Status: Not Yet Official on 17-Feb-2025
Official Date: 01-May-2026
Document Type: USP Monographs
DocId: GUID-8D7D89F9-25A8-4B43-AF49-5CDC4E68A4BA_5_en-US
DOI: https://doi.org/10.31003/USPNF_M1214_05_01
DOI Ref: s3t9e

Add the following:

▲Albuterol Inhalation Solution

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-albuterol-inhalation-sol-20250131.

DEFINITION

Albuterol Inhalation Solution is an isotonic sterile solution of albuterol sulfate. It may contain chelating agents, isotonicity agents, and pH adjusting agents. It contains NLT 90.0% and NMT 110.0% of the labeled amount of albuterol ($C_{13}H_{21}NO_3$) as albuterol sulfate.

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Solution A: 3.4 g/L of monobasic potassium phosphate and 1.1 g/L of sodium 1-heptanesulfonate in water. Adjust with phosphoric acid to a pH of 2.1.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	85	15
6	60	40
7.5	60	40
7.6	85	15
11.5	85	15

Diluent: 0.01 N hydrochloric acid

Standard solution: 0.1 mg/mL of USP Albuterol Sulfate RS (equivalent to 0.08 mg/mL of albuterol) in *Diluent*

Sample solution: Nominally 0.08 mg/mL of albuterol diluted with *Diluent* from a suitable volume of Inhalation Solution

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 210 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 2.6-µm packing L1

Column temperature: 37°

Flow rate: 0.75 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.7

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of albuterol ($C_{13}H_{21}NO_3$) in the portion of Inhalation Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times M \times 100$$

r_U = peak response of albuterol from the *Sample solution*

r_S = peak response of albuterol from the *Standard solution*

C_S = concentration of USP Albuterol Sulfate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of albuterol in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of albuterol, 239.31

M_{r2} = molecular weight of albuterol sulfate, 576.70

M = number of moles of albuterol per mole of albuterol sulfate, 2

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

IMPURITIES

• **Organic Impurities**

Solution A: 3.4 g/L of monobasic potassium phosphate and 1.1 g/L of sodium 1-heptanesulfonate in water. Adjust with phosphoric acid to a pH of 2.1.

Solution B: Acetonitrile

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	95	5
2.5	92.5	7.5
5	85	15
18	80.5	19.5
26	64	36
26.5	50	50
27.5	50	50
27.6	95	5
34	95	5

Diluent: 0.01 N hydrochloric acid

System suitability solution: 0.05 mg/mL each of USP Albuterol Sulfate RS, USP Albuterol Related Compound I RS, and USP Levalbuterol Related Compound H RS in *Diluent*

Standard solution: 1.25 µg/mL each of USP Albuterol Sulfate RS and USP Levalbuterol Related Compound D RS in *Diluent*

Sample solution: Nominally 200–800 µg/mL of albuterol diluted with *Diluent* from a suitable volume of Inhalation Solution

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 210 nm

Column: 2.1-mm × 15-cm; 1.7-µm packing L1

Temperatures

Autosampler: 10°

Column: 37°

Flow rate: 0.35 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—See *Table 3* for relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between albuterol and albuterol related compound I; NLT 2.0 between albuterol related compound I and levalbuterol related compound H, *System suitability solution*

Tailing factor: NMT 2.0 for albuterol and levalbuterol related compound D, *Standard solution*

Relative standard deviation: NMT 5.0% for albuterol and levalbuterol related compound D, *Standard solution*

Signal-to-noise ratio: NLT 10 for levalbuterol related compound D and albuterol, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of levalbuterol related compound D in the portion of Inhalation Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of levalbuterol related compound D from the *Sample solution*

r_S = peak response of levalbuterol related compound D from the *Standard solution*

C_S = concentration of USP Levalbuterol Related Compound D RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of albuterol in the *Sample solution* (µg/mL)

Calculate the percentage of any individual unspecified degradation product in the portion of Inhalation Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times M \times 100$$

r_U = peak response of any individual unspecified degradation product from the *Sample solution*

r_S = peak response of albuterol from the *Standard solution*

C_S = concentration of USP Albuterol Sulfate RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of albuterol in the *Sample solution* (µg/mL)

M_{r1} = molecular weight of albuterol, 239.31

M_{r2} = molecular weight of albuterol sulfate, 576.70

M = number of moles of albuterol per mole of albuterol sulfate, 2

Acceptance criteria: See *Table 3*. The reporting threshold is 0.05%.

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Albuterol	1.0	—
Albuterol related compound I[a]	1.12	—
Levalbuterol related compound H	1.17	—
Albuterol related compound A[a,b]	1.46	—
Levalbuterol related compound D	1.72	0.1
Deshydroxy albuterol[a,c]	1.79	—
N-Benzyl albuterol[a,d]	2.08	—
N-Benzyl albuterone[a,e]	2.35	—
Albuterol related compound E[a,f]	2.77	—
Levalbuterol related compound F[a,g]	3.27	—
Any individual unspecified degradation product	—	0.1
Total degradation products	—	1.0

[a] Process impurity controlled in the drug substance. Not included in total degradation products.

[b] 4-{2-[(1,1-Dimethylethyl)amino]-1-hydroxyethyl}-2-methylphenol.

[c] 4-[2-(*tert*-Butylamino)ethyl]-2-methylphenol.

[d] (1*RS*)-2-[Benzyl(1,1-dimethylethyl)amino]-1-[4-hydroxy-3-(hydroxymethyl)phenyl]ethanol.

[e] 2-[Benzyl(1,1-dimethylethyl)amino]-1-[4-hydroxy-3-(hydroxymethyl)phenyl]ethanone.

[f] 2,2'-Oxybis(methylene)bis{4-[2-(*tert*-butylamino)-1-hydroxyethyl]phenol}diacetate.

[g] 1-[4-(Benzyloxy)-3-(hydroxymethyl)phenyl]-2-(*tert*-butylamino)ethanol.

SPECIFIC TESTS

- **Sterility Tests ⟨71⟩:** Meets the requirements
- **pH ⟨791⟩:** 3.0–5.0
- **Particulate Matter in Injections ⟨788⟩,** *Method 1 Light Obscuration Particle Count Test*
  Sample: Pool the contents of NLT 10 units.
  Acceptance criteria: See *Table 4*.

Table 4

Particle Size (µm)	Limit NMT (particles/container)
≥10	6000
≥25	600

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Protect from light. Store in a pouch until the time of use. Store at controlled room temperature.
- **USP Reference Standards ⟨11⟩**

USP Albuterol Related Compound I RS

4-[2-(*tert*-Butylamino)-1-hydroxyethyl]phenol.

$C_{12}H_{19}NO_2$ 209.28

USP Albuterol Sulfate RS

USP Levalbuterol Related Compound D RS

5-[2-{(1,1-Dimethylethyl)amino}-1-hydroxyethyl]-2-hydroxy-benzaldehyde sulfate.

$(C_{13}H_{19}NO_3)_2 \cdot H_2SO_4$ 572.67

USP Levalbuterol Related Compound H RS

4-[2-(*tert*-Butylamino)-1-methoxyethyl]-2-(hydroxymethyl)phenol acetate.

$C_{14}H_{23}NO_3 \cdot C_2H_4O_2$ 313.39▲ (RB 1-May-2026)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
ALBUTEROL INHALATION SOLUTION	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(3)

Current DocID: GUID-8D7D89F9-25A8-4B43-AF49-5CDC4E68A4BA_5_en-US

DOI: https://doi.org/10.31003/USPNF_M1214_05_01

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