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

Salbutamol Injection

General Notices

Action and use

Beta$_2$-adrenoceptor agonist; bronchodilator.

DEFINITION

Salbutamol Injection is a sterile solution of Salbutamol Sulfate in Water for Injections.

The injection complies with the requirements stated under Parenteral Preparations and with the following requirements.

Content of salbutamol, $C_{13}H_{21}NO_3$

95.0 to 105.0% of the stated amount.

CHARACTERISTICS

A colourless or very pale yellow solution.

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. A volume containing the equivalent of 1 mg of salbutamol yields the reactions characteristic of *sulfates*, Appendix VI.

TESTS

Acidity

pH, 3.4 to 5.0, Appendix V L.

Related substances

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

(1) Dilute the injection to produce a solution containing the equivalent of 0.01% w/v of salbutamol.

(2) Dilute 1 volume of solution (1) to 20 volumes and further dilute 1 volume to 10 volumes.
(3) 0.012% w/v of *salbutamol sulfate BPCRS*, 0.00005% w/v of *salbutamol ketone BPCRS* (impurity J) and 0.00002% w/v of *salbutamol impurity Q BPCRS*.
(4) 0.012% w/v of *salbutamol for peak identification EPCRS*.
(5) 0.012% w/v of *salbutamol impurity standard BPCRS*.
(6) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *base-deactivated end-capped octylsilyl silica gel for chromatography* (3 µm) (Hypersil BDS C8 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 273 nm.
(f) Inject 50 µL of each solution.

MOBILE PHASE

Mobile phase A 0.5 volumes of *triethylamine* and 1000 volumes of 0.025M *sodium dihydrogen orthophosphate*, adjusted to pH 3.0 with 10% v/v of *orthophosphoric acid*.

Mobile phase B 350 volumes of *methanol* and 650 volumes of *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-5	95	5	isocratic
5-18	95→70	5→30	linear gradient
18-20	70	30	isocratic
20-20.1	70→10	30→90	linear gradient
20.1-25	10	90	isocratic
25-25.1	10→95	90→5	linear gradient
25.1-33	95	5	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (3), the *peak-to-valley ratio* is at least 6.0, where *Hp* is the height above the baseline of the peak due to impurity J and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to salbutamol;

in the chromatogram obtained with solution (6), the *signal-to-noise ratio* for the peak due to salbutamol is at least 20.

CALCULATION OF IMPURITIES

For impurities J and Q, use the concentration of each impurity in solution (3).

For all other impurities, use the concentration of salbutamol in solution (2).

For the reporting threshold, use the concentration of salbutamol in solution (6). For impurity N, apply the reporting threshold to the sum of impurity N peaks 1 and 2.

For peak identification, use solutions (3), (4) and (5).

Salbutamol retention time: about 8 minutes.

Relative retention: impurity J, about 0.95; impurity Q, about 1.4; impurity D, about 1.7; impurity N (peak 1), about 1.77; impurity N (peak 2), about 1.79; impurity F, about 1.9.

Correction factors: impurity D, multiply by 1.5.

LIMITS

— impurity D: not more than 1.0%;

— impurity J: not more than 0.5%;

— impurity F: not more than 0.3%;

— impurities N (sum of peaks 1 and 2) and Q: for each impurity, not more than 0.2%;

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

— total impurities: not more than 2.5%;

— reporting threshold: 0.1%.

ASSAY

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

(1) Dilute the injection to produce a solution containing the equivalent of 0.0025% w/v of salbutamol.
(2) 0.003% w/v of *salbutamol sulfate BPCRS*.
(3) 0.003% w/v of *salbutamol sulfate BPCRS* and 0.0025% w/v of *2-tert-butylamino-1-(4-hydroxy-3-methylphenyl)ethanol BPCRS* (impurity C).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *cyanosilyl silica gel for chromatography* (5µm) (Spherisorb CN is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 276 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

5 volumes of *propan-2-ol*, 30 volumes of 0.05M *ammonium acetate* and 65 volumes of *water*, adjusted to pH 4.5 with *glacial acetic acid*.

When the chromatograms are recorded under the prescribed conditions, the retention time of salbutamol is about 2 minutes.

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 C is at least 1.5.

DETERMINATION OF CONTENT

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

STORAGE

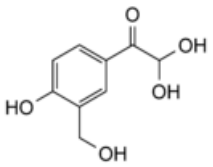
Salbutamol Injection should be protected from light.

LABELLING

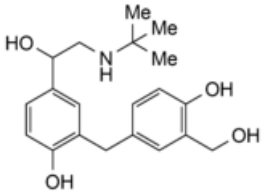
The quantity of active ingredient is stated in terms of the equivalent amount of salbutamol.

IMPURITIES

The impurities limited by the requirements of this monograph include impurity C, D, F, J, K, M, N, O and Q listed under Salbutamol Sulfate and:



1. 2,2-dihydroxy-1-[4-hydroxy-3-(hydroxymethyl)phenyl]ethanone (glyoxal impurity)



2. 2-[4-hydroxy-3-(hydroxymethyl)benzyl]-4-{1-hydroxy-2-[(2-methyl-2-propanyl)amino]ethyl}phenol (head-to-tail dimer impurity).