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# Ipratropium Bromide and Albuterol Sulfate Inhalation Solution

**DEFINITION**

Ipratropium Bromide and Albuterol Sulfate Inhalation Solution is an isotonic sterile solution of ipratropium bromide and 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 ipratropium bromide ( $C_{20}H_{30}BrNO_3$ ) and albuterol ( $C_{13}H_{21}NO_3$ ) as albuterol sulfate.

**IDENTIFICATION**

- A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.
- B.** The UV spectra of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

**ASSAY**

*Change to read:*

**PROCEDURE**

**Buffer:** 2.7 g/L of [monobasic potassium phosphate](#) in [water](#)  
**Solution A:** [Acetonitrile](#) and *Buffer* (5:95). [NOTE—The pH of the solution is about 4.7.]  
**Solution B:** [Acetonitrile](#) and *Buffer* (40:60). [NOTE—The pH of the solution is about 5.4.]  
**Mobile phase:** See [Table 1](#).

Table 1

| Time<br>(min) | Solution A<br>(%) | Solution B<br>(%) |
|---------------|-------------------|-------------------|
| 0             | 100               | 0                 |
| 3             | 100               | 0                 |
| 30            | 50                | 50                |
| 35            | 100               | 0                 |
| 40            | 100               | 0                 |

**System suitability solution:** 0.1 mg/mL of [USP Ipratropium Bromide RS](#), 0.5 mg/mL of [USP Albuterol Sulfate RS](#), and 0.05 mg/mL each of [USP Ipratropium Bromide Related Compound B RS](#) and [USP Ipratropium Bromide Related Compound C RS](#) in [water](#)  
**Standard solution:** 0.04 mg/mL of [USP Ipratropium Bromide RS](#) and 0.25 mg/mL of [USP Albuterol Sulfate RS](#) in [water](#)  
**Sample solution:** Nominally 0.04 mg/mL of ipratropium bromide and 0.25 mg/mL of albuterol sulfate from the pooled contents of NLT 20 vials of Inhalation Solution prepared as follows. Transfer a suitable volume of the pooled composite Inhalation Solution to a suitable volumetric flask. Dilute with [water](#) to obtain the final nominal concentration.

**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 200–300 nm.  
**Column:** 4.6-mm × 15-cm; 5-µm packing [L7](#)  
**Column temperature:** 15°  
**Flow rate:** 1 mL/min  
**Injection volume:** 20 µL

**System suitability**

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

[NOTE—The relative retention times for the components relative to ipratropium are shown in [Table 2](#).]

Table 2

| Component                      | Relative Retention Time |
|--------------------------------|-------------------------|
| Albuterol                      | 0.3                     |
| Ipratropium related compound C | 0.7                     |
| Ipratropium                    | 1.0                     |
| Ipratropium related compound B | 1.05                    |

**Suitability requirements**

**Resolution:** NLT 2.0 between ipratropium and ipratropium related compound B, *System suitability solution*

**Tailing factor:** NMT 2.0 for ▲albuterol and ipratropium, ▲ (USP 1-May-2021) *Standard solution*

**Relative standard deviation:** NMT 1.0% for ▲albuterol and ipratropium, ▲ (USP 1-May-2021) *Standard solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ipratropium bromide ( $C_{20}H_{30}BrNO_3$ ) 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 ipratropium from the *Sample solution*

$r_S$  = peak response of ipratropium from the *Standard solution*

$C_S$  = concentration of [USP Ipratropium Bromide RS](#) in the *Standard solution* (mg/mL)

$C_U$  = nominal concentration of ipratropium bromide in the *Sample solution* (mg/mL)

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

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

$r_U$  = 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

$N$  = number of moles of albuterol per mole of albuterol sulfate, 2

**Acceptance criteria**

**Ipratropium bromide:** 90.0%–110.0%

**Albuterol:** 90.0%–110.0%

**PERFORMANCE TESTS**

- [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meets the requirements

**IMPURITIES**

**Change to read:**

- **ORGANIC IMPURITIES**

**Solution A:** Dissolve 2.7 g of [monobasic potassium phosphate](#) in 1 L of [water](#). Adjust with [phosphoric acid](#) to a pH of 3.9.

**Solution B:** [Acetonitrile](#)

**Mobile phase:** See [Table 3](#).

**Table 3**