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Ipratropium Bromide Inhalation Solution

DEFINITION

Ipratropium Bromide Inhalation Solution is an isotonic sterile solution of ipratropium bromide monohydrate ($C_{20}H_{30}BrNO_3 \cdot H_2O$). It may contain isotonicity agents and pH-adjusting agents. It contains NLT 90.0% and NMT 110.0% of the labeled amount of ipratropium bromide ($C_{20}H_{30}BrNO_3$).

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.
- Protect solutions containing ipratropium bromide from light.

ASSAY

• **PROCEDURE**

Phosphate solution: Dissolve 8.9 g of [dibasic sodium phosphate dihydrate](#) in 100 mL of [water](#).

Buffer: Dissolve 14.3 g of [monobasic sodium phosphate dihydrate](#) and 2 g of [tetrapropylammonium chloride](#) in 1 L of [water](#). Adjust with *Phosphate solution* to a pH of 5.5.

Solution A: *Buffer*

Solution B: [Methanol](#)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	87	13
7.0	87	13
7.1	10	90
9.0	10	90
9.1	87	13
12.0	87	13

Diluent: [Methanol](#) and *Buffer* (13:87)

System suitability solution: 0.1 mg/mL each of [USP Ipratropium Bromide RS](#) and [USP Ipratropium Bromide Related Compound C RS](#) in *Diluent*. Sonicate to dissolve.

Standard solution: 0.1 mg/mL of [USP Ipratropium Bromide RS](#) in *Diluent*. Sonicate to dissolve.

Sample solution: Nominally 0.1 mg/mL of ipratropium bromide from Inhalation Solution prepared as follows. Pool the contents from NLT 8 vials of Inhalation Solution. Transfer a suitable volume of the pooled Inhalation Solution to a suitable volumetric flask and dilute with *Diluent* to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 220 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 3.9-mm × 15-cm; 4-μm packing [L1](#)

Column temperature: 30°

Flow rate: 2 mL/min

Injection volume: 25 μL

System suitability

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

[NOTE—The relative retention times for ipratropium bromide related compound C and ipratropium are 0.65 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.5 between ipratropium bromide related compound C and ipratropium, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 1.0%, *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)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

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

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**

Buffer: 13.6 g/L of [monobasic potassium phosphate](#) in [water](#). Adjust with [10% phosphoric acid](#) to a pH of 4.0.

Solution A: [Acetonitrile](#) and *Buffer* (5:95)

Solution B: [Acetonitrile](#) and *Buffer* (30:70)

Mobile phase: See [Table 2](#).

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	82	18
5.0	82	18
19.0	77	23
34.0	77	23
37.0	73	27
46.0	67	33
48.0	67	33
59.0	50	50
68.0	0	100
74.0	0	100
74.1	82	18
85.0	82	18

Diluent: [Acetonitrile](#) and [water](#) (5:95)

System suitability solution: 10 µg/mL of [USP Ipratropium Bromide RS](#) and 1 µg/mL each of [USP Ipratropium Bromide Related Compound B RS](#) and [USP Ipratropium Bromide Related Compound C RS](#) in *Diluent*

Sensitivity solution: 0.1 µg/mL of [USP Ipratropium Bromide RS](#) in *Diluent*