

**IPRATROPIUM BROMIDE 250MCG/1ML NEBULISER SOLUTION
IPRATROPIUM BROMIDE 500MCG/2ML NEBULISER SOLUTION
PL 18023/0011**

UKPAR

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LAY SUMMARY

The UK granted a marketing authorisation for the medicinal product Ipratropium Bromide 250mcg/1ml Nebuliser Solution, Ipratropium Bromide 500mcg/2ml Nebuliser Solution (PL 18023/0011) to Breath Limited on 23rd February 2010. The product is available as a prescription only medicine (POM) to make breathing easier in patients with asthma and other breathing difficulties, such as chronic obstructive pulmonary disease. Ipratropium Bromide Nebuliser Solution can be used at the same time as medicines called beta₂-agonist bronchodilators ('relievers'), for example salbutamol.

The active ingredient ipratropium bromide belongs to a group of medicines called "bronchodilators", which help to open up the air passages in your lungs so that you can breathe more easily.

This application is a duplicate of a previously granted application for Ipratropium Bromide 250mcg/1ml Nebuliser Solution (PL 18023/0003), approved on 21st August 2000 to the marketing authorisation holder Breath Limited.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Ipratropium Bromide 250mcg/1ml Nebuliser Solution, Ipratropium Bromide 500mcg/2ml Nebuliser Solution outweigh the risks, hence a Marketing Authorisation has been granted.

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PL 18023/0011**

SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted a marketing authorisation for the medicinal product Ipratropium Bromide 250mcg/1ml Nebuliser Solution, Ipratropium Bromide 500mcg/2ml Nebuliser Solution (PL 18023/0011) to Breath Limited on 23rd February 2010. The product, available as a prescription only medicine (POM), is indicated for the treatment of reversible bronchospasm associated with chronic obstructive pulmonary disease (COPD). It is also indicated, when used concomitantly with inhaled beta₂-agonists, for treatment of reversible airways obstruction as in acute and chronic asthma.

The application was submitted as a simple abridged application according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, cross-referring to Ipratropium Bromide 250mcg/1ml Nebuliser Solution (PL 18023/0003), approved on 21st August 2000 to the marketing authorisation holder Breath Limited.

No new data was submitted nor was it necessary for this simple application, as the data are identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no PAR was generated for it.

Ipratropium bromide is an anticholinergic medicine, which blocks muscarinic cholinergic receptors in smooth muscle of the bronchi of the lungs. This opens the bronchi and provides relief in chronic obstructive pulmonary disease

PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 18023/0011

PROPRIETARY NAME: Ipratropium Bromide 250mcg/1ml Nebuliser Solution,
Ipratropium Bromide 500mcg/2ml Nebuliser Solution

ACTIVE(S): Ipratropium bromide

COMPANY NAME: Breath Limited

E.C. ARTICLE: Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC

LEGAL STATUS: POM

1. INTRODUCTION

This is a simple, piggy back application for Ipratropium Bromide 250mcg/1ml Nebuliser Solution, Ipratropium Bromide 500mcg/2ml Nebuliser Solution submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Breath Limited, Unit 2, Eastman Way, Stevenage, Hertfordshire, SG1 4SZ, UK.

The application cross-refers to Ipratropium Bromide 250mcg/1ml Nebuliser Solution (PL 18023/0003), approved on 21st August 2000 to the marketing authorisation holder Breath Limited. The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed names of the product are Ipratropium Bromide 250mcg/1ml Nebuliser Solution and Ipratropium Bromide 500mcg/2ml Nebuliser Solution. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

The product contains ipratropium bromide, equivalent to 250micrograms per millilitre. It is to be stored in sterile polyethylene ampoules, containing either 1ml or 2ml solution. Ampoules in strips of 10 are overwrapped in aluminium foil and packed into cartons of 20 or 60 ampoules. The proposed shelf-life (36 months) and storage conditions (Do not store above 25°C. Store in the original package. The ampoule should be opened immediately before use and any solution remaining after use should be discarded) are consistent with the details registered for the cross-reference product.

2.3 Legal status

On approval, the products will be available as prescription-only medicines (POM).

2.4 Marketing authorisation holder/Contact Persons/Company

Breath Limited, Unit 2, Eastman Way, Stevenage, Hertfordshire, SG1 4SZ, UK.

The QP responsible for pharmacovigilance is stated and her CV is included.

2.5 Manufacturers

The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of GMP compliance has been provided.

2.6 Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process

The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specification

The proposed finished product specification is in line with the details registered for the cross-reference product.

2.9 Drug substance specification

The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance

No materials of animal or human origin are included in the product. This is consistent with the cross reference product.

3. EXPERT REPORTS

The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts' CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4. PRODUCT NAME & APPEARANCE

See 2.1 for details of the proposed product names. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS

The proposed summary is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET/CARTON

PIL

The patient information leaflet has been prepared in-line with the details registered for the cross-reference product.

Carton and blister

The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS

The data submitted with the application are acceptable. A Marketing Authorisation should be granted.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.

CLINICAL ASSESSMENT

As this is a duplicate application, no new clinical data have been supplied and none are required.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The data for this application are consistent with that previously assessed for the cross-reference product and as such have been judged to be satisfactory.

PRECLINICAL

No new preclinical data were submitted and none are required for an application of this type.

EFFICACY

This application is identical to a previously granted application for Ipratropium Bromide 250mcg/1ml Nebuliser Solution (PL 18023/0003).

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. Extensive clinical experience with ipratropium bromide is considered to have demonstrated the therapeutic value of the compound. The risk:benefit is, therefore, considered to be positive.

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STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation application on 29 th May 2009.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 9 th June 2009.
3	Following assessment of the application the MHRA requested further information on 14 th August 2009.
4	The applicant responded to the MHRA's requests, providing further information on 4 th November 2009
5	The application was determined on 23 rd February 2010

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STEPS TAKEN AFTER ASSESSMENT

Date submitted	Application type	Scope	Outcome

**IPRATROPIUM BROMIDE 250MCG/1ML NEBULISER SOLUTION
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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ipratropium Bromide 250 micrograms/1ml Nebuliser Solution
Ipratropium Bromide 500 micrograms/2ml Nebuliser Solution.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ampoule contains ipratropium bromide at 250 micrograms/1ml i.e. 250 micrograms in 1ml and 500 micrograms in 2ml.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Nebuliser Solution.
A clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ipratropium bromide is indicated for the treatment of reversible bronchospasm associated with chronic obstructive pulmonary disease (COPD).

Ipratropium bromide is indicated, when used concomitantly with inhaled beta₂-agonists, for treatment of reversible airways obstruction as in acute and chronic asthma.

4.2 Posology and method of administration

This medicinal product is for inhalation use only.

The dosage should be adapted to the individual needs of the patient. In children aged 12 years and under, only Ipratropium Bromide Nebuliser Solution 1 ml should be used. The following doses are recommended:

Adults (including the elderly) and children over 12 years of age:

250 - 500 micrograms (i.e. one vial of 250 micrograms in 1 ml or one vial of 500 micrograms in 2ml) 3 to 4 times daily. The exact starting dose may vary depending on local guidelines.

For treatment of acute bronchospasm, 500 micrograms.

Repeated doses can be administered until the patient is stable. The time interval between the doses may be determined by the physician.

It is advisable not to exceed the recommended daily dose during either acute or maintenance treatment. Daily doses exceeding 2 mg in adults and children over 12 years of age should only be given under medical supervision.

Children 6 - 12 years of age:

250 micrograms (i.e. one vial of 250 micrograms in 1ml) up to a total daily dose of 1mg (4 vials). The time interval between doses may be determined by the physician.

Children 0 – 5 years of age (for treatment of acute asthma only):

125 – 250 micrograms (i.e. half to one vial of 250 micrograms in 1ml) up to a total daily dose of 1 mg (4 vials).

Ipratropium bromide should be administered no more frequently than 6 hourly in children under 5 years of age.

For acute bronchospasm, repeated doses may be administered until the patient is stable.

If therapy does not produce a significant improvement or if the patient's condition gets worse, medical advice must be sought. In the case of acute or rapidly worsening dyspnoea (difficulty in breathing) a doctor should be consulted immediately.

Ipratropium bromide may be combined with a short-acting beta₂-agonist in the same nebuliser chamber, for simultaneous administration where co-administration is required, in line with local prescribing guidelines. The solution should be used as soon as possible after mixing and any unused solution should be discarded.

Ipratropium bromide can be administered using a range of commercially available nebulising devices. The dose of nebuliser solution may need to be diluted according to local prescribing guidelines and in order to obtain a final volume suitable for the particular nebuliser being used (usually 2 – 4 ml); if dilution is necessary use only sterile sodium chloride 0.9% solution.

4.3 Contraindications

Known hypersensitivity to atropine or ipratropium bromide.

4.4 Special warnings and precautions for use

Use of the nebuliser solution should be subject to close medical supervision during initial dosing.

Caution is advocated in the use of anticholinergic agents in patients with narrow-angle glaucoma, or with prostatic hyperplasia or bladder-outflow obstruction.

As patients with cystic fibrosis may be prone to gastro-intestinal motility disturbances, ipratropium bromide, as with other anticholinergics, should be used with caution in these patients.

Immediate hypersensitivity reactions following the use of ipratropium bromide have been demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, oropharyngeal oedema and anaphylaxis.

There have been isolated reports of ocular complications (i.e. mydriasis, increased intra-ocular pressure, narrow-angle glaucoma, eye pain) when aerosolised ipratropium bromide, either alone or in combination with an adrenergic beta₂-agonist, has come into contact with the eyes during nebuliser therapy.

Eye pain or discomfort, blurred vision, visual halos or coloured images in association with red eyes from conjunctival congestion and corneal oedema may be signs of acute narrow-angle glaucoma. Should any combination of these symptoms develop, treatment with miotic drops should be initiated and specialist advice sought immediately.

Patients must be instructed in the correct administration of ipratropium bromide. Care must be taken not to allow the solution or mist to enter the eyes. It is recommended that the nebulised solution is administered via a mouthpiece. If this is not available and a nebuliser mask is used, it must fit properly. Patients who may be predisposed to glaucoma should be warned specifically to protect their eyes.

4.5 Interaction with other medicinal products and other forms of interaction

There is evidence that the administration of ipratropium bromide with beta-adrenergic drugs and xanthine preparations may produce an additive bronchodilatory effect.

The risk of acute glaucoma in patients with a history of narrow-angle glaucoma (see Special Warnings and Precautions for Use) may be increased when nebulised ipratropium bromide and beta₂-agonists are administered simultaneously.

4.6 Pregnancy and lactation

The safety of ipratropium bromide during human pregnancy has not been established. The benefits of using ipratropium bromide during a confirmed or suspected pregnancy must be weighed against the possible hazards to the unborn child. Preclinical studies have shown no embryotoxic or teratogenic effects following inhalation or intranasal application at doses considerably higher than those recommended in man.

It is not known whether ipratropium bromide is excreted into breast milk. It is unlikely that ipratropium bromide would reach the infant to an important extent, however caution should be exercised when ipratropium bromide is administered to nursing mothers.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

The most common non-respiratory adverse reactions reported in clinical trials are headache, nausea (with or without vomiting) and dryness of the mouth.

Common (>1/100, <1/10):

Nervous system disorders:	Headache
Respiratory, thoracic and mediastinal disorders:	Cough, local irritation
Gastrointestinal disorders:	Dryness of the mouth, nausea and disturbances in gastrointestinal motility (constipation, diarrhoea and vomiting).

Uncommon (>1/1000, <1/100)

Immune system disorders:	Urticaria.
Eye disorders:	Accommodation disturbances, narrow-angle glaucoma
Cardiac disorders:	Tachycardia
Respiratory, thoracic and mediastinal disorders:	Spasms of larynx
Skin and subcutaneous tissue disorders:	Exanthema

Rare (>1/10,000, <1/1000):

Immune system disorders:	Anaphylactic reactions, angio-oedema on the tongue, lips and face
Eye disorders:	Increased intraocular pressure, pain in the eyes, mydriasis
Cardiac disorders:	Palpitations, supraventricular tachycardia, atrial fibrillation
Respiratory, thoracic and mediastinal disorders:	Bronchospasms induced by the inhalation
Renal and urinary disorders:	Urinary retention

4.9 Overdose

Palpitation and increases in heart rate have been produced with inhaled doses of 5 mg. Side effects have not been caused by single inhaled doses of 2 mg in adults and 1 mg in children. Single oral doses of 30 mg of ipratropium bromide caused anticholinergic side effects, but these did not require treatment.

Severe overdose is characterized by atropine-like symptoms like tachycardia, tachypnea, high fever and central effects like restlessness, confusion and hallucinations. These symptoms should be treated symptomatically. The use of fysostigmine is not recommended because of worsening of cardiotoxic symptoms and induction of convulsions.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anticholinergics, ATC code: R03BB01

Ipratropium bromide is a competitive antagonist of muscarinic acetylcholine receptors. It exhibits its greatest potency on bronchial receptors, whether given intravenously or inhaled, but causes no tachycardia. No anticholinergic effects have been observed on cardiac function, bladder function or in the eye.

Ipratropium bromide is able to inhibit reflex-induced bronchoconstriction following exercise, inhalation of cold air and the early response to inhaled antigens. It also reverses the bronchoconstriction induced by inhaled cholinergic agonists.

Inhalation of 0.04mg of ipratropium from a metered dose aerosol causes bronchodilation, the maximal effect is seen after 30-60 minutes, with a duration of 4 hours. This is a dose related effect and use of a nebuliser produces greater bronchodilation, a dose of 0.5mg producing maximal bronchodilation.

5.2 Pharmacokinetic properties

Depending on the formulation and the inhalation technique, approximately 10-30 % of the inhaled dose reaches the lungs. The major part of the dose is swallowed.

Because of the negligible gastro-intestinal absorption, the bioavailability of the swallowed dose is only about 2 % of the total dose administered. The part of the dose that reaches the lungs has an almost complete systemic bioavailability and reaches the circulation within a few minutes.

From data on renal excretion (0-24 h) the total systemic bioavailability of inhaled ipratropium bromide is estimated to be 7-28 % (averages from three studies). It can be assumed that this interval is valid for the solution for nebuliser as well.

The kinetic parameters have been calculated from plasma concentrations after intravenous administration. The plasma concentration falls rapidly. The volume of distribution (V_z) is 338 L (approximately 4.6 L/kg). Ipratropium has a low degree of protein binding (<20 %). Because of its ammonium ion structure, ipratropium does not pass the blood-brain barrier. The elimination of ipratropium is biphasic. The half-life of elimination of the drug and metabolites is 3.6 hours. The half-life of the terminal elimination phase is about 1.6 hours.

The average total clearance has been estimated to be 2.3 L/min. About 60 % of the systemic available dose is metabolised, probably in the liver. The main metabolites that are found in the urine have a low affinity for muscarinic receptors and do not possess significant anticholinergic activity.

About 40 % of the systemic available dose is excreted via the kidneys, which corresponds to a renal clearance of 0.9 L/min.

From studies using radioactively labelled ipratropium, less than 10 % of the dose (ipratropium and metabolites) is excreted via bile and faeces. The major part of the radio labelled dose is excreted via the kidneys.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction, genotoxicity or carcinogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride
Water for Injections
Concentrated Hydrochloric Acid (for pH adjustment)

6.2 Incompatibilities

Ipratropium Nebuliser Solution can be diluted only with sterile 0.9% sodium chloride solution.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package.
The ampoule should be opened immediately before use and any solution remaining after use should be discarded.

6.5 Nature and contents of container

Sterile unit dose polyethylene ampoules, containing Ipratropium Bromide Nebuliser Solution are available in two sizes: 1 ml and 2 ml. Ampoules, in strips of 10 overwrapped in aluminium foil, are packed into cartons available in packs of 20 or 60 ampoules. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Ipratropium Bromide Nebuliser Solution is for inhalation from an intermittent positive pressure ventilator or from a suitable nebuliser which should be operated according to the manufacturer's instructions.

To open the plastic ampoule, take a strip of ampoules from the foil pack, remove one ampoule, replacing the rest back in the foil pack and replace the foil pack back in the carton. Hold the ampoule upright and open by twisting off the top. Squeeze the liquid into the solution holder of the machine.

7 MARKETING AUTHORISATION HOLDER

Breath Limited
Unit 2, Eastman Way,
Stevenage, Hertfordshire,
SG1 4SZ, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL: 18023/0011

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/02/2010

10 DATE OF REVISION OF THE TEXT

23/02/2010

IPRATROPIUM BROMIDE 250MCG/1ML NEBULISER SOLUTION

IPRATROPIUM BROMIDE 500MCG/2ML NEBULISER SOLUTION

PL 18023/0011

PACKAGE LEAFLET: INFORMATION FOR THE USER

Ipratropium Bromide 250 micrograms/1ml Nebuliser Solution

Ipratropium Bromide 500 micrograms/2ml Nebuliser Solution

(Ipratropium Bromide)

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Ipratropium Bromide Nebuliser Solution is and what it is used for
2. Before you take Ipratropium Bromide Nebuliser Solution
3. How to take Ipratropium Bromide Nebuliser Solution
4. Possible side effects
5. How to store Ipratropium Bromide Nebuliser Solution
6. Further information

1. WHAT IPRATROPIUM BROMIDE NEBULISER SOLUTION IS AND WHAT IT IS USED FOR

Ipratropium belongs to a group of medicines called "bronchodilators" which help to open up the air passages in your lungs so that you can breathe more easily.

This medicine helps to make breathing easier in patients with asthma and other breathing difficulties such as chronic obstructive pulmonary disease.

Ipratropium Bromide Nebuliser Solution can be used at the same time as medicines called beta₂-agonist bronchodilators ('relievers'), for example salbutamol.

2. BEFORE YOU TAKE IPRATROPIUM BROMIDE NEBULISER SOLUTION

Do not take Ipratropium Bromide Nebuliser Solution

- if you are allergic (hypersensitive) to ipratropium bromide or a related medicine called atropine
- if you are allergic to any of the other ingredients of Ipratropium Bromide Nebuliser Solution (these are listed in section 6, Further information).

Take special care with Ipratropium Bromide Nebuliser Solution

Talk to your doctor before taking this medicine if any of the following apply to you:

- if you suffer from cystic fibrosis
- if you have a condition which makes passing urine difficult
- if you suffer from raised pressure in the eyes (glaucoma), as you will need to make sure the mist does not get into your eyes
- if you are a man suffering from prostate problems.

Taking other medicines

Tell your doctor if you are taking or have taken any of the following medicines as they may interact with Ipratropium Bromide Nebuliser Solution:

- medicines called xanthines such as theophylline
- other medicines containing bronchodilators (which also help you to breathe more easily), such as salbutamol or terbutaline.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding

If you are pregnant, think you are pregnant or are breast-feeding you should not use Ipratropium Bromide Nebuliser Solution unless your doctor tells you to. If you become pregnant whilst taking this medicine you should tell your doctor as soon as possible.

Driving and using machines

Ipratropium Bromide Nebuliser Solution has no known effects on the ability to drive and use machines.

3. HOW TO TAKE IPRATROPIUM BROMIDE NEBULISER SOLUTION

Always use Ipratropium Bromide Nebuliser Solution exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Your doctor may tell you to use your nebuliser at regular times each day or only when you are wheezy or short of breath.

Adults, the elderly and children over 12 years

The usual dose is 250-500 micrograms (1–2ml of solution) three or four times a day.

For acute attacks of breathlessness use 500 micrograms (2ml) of solution.

Children 6 - 12 years

The usual dose is 250 micrograms (1ml). The time between doses should be decided by the doctor.

Children up to 5 years

This medicine should only be used for acute attacks of breathlessness in children up to 5 years.

The usual dose is 125 - 250 micrograms (0.5–1ml of solution). The time between doses should be decided by the doctor but there should be at least 6 hours between doses.

In all cases, if breathlessness persists or becomes worse, tell your doctor.

General instructions:

Ipratropium Bromide Nebuliser Solution should be used with a suitable nebuliser. The "mist" produced is then inhaled through a face mask or mouthpiece. Your doctor will advise you on choosing an appropriate nebuliser and how it should be used.

Sometimes, this medicine is given using an intermittent positive pressure ventilator, in which case treatment will be started by your specialist.

Instructions for use:

1. Prepare your nebuliser following the manufacturer's instructions and/or the dosing instructions given by your doctor. Make sure it is clean.
2. Take a strip of ampoules from the foil sachet. Remove one or two ampoules (depending on your dose) (Diagram 1) and put the rest back in the foil sachet and replace the foil sachet in the carton. Never use an ampoule that has been opened already or if the solution is discoloured.
3. Hold the ampoule upright and open it by twisting off the top (Diagram 2).

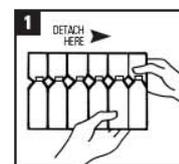


Diagram 1

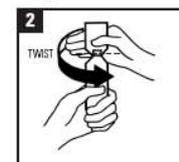


Diagram 2

4. Unless otherwise instructed by your doctor, squeeze all the liquid from the ampoule into the nebuliser chamber.
5. Throw away the empty plastic ampoule
6. If your doctor has told you to dilute the solution, this should be carried out using ONLY sterile sodium chloride 0.9% solution. Use the amount which your doctor has told you to use.
7. Turn on the nebuliser and breathe in the "mist" calmly and deeply using the face mask or mouthpiece. If you are using a face mask make sure that it is fitted correctly. Be sure to protect your eyes from the mist produced as it can cause pain or discomfort if it gets into them. This is especially important if you suffer from glaucoma. If a lot of the mist gets into your eyes or you start suffering from eye pain or discomfort after using this medicine you should contact your doctor or pharmacist.
8. The length of time it takes your nebuliser to turn your medicine into a mist will depend on the type of equipment you use. You will know when your treatment is complete because the fine mist will stop coming out of your mask or mouthpiece.
9. You must wash your nebuliser, face mask and/or mouthpiece in warm soapy water and rinse well after each use.

Contact your doctor immediately if:

- You are not getting relief from your current dose
- Your breathing is getting worse
- Your chest feels tight.

These are signs that your condition is not being controlled and you may need different or additional treatment.

If you take more Ipratropium Bromide Nebuliser Solution than you should

You may feel that your heart is beating faster than usual or that your breathing becomes rapid. You may have a high fever, restlessness, confusion or hallucinations.

Call your doctor immediately or go to the nearest hospital casualty department. Take this leaflet or an ampoule of your medicine with you so that the doctor will know what you have taken.

If you forget to take Ipratropium Bromide Nebuliser Solution

If you forget to take your Ipratropium Bromide Nebuliser Solution, take the next dose when it is due, or before you become wheezy.

Do not take a double dose to make up for the one that you missed.

If you stop taking Ipratropium Bromide Nebuliser Solution this may make your condition worse. Do not stop taking your medicine unless your doctor tells you to do so.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Ipratropium Bromide Nebuliser Solution can cause side effects, although not everybody gets them.

All medicines can cause allergic reactions, although serious allergic reactions are very rare. Tell your doctor immediately if you get any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body). This is known as 'angioedema'.

Rarely, inhaled drugs such as Ipratropium Bromide Nebuliser Solution can cause acute wheezing and/or shortness of breath. If this occurs, stop using your medicine immediately and seek medical advice.

The following side effects have also been reported:

Common side effects (probably affecting up to 1 in 10 people)

- Headache
- Irritation of the nose and mouth
- Nausea and/or vomiting (feeling or being sick).
- Cough
- Dryness of the mouth
- Constipation
- Diarrhoea

Uncommon side effects (probably affecting fewer than 1 in 100 people)

- Skin rashes (a rash of red spots or itchy 'nettle' rash)
- Rapid heartbeat
- Blurred vision, difficulty focusing or other visual disturbances
- Glaucoma (increased pressure in the eye).

Rare side effects (probably affecting fewer than 1 in 1,000 people)

- Allergic reactions
- Difficulty passing urine
- Pain in the eyes
- Swelling of the tongue, lips and face
- Irregular heartbeat
- Widening of the pupils.
- Increased awareness of your heartbeat
- Increased pressure in the eye

If any of the solution or mist accidentally gets into your eyes you may experience red eyes, discomfort or pain in your eyes, blurred vision, or you may see halos or coloured images.

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE IPRATROPIUM BROMIDE NEBULISER SOLUTION

Keep out of the reach and sight of children.

Do not store your medicine above 25°C. Store in the original package in order to protect from light.

Do not use Ipratropium Bromide Nebuliser Solution after the expiry date which is stated on the ampoule label, foil sachet and carton. The expiry date refers to the last day of that month.

Do not use Ipratropium Bromide Nebuliser Solution if you notice any cloudiness when the solution is poured into the nebuliser cup. Discard the solution and wash the nebuliser cup before selecting a fresh ampoule for use.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION**What Ipratropium Bromide Nebuliser Solution contains**

- The active ingredient is Ipratropium Bromide 250 micrograms/ml (0.025% w/v).
- The other ingredients are sodium chloride, water for injections and hydrochloric acid

What Ipratropium Bromide Nebuliser Solution looks like and contents of the pack

Your medicine comes in the form of plastic ampoules containing a clear colourless solution to be nebulised (made into a fine mist for inhalation).

Two sizes of ampoules are available:

Ampoule containing 1ml of solution (250 micrograms of Ipratropium Bromide)
Ampoule containing 2ml of solution (500 micrograms of Ipratropium Bromide)

The ampoules are packed in strips of 10 inside a foil sachet which are then packed into a carton. Cartons are available in packs of 20 or 60 ampoules. Not all pack sizes may be marketed.

Marketing Authorisation Holder:

Breath Limited,
Unit 2, Eastman Way, Stevenage, Hertfordshire, SG1 4SZ, UK

Manufacturer:

Laboratoire Unither,
Z.I. Longpre, 10 rue Andre Durouchez, 80084 Amiens Cedex 2, France

This leaflet was last approved in: 10/2009

Item code

Pharmacode

**IPRATROPIUM BROMIDE 250MCG/1ML NEBULISER SOLUTION
IPRATROPIUM BROMIDE 500MCG/2ML NEBULISER SOLUTION
PL 18023/0011**

LABELLING



**Ipratropium Bromide 250 micrograms / 1ml
Nebuliser Solution**

(Ipratropium Bromide)

Each 1ml ampoule contains 250 micrograms of ipratropium bromide.
This medicinal product also contains sodium chloride, hydrochloric acid and water for injections.

For inhalation use only. Read the package leaflet before use. Use as directed by your doctor. Each ampoule is for single use only and should be opened immediately before use. Discard any unused contents after each use. Do not store above 25°C. Store in the original package in order to protect from light.

10 x 1ml ampoules

FOR INHALATION USE ONLY

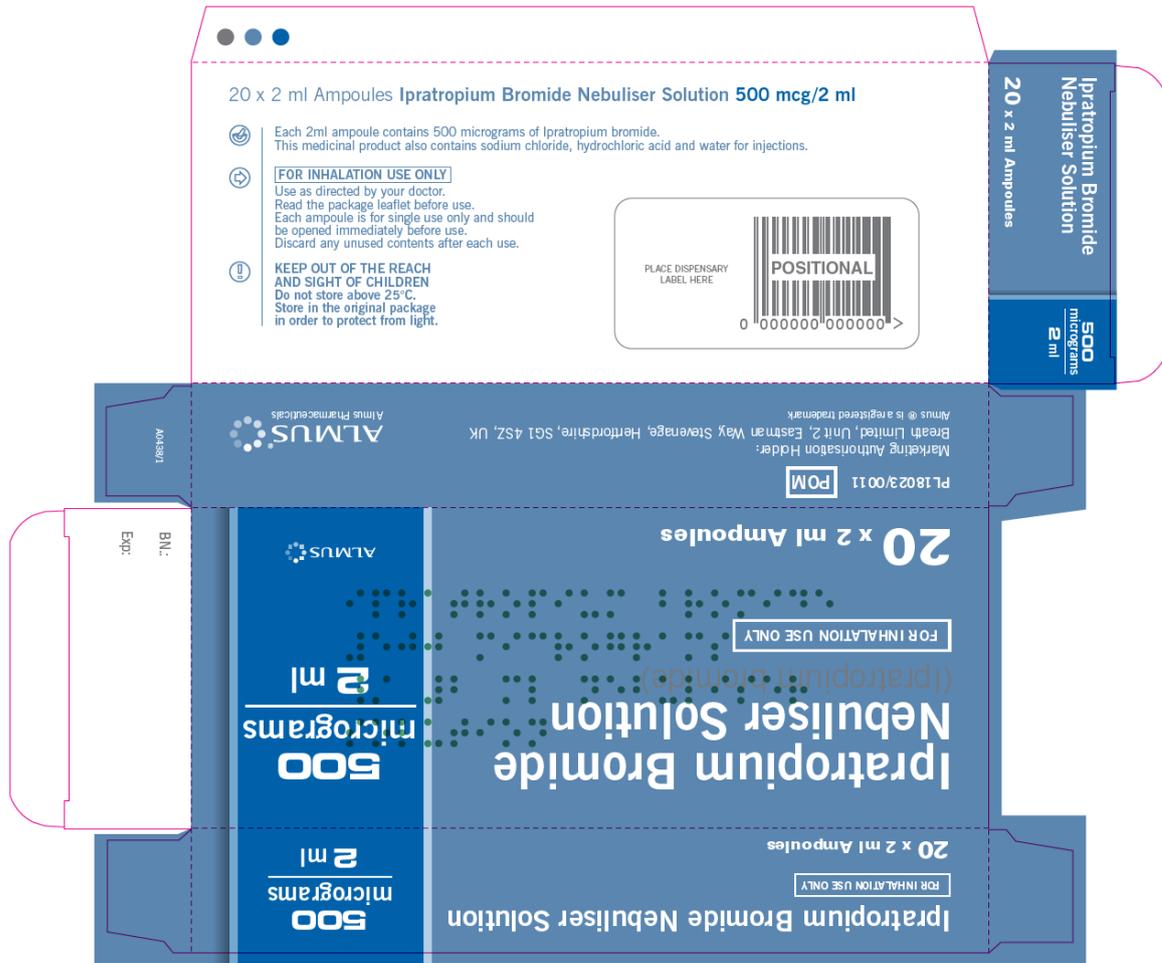
Keep out of the reach and sight of children.

PL 18023/0011
Marketing Authorisation Holder:
Breath Limited,
Unit 2, Eastman Way,
Stevenage,
Hertfordshire,
SG1 4SZ, UK

POM

Ipratropium Bromide
250 micrograms / 1ml Nebuliser
Solution. For inhalation use only.

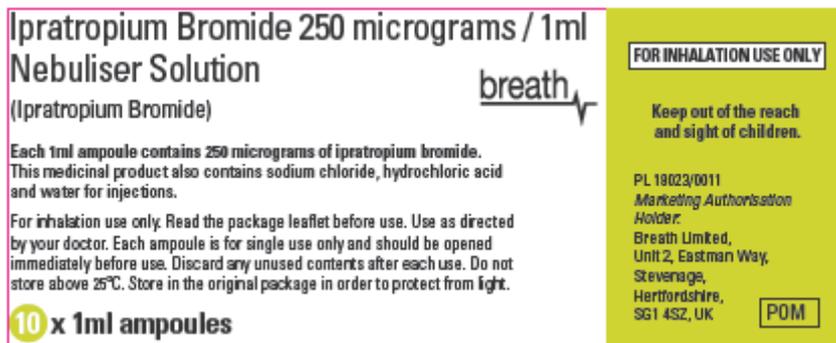
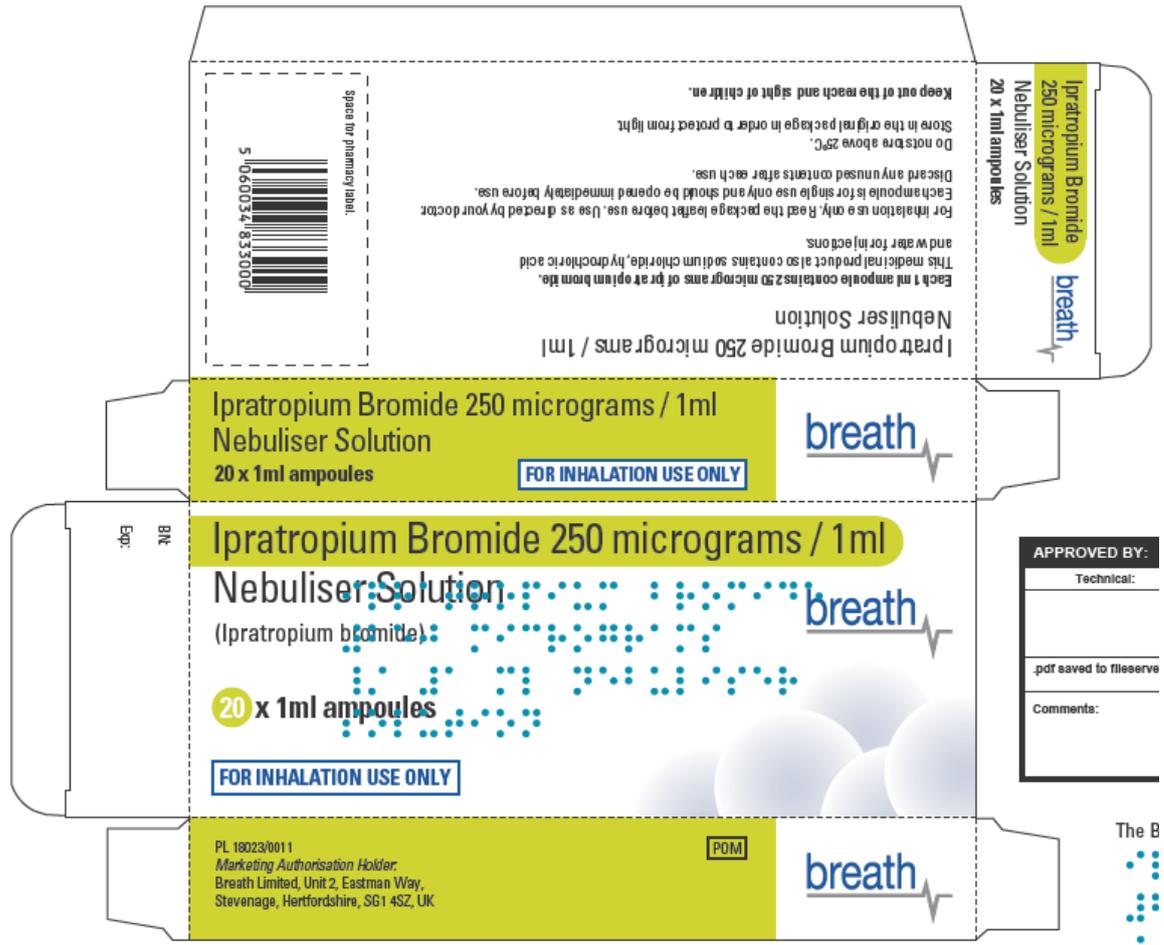
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Exp:



<p>Ipratropium Bromide 500 micrograms / 2ml Nebuliser Solution (Ipratropium Bromide)</p> <p>Each 2ml ampoule contains 500 micrograms of ipratropium bromide. This medicinal product also contains sodium chloride, hydrochloric acid and water for injections.</p> <p>For inhalation use only. Read the package leaflet before use. Use as directed by your doctor. Each ampoule is for single use only and should be opened immediately before use. Discard any unused contents after each use. Do not store above 25°C. Store in the original package in order to protect from light.</p> <p>10 x 2ml ampoules</p>	<p>FOR INHALATION USE ONLY</p> <p>Keep out of the reach and sight of children.</p> <p>PL 18023/0011 Marketing Authorisation Holder: Breath Limited, Unit 2, Eastman Way, Stevenage, Hertfordshire, SG1 4SZ, UK</p> <p>POM</p>
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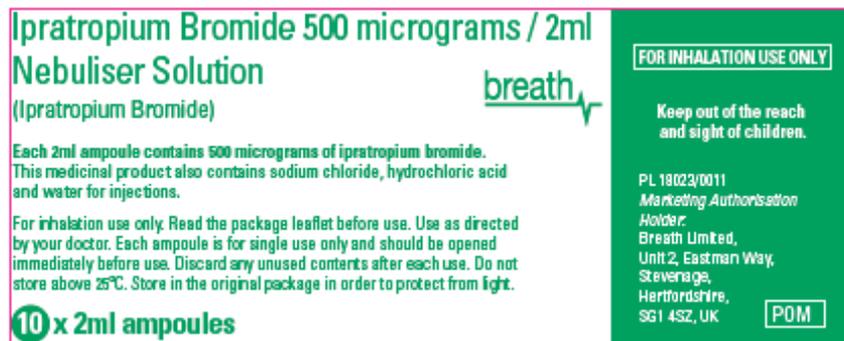
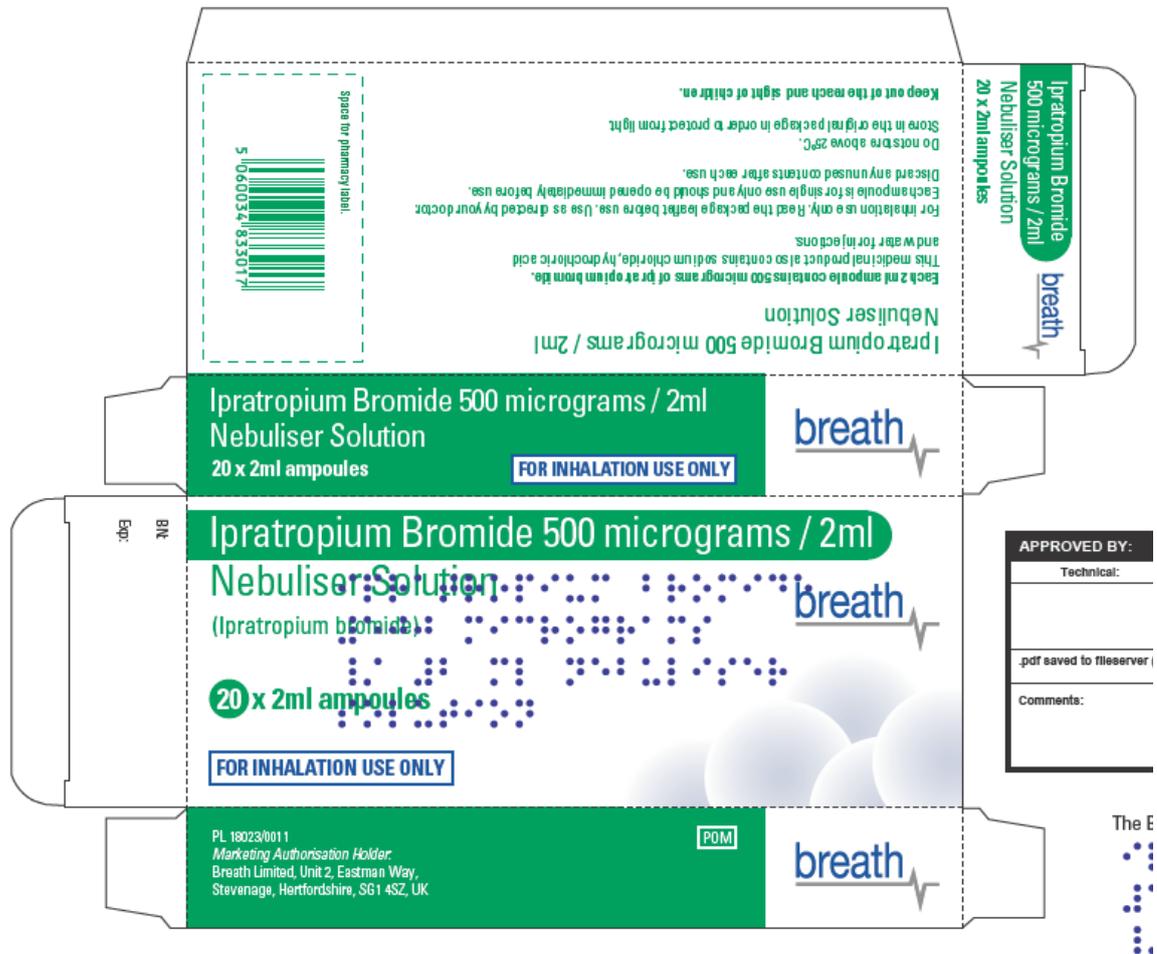
Ipratropium Bromide
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