 Assay, 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

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

- (1) To a quantity of the nebuliser suspension containing 1 mg of Budesonide add 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) 0.01% w/v of [budesonide BPCRS](#) in solvent A (as described under Related substances).

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 20 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 content of $C_{25}H_{34}O_6$ in the nebuliser suspension from the sum of the areas of the two budesonide epimer peaks and using the declared content of $C_{25}H_{34}O_6$ in [budesonide BPCRS](#).

STORAGE

Budesonide Nebuliser Suspension should be protected from light.

IMPURITIES

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