



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

Salbutamol Nebuliser Solution

[General Notices](#)

Action and use

Beta₂-adrenoceptor agonist; bronchodilator.

DEFINITION

Salbutamol Nebuliser Solution is a solution of [Salbutamol Sulfate](#) in a suitable vehicle, intended to be converted into aerosols by a nebuliser.

The nebuliser solution complies with the requirements stated under [Preparations for Inhalation](#) and with the following requirements.

Content of salbutamol, C₁₃H₂₁NO₃

95.0 to 105.0% of the stated amount.

IDENTIFICATION

- A. Dilute the solution being examined with sufficient 0.1M [hydrochloric acid](#) to produce a solution containing the equivalent of 0.008% w/v of salbutamol. The [light absorption](#) of the resulting solution, [Appendix II B](#), in the range 230 nm to 350 nm exhibits a maximum only at 276 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 peak in the chromatogram obtained with solution (2).
- C. Dilute the solution being examined with sufficient [water](#) to produce a solution containing the equivalent of 0.025% w/v of salbutamol. The resulting solution yields reaction A characteristic of [sulfates](#), [Appendix VI](#).

TESTS

Acidity

pH, 3.0 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 a quantity of the nebuliser solution to produce a solution containing the equivalent of 0.015% w/v of salbutamol and mix with the aid of ultrasound.
- (2) Dilute 1 volume of solution (1) to 50 volumes and further dilute 1 volume to 10 volumes.
- (3) 0.018% w/v of [salbutamol sulfate BPCRS](#), 0.000075% w/v of [salbutamol ketone BPCRS](#) (impurity J) and 0.00003% w/v of [salbutamol impurity Q BPCRS](#).
- (4) 0.018% w/v of [salbutamol for peak identification EPCRS](#).

(5) 0.018% w/v of [salbutamol impurity standard BPCRS](#).

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](#), adjust 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 *H_p* is the height above the baseline of the peak due to impurity J and *H_v* 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 (2), the [signal-to-noise ratio](#) for the peak due to salbutamol is at least 30.

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 (2). 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 1, about 0.6; impurity 3, about 0.8; 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; impurity 2, about 2.2.

Correction factors: impurity D, multiply by 1.5.

LIMITS

- impurities D, F and J: for each impurity, not more than 0.5%;
- impurity 1: not more than 0.4%;
- impurities N (sum of peaks 1 and 2), 2 and 3: for each impurity, not more than 0.3%;

- impurity Q: not more than 0.2%;
- unspecified impurities: for each impurity, not more than 0.2%;
- total impurities: not more than 2.0%;
- reporting threshold: 0.1%.

ASSAY

Carry out the method for [liquid chromatography, Appendix III D](#), using the following solutions prepared in [water](#).

- (1) Dilute a volume of the nebuliser solution to produce a solution containing the equivalent of 0.05% w/v of salbutamol.
- (2) 0.06% w/v of [salbutamol sulfate BPCRS](#).
- (3) 0.06% w/v of [salbutamol sulfate BPCRS](#) and 0.04% w/v of [2-tert-butylamino-1-\(4-hydroxy-3-methylphenyl\)ethanol BPCRS](#) (impurity C).

CHROMATOGRAPHIC CONDITIONS

- Use a stainless steel column (20 cm × 5 mm) packed with [cyanosilyl silica gel for chromatography](#) (5 µm) (Spherisorb CN is suitable).
- Use isocratic elution and the mobile phase described below.
- Use a flow rate of 2 mL per minute.
- Use an ambient column temperature.
- Use a detection wavelength of 276 nm.
- Inject 10 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 [dilute 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;

in the chromatogram obtained with solution (2), the [symmetry factor](#) for the peak due to salbutamol is within 0.8 to 2.8.

DETERMINATION OF CONTENT

Calculate the content of $C_{13}H_{21}NO_3$ in the nebuliser solution from the chromatograms obtained and using the declared content of $C_{13}H_{21}NO_3$ in [salbutamol sulfate BPCRS](#).

STORAGE

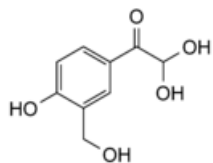
Salbutamol Nebuliser Solution should be protected from light.

LABELLING

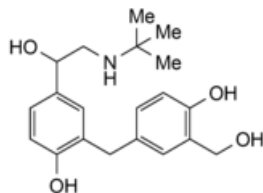
The quantity of active ingredient is stated in terms of the equivalent amount of salbutamol.

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)

3. salbutamol-benzalkonium chloride adduct, unknown structure.