PRODUCT INFORMATION

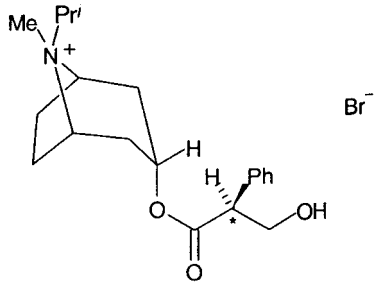
IPRAVENT® Inhalation Solution – Unit Dose

NAME OF THE MEDICINE

Ipratropium Bromide BP

Ipratropium bromide is a quaternary isopropyl derivative of atropine. Its chemical name is (1R, 3r, 5S, 8r)-3-[(RS) - (3 - hydroxy - 2 - phenylpropanoyl) oxy] - 8 - methyl - 8 - (1 - methylethyl) - 8 - azoniabicyclo [3.2.1] octane bromide. It appears as a white or almost white, crystalline powder, soluble in water, freely soluble in methanol and slightly soluble in alcohol. The addition of an N-isopropyl group distinguishes the molecule from atropine and is responsible for a lower lipid solubility.

The structural formula is represented below.



and epimer at C*

Molecular Formula: $C_{20}H_{30}BrNO_3$

Molecular Weight: 412.4

CAS Number: 22254-24-6

DESCRIPTION

Ipravent Inhalation Solution in Sterinebs is a clear, colourless to almost colourless, sterile solution. It contains ipratropium bromide monohydrate 261μg/mL equivalent to 250μg ipratropium bromide (anhydrous) or ipratropium bromide monohydrate 522μg/mL equivalent to 500μg ipratropium bromide (anhydrous) and Sodium Chloride BP in Water for Injections BP. It does not contain preservatives.

PHARMACOLOGY

Class of Drug

Anticholinergic bronchodilator.

Mode of Action

Ipratropium bromide allows bronchodilation by inhibiting cholinergic bronchomotor tone and consequently, vagal reflexes mediating bronchoconstriction are blocked. In this respect ipratropium bromide is fundamentally different from β_2 agonists. The onset of bronchodilator response is seen within three to five minutes of administration. Peak response is reached 1.5 to 2 hours after inhalation. The duration of significant bronchodilator action is up to 6 hours. Ipravent can be used in combination with β_2 agonists.

There is evidence that in patients who respond to ipratropium bromide greater relief of bronchospasm can be achieved by the concurrent use of ipratropium bromide, and β_2 agonists, as compared to that achieved by using either drug alone. Ipratropium bromide inhibits bronchospasm induced by acetylcholine and offers partial protection against histamine and allergen-induced bronchospasm. No significant alteration in sputum viscosity, sputum volume or mucociliary clearance has been observed.

Pharmacokinetics

There are no data available relating to systemic levels of inhaled nebulised solution. Like other substances administered by inhalation, most of the dose enters the gastrointestinal tract, is unabsorbed and is excreted in the faeces. In healthy volunteers, the elimination half-life is 3.5 hours (range 1.5 to 4 hours). Eight metabolites possessing little or no anticholinergic activity have been detected.

INDICATIONS

- moderate asthmatic attacks
- chronic forms of asthma
- asthma in patients with diminished cardiac reserve
- bronchospasm during or after surgery
- chronic obstructive bronchitis with bronchospasm
- use during assisted ventilation with a respirator.

CONTRAINDICATIONS

Hypersensitivity to ipratropium bromide or any of the ingredients.

PRECAUTIONS

Like other drugs with anticholinergic activity, ipratropium bromide should be avoided or used with caution in patients where atropine-like effects may precipitate or exacerbate a pre-existing clinical condition. Patients at particular risk are those with:

- eyes with narrow iridocorneal angles (as acute angle-closure glaucoma may precipitate)
- tendency towards urinary retention
- tendency towards constipation.

Patients with cystic fibrosis may be more prone to gastrointestinal motility disturbances.

Ipratropium bromide should be used with caution in patients with pre-existing urinary outflow tract obstruction (e.g. prostatic hyperplasia or bladder-neck obstruction).*

Patients must be instructed on the correct administration of Ipravent and warned to not allow the solution to enter the eyes. There have been isolated reports of ocular complications e.g. mydriasis, increased intraocular pressure, acute angle closure glaucoma and eye pain as a result of direct contact of the solution.

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

Immediate hypersensitivity reactions may occur after administration of Ipravent, as demonstrated by rare cases of urticaria, angio-oedema, rash, bronchospasm, oropharyngeal oedema and anaphylaxis.*

Use in Pregnancy

Category B1. Ipratropium bromide has been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals have not shown evidence of an increased occurrence of foetal damage.

Care is recommended during pregnancy, particularly in the first trimester. The benefits of using ipratropium bromide when pregnancy is present or suspected must be weighed against possible hazards to the foetus.

Use in Lactation

No specific studies are available to determine the excretion of ipratropium bromide in human breast milk. The benefit of using ipratropium bromide during lactation should therefore be weighed against possible effects on the child.

Use in Children

Ipravent Inhalation Solution is not recommended for use in infants less than 8 weeks old.

Mutagenicity

Studies in rats, mice and rabbits showed no embryo-toxic or teratogenic effects.

Effects on Ability to Drive or Operate Machinery

No studies on the effects on the ability to drive and use machines have been performed. However, patients should be advised that they may experience undesirable effects such as dizziness, accommodation disorder, mydriasis and blurred vision during treatment with Ipravent. Therefore, caution should be recommended when driving a car or operating machinery. If patients experience the above mentioned side effects they should avoid potentially hazardous tasks such as driving or operating machinery.*

INTERACTIONS WITH OTHER MEDICINES

No significant drug interactions have been reported with ipratropium bromide, although there is some potential for an additive interaction with other concomitantly administered anticholinergic medications.

Effective bronchodilation with ipratropium bromide has been demonstrated in patients receiving β-adrenergics and xanthine preparations.

The risk of acute glaucoma in patients with a history of narrow-angle glaucoma (see PRECAUTIONS) may be increased when nebulised ipratropium bromide and beta-mimetics are administered simultaneously.*

ADVERSE EFFECTS

Many of the listed undesirable effects can be assigned to the anticholinergic properties of ipratropium bromide. As with all inhalation therapy, ipratropium bromide may show signs of local irritation.*

The most frequent side effects reported in clinical trials with ipratropium bromide were headache, dizziness, throat irritation, cough, gastrointestinal disorders (including constipation, diarrhoea, gastrointestinal motility disorder, dry mouth, nausea, stomatitis, oedema mouth and vomiting).*

If the substance enters the eye by inappropriate handling, mild and reversible disturbance of accommodation may occur. Other ocular complications have also been reported (see PRECAUTIONS). However, acute angle-closure glaucoma has been reported following direct eye contact.*

Allergic type reactions such as angio-oedema of the tongue, lips and face may occur.*

The following adverse reactions were reported in the clinical studies of ipratropium bromide at the following frequency: very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare (<1/10,000).*

Immune System Disorders*

Uncommon: hypersensitivity, anaphylactic reaction

Nervous System Disorders*

Common: headache, dizziness

Eye Disorders*

Uncommon: vision blurred, mydriasis, intraocular pressure increased, glaucoma, eye pain, halo vision, conjunctival hyperaemia, corneal oedema,

Rare: accommodation disorder

Cardiac Disorders*

Uncommon: palpitations, supraventricular tachycardia

Rare: atrial fibrillation, heart rate increased

Respiratory, Thoracic and Mediastinal Disorders*

Common: throat irritation, cough

Uncommon: bronchospasm, bronchospasm paradoxical, laryngospasm, pharyngeal oedema, dry throat

Gastrointestinal Disorders*

Common: dry mouth, nausea, gastrointestinal motility disorder (including reports of change in bowel motions and habits, dyspepsia, gastrointestinal reflux and flatulence)[1]

Uncommon: diarrhoea, constipation, vomiting, stomatitis, oedema mouth

Skin and Subcutaneous Tissue Disorders*

Uncommon: rash, pruritus, angioedema

Rare: urticaria

Renal and Urinary Disorders*

Uncommon: urinary retention

DOSAGE AND ADMINISTRATION

Ipravent Inhalation Solution in unit dose ampoules does not contain preservatives and is therefore intended for single use only. Any unused portion should be discarded.

Adults

The recommended dosage is 250 to 500μg, diluted to 2 to 3mL with normal saline and nebulised until the entire volume of solution is consumed, every six hours. Daily doses exceeding 2mg of ipratropium bromide in adults should be given under medical supervision.

In cases of moderate bronchospasm or with assisted ventilation, a dose in the lower range of 250μg is recommended. In severely distressed patients, 500μg has been shown to produce optimal bronchodilation. Inhalation may be repeated after two hours.

Dosage in Children (over 8 weeks old)

A dose of 250μg diluted to 2 to 3mL with normal saline is recommended for children, administered in the same manner as for adults. Daily doses exceeding 1mg of ipratropium bromide in children under 12 years of age should be given under medical supervision.

Ipravent solution can be administered via a range of commercially available nebulising devices. Solutions are best administered at a flow rate of 4 to 6L/minute when using wall oxygen. Dosage is dependent on the mode of inhalation and the specific nebuliser used and should be modified to suit individual patient requirements.

[1] The definition is based on a post-hoc review of all ADR terms reported in the defined study dataset. Terms that report a clinically related term with greater medical specificity were excluded and added to the more specific term (e.g. "nausea", "vomiting").

Compatibility

Sodium cromoglycate may not be compatible with ipratropium bromide inhalation solution as precipitation may occur.

Dilution of Ipravent Inhalation Solution should be carried out immediately before use. Should visible turbidity or crystallisation appear in the solution before or during inhalation, the preparation should be discarded. Any solution remaining in the nebuliser on completion of inhalation should be discarded immediately. Nebuliser bowls and associated equipment should be cleaned and maintained prior to each use according to the manufacturer's recommendations.

OVERDOSAGE

Accidental overdose by inhalation is unlikely. Adverse effects from overdosage may be expected to follow the pattern listed under **ADVERSE EFFECTS**. Anticholinergic side effects are not severe and do not require specific reversal.

PRESENTATION AND STORAGE CONDITIONS

AUST R 75644 Ipravent Inhalation Solution 250μg in 1mL (sterile) Sterineb ampoules (30s)

AUST R 75645 Ipravent Inhalation Solution 500μg in 1mL (sterile) Sterineb ampoules (30s)

Store below 25ºC. Protect from light. Single use only. Discard unused portion.

Ipratropium Bromide is sensitive to light. All ampoules must be stored in the carton or protected from light.

The expiry date (month/year) is stated on the package after the word EXP.

NAME AND ADDRESS OF THE SPONSOR

Pfizer Australia Pty Ltd
ABN 50 008 422 348
38-42 Wharf Road
West Ryde NSW 2114
Australia

POISON SCHEDULE OF THE MEDICINE

Prescription Only Medicine (S4)

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS

01 September 2000

DATE OF MOST RECENT AMENDMENT

30 May 2012

* Please note change(s) in Product Information

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Sterinebs® are plastic ampoules produced by Pfizer