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

Salbutamol Oral Solution

General Notices

Action and use

Beta$_2$-adrenoceptor agonist; bronchodilator.

DEFINITION

Salbutamol Oral Solution is a solution of Salbutamol Sulfate in a suitable flavoured vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements.

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

95.0 to 105.0% of the stated amount.

IDENTIFICATION

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).

TESTS

Acidity

pH, 3.3 to 4.0, 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 volume of the oral solution to produce a solution containing the equivalent of 0.01% w/v of salbutamol.
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) 0.012% w/v of *salbutamol sulfate BPCRS*, 0.00005% w/v each of *salbutamol ketone BPCRS* (impurity J) and *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 *octylsilyl silica gel for chromatography* (3 µm) (Luna C-8 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate as described below.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 225 nm.
(f) Inject 40 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 35 volumes of *methanol* and 65 volumes of *acetonitrile*.

Time (Minutes)	Flow rate (mL/min)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-5	1.0	95	5	isocratic
5-10	1.0	95→90	5→10	linear gradient
10-25	1.0→1.5	90	10	isocratic
25-45	1.5	90	10	isocratic
45-45.1	1.5	90→10	10→90	linear gradient
45.1-47.0	1.5	10	90	isocratic
47.0-47.1	1.5	10→95	90→5	linear gradient
47.1-55.0	1.5	95	5	re-equilibration
55.0-55.1	1.5→1.0	95	5	re-equilibration
55.1-60.0	1.0	95	5	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity J and salbutamol is at least 1.2;

in the chromatogram obtained with solution (6), the *signal-to-noise ratio* for the peak due to salbutamol is at least 30.

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 (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 0.9; impurity Q, about 1.7; impurity D, about 2.4; impurity N (peak 1), about 3.1; impurity N (peak 2), about 3.2; impurity O, about 3.3 and impurity F, about 3.8.

Correction factors: impurity F, multiply by 0.3; impurity N, multiply by 0.6; impurity O, multiply by 0.3; impurity Q, multiply by 2.4.

LIMITS

— impurities D and F: for each impurity, not more than 0.6%;

— impurities J, N (sum of peaks 1 and 2), O and Q: for each impurity, 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%.

ASSAY

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

(1) Dilute a weighed amount of the oral solution to produce a solution containing the equivalent of 0.01% w/v of salbutamol.
(2) 0.012% w/v of *salbutamol sulfate BPCRS*.
(3) 0.012% w/v of *salbutamol sulfate BPCRS* and 0.00005% w/v of *salbutamol ketone BPCRS* (impurity J).

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity J and salbutamol is at least 1.2.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral solution, Appendix V G, and calculate the content of $C_{13}H_{21}NO_3$, weight in volume, using the declared content of $C_{13}H_{21}NO_3$ in *salbutamol sulfate BPCRS*.

STORAGE

Salbutamol Oral 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, I, J, K, M, N, O and Q listed under Salbutamol Sulfate.