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# Ipratropium Nebuliser Solution

General Notices

*Details for the public consultation of this monograph are as follows:*

| EAG/Panel/Working Party | Medicinal Chemicals 2 |
|---|---|
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| **Deadline for Comment** | 30th September 2026 |
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| **Notes** | Revised monograph<br>If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.<br>**Content** Revised expression of content. Please note that this amendment does not require a labeling change for established products. Tightening of the upper content limits.<br>**Identification** HPLC-DAD method introduced, harmonised with Assay .<br>**Related substances and named impurity** Inclusion of relative retention times, quantitative limits introduced .<br>**Labelling** Included that the active ingredient is stated in terms of equivalent amount of anhydrous ipratropium bromide.<br>**Impurities** Correction of impurities controlled in the related substances test. |



**Action and use**

Anticholinergic (antimuscarinic) bronchodilator.

## DEFINITION

Ipratropium Nebuliser Solution is a solution of Ipratropium Bromide 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 anhydrous ipratropium bromide, $C_{20}H_{30}NO_3Br$**

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, 3.0 to 4.0, Appendix V L.

### Related substances

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

(1) Dilute a quantity of the nebuliser solution, if necessary, with sufficient 0.001M *hydrochloric acid* to produce a solution containing the equivalent of 0.02% w/v of anhydrous ipratropium bromide.
(2) Dilute 1 volume of solution (1) to 200 volumes with 0.001M *hydrochloric acid*.
(3) 0.005% w/v of *ipratropium bromide impurity B EPCRS* and 0.005% w/v of *ipratropium bromide BPCRS* in 0.001M *hydrochloric acid*.
(4) Dilute 1 volume of solution (2) to 5 volumes with 0.001M *hydrochloric acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4.6 mm) packed with *octylsilyl silica gel for chromatography* (5 µm) (Columbus C8 is suitable).
(b) Use isocratic elution using the mobile phase described below.
(c) Use a flow rate of 0.5 mL per minute.
(d) Use an ambient column temperature.
(e) Detection wavelength of 210 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for 6 times the retention time of ipratropium.

MOBILE PHASE

A mixture of 4 volumes of freshly distilled *triethylamine*, 50 volumes of *propan-2-ol R1*, 100 volumes of *acetonitrile R1* and 850 volumes of a 0.1% w/v solution of *sodium methanesulfonate*. Adjust the pH of the mixture to 3.0 with *orthophosphoric acid*.

SYSTEM SUITABILITY

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

CALCULATION OF IMPURITIES

For each impurity, use the concentration of anhydrous ipratropium bromide in solution (2).

For the reporting threshold, use the concentration of anhydrous ipratropium bromide in solution (4).

For peak identification, use solution (3).

Ipratropium retention time: about 11 minutes.

Relative retentions: impurity B, about 1.1; impurity D, about 1.4; impurity C, about 2.1; impurity F, about 4.5.

LIMITS

— unspecified impurities: for each impurity, not more than 0.5%;

— total impurities: not more than 1.5%;

— reporting threshold: 0.1%.

## ASSAY

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

(1) Dilute a quantity of the nebuliser solution, if necessary, with sufficient 0.001M *hydrochloric acid* to produce a solution containing the equivalent of 0.02% w/v of anhydrous ipratropium bromide.
(2) 0.0209% w/v of *ipratropium bromide BPCRS* in 0.001M *hydrochloric acid*.
(3) 0.005% w/v of *ipratropium bromide impurity B EPCRS* and 0.005% w/v of *ipratropium bromide BPCRS* in 0.001M *hydrochloric acid*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic procedure 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 ipratropium and impurity B is at least 1.2.

DETERMINATION OF CONTENT

Calculate the content of $C_{20}H_{30}NO_3$ in the solution using the declared content of $C_{20}H_{30}NO_3Br,H_2O$ in *ipratropium bromide BPCRS*. Each mg of $C_{20}H_{30}BrNO_3,H_2O$ is equivalent to 0.9581 mg of $C_{20}H_{30}BrNO_3$.

## STORAGE

Ipratropium Nebuliser Solution should be stored protected from light in a sealed container.

## LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of anhydrous ipratropium bromide.

## IMPURITIES

The impurities limited by the requirements of this monograph include B, C, D and F listed under Ipratropium Bromide.