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Salbutamol Inhalation Powder, pre-metered

General Notices

Salbutamol Inhalation Powder, pre-dispensed

Action and use

Beta$_2$-adrenoceptor agonist; bronchodilator.

DEFINITION

Salbutamol Inhalation Powder, pre-metered consists of Salbutamol Sulfate 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 salbutamol, $C_{13}H_{21}NO_3$

95.0 to 105.0% of the stated amount per pre-metered unit.

IDENTIFICATION

A. In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

B. Dissolve a quantity of the inhalation powder containing the equivalent of 4 mg of salbutamol in 5 mL of *water*. The resulting solution yields reaction A characteristic of *sulfates*, Appendix VI.

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in the mobile phase.

(1) Dissolve a quantity of the inhalation powder in sufficient mobile phase to produce a solution containing the equivalent of 0.02% w/v of salbutamol and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes and further dilute 1 volume of this solution to 5 volumes.
(3) 0.02% w/v of *salbutamol for peak identification EPCRS*.
(4) 0.02% w/v of *salbutamol impurity standard BPCRS*.
(5) 0.00004% w/v of each of *salbutamol sulfate BPCRS* and *salbutamol impurity B BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 3.9 mm) packed with *end-capped octylsilyl silica gel for chromatography* (5 µm) (Symmetry C8 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 220 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for 25 times the retention time of salbutamol.

MOBILE PHASE

22 volumes of *acetonitrile R1* and 78 volumes of a solution containing 0.287% w/v of *sodium heptanesulfonate* and 0.25% w/v of *potassium dihydrogen orthophosphate* previously adjusted to pH 3.7 with 2M *orthophosphoric acid*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (5), the *resolution* between the peaks due to salbutamol and impurity B is at least 3.0.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of salbutamol in solution (2).

For the reporting threshold, use the concentration of salbutamol in solution (2).

For peak identification, use solutions (3) and (4).

Salbutamol retention time: about 3 minutes.

Relative retention: impurity B, about 1.4; impurity D, about 2.7; impurity F, about 6.3.

Correction factors: impurity D, multiply by 0.5.

LIMITS

— impurity F: not more than 0.8%;

— impurity D: not more than 0.3%;

— unspecified impurities: for each impurity, not more than 0.2%;

— total impurities: not more than 2.0%;

— reporting threshold: 0.1%.

Uniformity of delivered dose

Complies with the requirements for *Inhalation Powders* stated under *Preparations for Inhalation* 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 mobile phase to produce a solution containing the

equivalent of 0.00008% w/v of salbutamol.
(2) 0.0001% w/v of *salbutamol sulfate BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used, excluding (g).

DETERMINATION OF CONTENT

Calculate the content of salbutamol, $C_{13}H_{21}NO_3$, per delivered dose using the declared content of $C_{13}H_{21}NO_3$ in *salbutamol sulfate BPCRS*. Repeat the procedure as described for pre-metered systems under *Inhalation Powders, Uniformity of delivered dose*.

ASSAY

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-metered units in sufficient *water* to produce a solution containing the equivalent of 0.0001% w/v of salbutamol.
(2) 0.00012% w/v of *salbutamol sulfate BPCRS* in *water*.
(3) 0.0001% w/v of *salbutamol sulfate BPCRS* and 0.0001% w/v of *salbutamol impurity B BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used, excluding (g).

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to salbutamol and impurity B is at least 3.0.

DETERMINATION OF CONTENT

Calculate the content of salbutamol, $C_{13}H_{21}NO_3$, using the declared content of $C_{13}H_{21}NO_3$ in *salbutamol sulfate BPCRS*.

LABELLING

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

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B, C, D, E, F, G, H, I, J and P listed under Salbutamol Sulfate.