**AUSTRALIAN PRODUCT INFORMATION**

# AERON® 250/500

*ipratropium bromide monohydrate conventional inhalation*

## 1 NAME OF THE MEDICINE

Ipratropium bromide monohydrate

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each AERON ampoule contains 250 micrograms/mL or 500 micrograms/mL of ipratropium bromide as the active ingredient.

For the full list of excipients, see section 6.1 List of Excipients.

## 3 PHARMACEUTICAL FORM

AERON is a clear colourless solution essentially free from foreign particles.

## 4 CLINICAL PARTICULARS

### 4.1 THERAPEUTIC INDICATIONS

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

### 4.2 DOSE AND METHOD OF ADMINISTRATION

AERON can be administered via a range of commercially available nebulising devices. Where wall oxygen is available, solutions are best administered at a flow rate of 6 to 8 L/minute. Administration of AERON via a nebuliser is intended for those patients who cannot use a metred dose aerosol.

Dosage is dependent on the mode of inhalation and the quality of nebulisation. The duration of inhalation can be controlled by the dilution volume. It is advisable not to greatly exceed the recommended daily dose as this suggests additional therapeutic modalities may be needed.

Diluted solutions should be freshly prepared before use and any solution remaining in the nebuliser on completion of inhalation should be discarded.

After opening the unit dose ampoule, the solution should be used as soon as possible and any unused solution discarded immediately.

Note:
The dosage should be adapted to the individual requirements of the patient; patients should also be kept under medical supervision during treatment. Unless otherwise prescribed, the following doses are recommended:

#### Adults

The recommended dosage is 261 to 522 micrograms (equivalent 250 to 500 micrograms ipratropium bromide) four times daily, diluted to 2 to 3 mL with normal saline and nebulised until the entire volume of solution is consumed. Daily dose exceeding 2.088 mg (equivalent 2 mg 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 261 micrograms (equivalent 250 micrograms ipratropium bromide) is recommended. In more severely distressed patients, 522 micrograms ipratropium bromide (equivalent 500 micrograms ipratropium bromide) has been shown to produce optimal bronchodilatation.

### Children

The recommended dose is 261 micrograms (equivalent 250 micrograms ipratropium bromide) four times daily diluted to 2 to 3 mL with normal saline and nebulised until the entire volume of solution is consumed.

Daily doses exceeding 1.044 mg (equivalent 1 mg ipratropium bromide) in children under 12 years of age should be given under medical supervision.

It is advisable not to greatly exceed the recommended daily dose.

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

## 4.3 CONTRAINDICATIONS

Known hypersensitivity to atropine or its derivatives (such as the active substance ipratropium bromide) or to any of the ingredients in AERON.

## 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

### Hypersensitivity

Immediate hypersensitivity reactions may occur after administration of ipratropium bromide, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, oropharyngeal oedema and anaphylaxis.

### Paradoxical Bronchospasm

As with other inhaled medicines, AERON may result in paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs, AERON should be discontinued immediately and substituted with an alternative therapy.

### Anticholinergic Effects

Like other drugs with anticholinergic activity, ipratropium bromide should be avoided or used with caution in patients in whom atropine-like effects may precipitate or exacerbate a pre-existing clinical condition. Patients at particular risk are those with eyes with narrow iridocorneal angles since acute angle closure glaucoma may be precipitated, or patients with a tendency towards urinary retention or constipation.

### Ocular Complications

AERON should be used with caution in patients predisposed to narrow-angle glaucoma.

There have been isolated reports of ocular complications (mydriasis, increased intraocular pressure, acute angle closure glaucoma, eye pain) as a result of direct eye contact of ipratropium bromide formulations. Thus, patients must be instructed in the correct administration of AERON, and warned not to allow the solution or mist to enter the eyes. A nebuliser mask must be fitted properly during inhalation.

Patients who may be predisposed to glaucoma should be specifically warned to 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.

### Renal and Urinary Effects

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

### Gastro-intestinal Motility Disturbances

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

### Use in the Elderly

No data available.

### Paediatric Use

Paediatric patients can use AERON at the recommended dose (see section 4.2 Dose and Method of Administration).

### Effects on Laboratory Tests

No data available.

## 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

The chronic co-administration of ipratropium bromide with other anticholinergic drugs has not been studied. Therefore, the chronic co-administration of ipratropium bromide with other anticholinergic drugs is not recommended. Beta-adrenergics and xanthine preparations may intensify the 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 beta-mimetics are administered simultaneously.

### Physical Compatibility

AERON and disodium cromoglycate inhalation solutions that contain the preservative benzalkonium chloride should not be administered simultaneously in the same nebuliser as precipitation may occur.

## 4.6 FERTILITY, PREGNANCY AND LACTATION

### Effects on Fertility

No data available.

### Use in Pregnancy

Pregnancy category: B1

Care is recommended during pregnancy, particularly in the first trimester. The safety of ipratropium bromide during pregnancy has not been established. The benefits of using ipratropium bromide when pregnancy is present or suspected must be weighed against possible hazards to the fetus. Studies in rats, mice and rabbits showed no embryotoxic or teratogenic effects.

### Use in Lactation

No specific studies are available to determine the excretion of ipratropium bromide in human breast milk. Although lipid-insoluble quaternary cations pass into breast milk, it is unlikely that ipratropium bromide would reach the infant to an important extent, especially when administered by inhalation. However, as many drugs are excreted into breast milk, caution should be exercised when ipratropium bromide is administered to breastfeeding mothers.

## 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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 AERON. Therefore, caution should be recommended when driving a car or operating machinery. If patients experience any of the above side effects they should avoid potentially hazardous tasks such as driving or operating machinery.

## 4.8 ADVERSE EFFECTS (UNDESIRABLE 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 symptoms of local irritation.

The most frequent side effects reported in clinical trials 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 eyes due to inappropriate handling, mild and reversible disturbance of accommodation may occur. Other ocular complications have also been reported (see section 4.4 Special Warnings and Precautions for Use). However, acute angle-closure glaucoma has been reported following direct eye contact.

Allergic type reactions such as angioedema of the tongue, lips and face may occur.

The following adverse reactions have been reported during use of ipratropium bromide in clinical trials and during the post-marketing experience 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).

| System Organ Class | Common | Uncommon | Rare |
|---|---|---|---|
| **Immune system disorders** | | hypersensitivity<br>anaphylactic reaction | |
| **Nervous system disorders** | headache<br>dizziness | | |
| **Eye disorders** | | vision blurred<br>mydriasis<br>intraocular pressure increased<br>glaucoma<br>eye pain<br>halo vision<br>conjunctival hyperaemia<br>corneal oedema | accommodation disorder |
| **Cardiac disorders** | | palpitations<br>supraventricular tachycardia | atrial fibrillation<br>heart rate increased |
| **Respiratory, thoracic and mediastinal disorders** | throat irritation<br>cough | bronchospasm<br>bronchospasm paradoxical<br>laryngospasm<br>pharyngeal oedema<br>dry throat | |
| **Gastrointestinal disorders** | dry mouth<br>nausea<br>gastrointestinal motility disorder (including reports of change in bowel motions and habits, dyspepsia, gastrointestinal reflux and flatulence)[1] | diarrhoea<br>constipation<br>vomiting<br>stomatitis<br>oedema mouth | |
| **Skin and subcutaneous tissue disorders** | | rash<br>pruritus<br>angioedema | urticaria |
| **Renal and urinary disorders** | | urinary retention | |

[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”).

## Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

## 4.9 OVERDOSE

No symptoms specific to overdosage have been encountered. In view of the wide therapeutic range and topical administration of ipratropium bromide inhalation solutions, no serious anticholinergic symptoms are to be expected. Minor systemic manifestations of anticholinergic action, including dry mouth, visual accommodation disturbances and tachycardia may occur.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 PHARMACODYNAMIC PROPERTIES

### Mechanism of Action

Ipratropium bromide is an anticholinergic bronchodilator. It differs fundamentally from the beta2- agonists in that it allows bronchodilation by inhibiting cholinergic bronchomotor tone; vagal reflexes that mediate bronchoconstriction are blocked. Bronchodilation following inhalation of ipratropium bromide is primarily a local, site specific effect.

The time course of action of ipratropium bromide also differs from the beta2-agonists in that although the onset of bronchodilator response is seen within three to five minutes of administration, peak response is not reached until 1.5 to 2 hours after inhalation. The duration of significant bronchodilator action is up to six hours.

Ipratropium bromide may be used in combination with beta2-agonists. There is evidence that in patients who respond to ipratropium bromide, the concurrent administration of ipratropium bromide and beta2-agonists produces a greater relief of bronchospasm than either drug given alone.

Ipratropium bromide inhibits acetylcholine induced bronchospasm and provides partial protection against histamine and allergen induced bronchospasm. No significant alteration in sputum viscosity, sputum volume or mucociliary clearance has been observed.

### Clinical Trials

No data available.

## 5.2 PHARMACOKINETIC PROPERTIES

### Absorption

From limited pharmacokinetic data using the metered dose aerosol in humans, it has been shown that approximately 5% of an inhaled dose is absorbed systemically and, thus, very low plasma levels are reached. No data are available on the nebulising solution and, although it may be assumed that a similar pattern applies, the systemic levels are likely to be higher due to the increased dose administered.

### Distribution

As with other substances administered by inhalation, most of the dose enters the gastrointestinal tract, is unabsorbed and excreted in the faeces.

### Metabolism

Eight metabolites with little or no anticholinergic activity have been detected.

### Excretion

Renal excretion of the active ingredient is given as 3% of the dose after oral inhalation via the nebuliser (compared to 46% of the dose after intravenous administration) and the drug is minimally (< 20%) bound to plasma proteins. The elimination half-life in healthy volunteers is 3.5 hours (range 1.5 to 4 hours).

## 5.3 PRECLINICAL SAFETY DATA

### Genotoxicity

### No data available. Carcinogenicity

No data available.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 LIST OF EXCIPIENTS

The ampoules also contain sodium chloride, hydrochloric acid and water for injections.

## 6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

## 6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

Unopened ampoules should be used within 28 days of opening the pouch. Unused ampoules should be discarded.

## 6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Protect from Light.

## 6.5 NATURE AND CONTENTS OF CONTAINER

Container type: ampoule (LDPE)

Pack size: 30

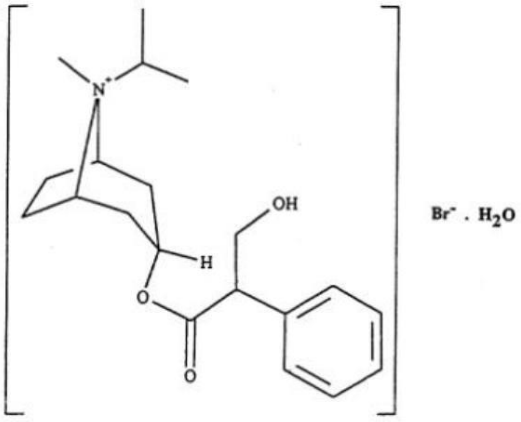
Some strengths, pack sizes and/or pack types may not be marketed.

## 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

## 6.7 PHYSICOCHEMICAL PROPERTIES

### Chemical Structure




Ipratropium bromide monohydrate is a white or almost white crystalline powder. It is soluble in water, freely soluble in methanol and slightly soluble in alcohol.

The chemical name for ipratropium bromide (as monohydrate) is (1R,3r,5S,8r)-3-[(RS)-(3-hydroxy-2-phenyl-propanoyl)oxy]-8-methyl-8-(1-methylethyl)-8-azoniabicyclo[3.2.1]octane bromide monohydrate.

Molecular formula: $C_{20}H_{30}NO_3Br.H_2O$

Molecular weight: 430.4

### CAS Number

66985-17-9

## 7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 (Prescription Only Medicine)

## 8 SPONSOR

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## 9 DATE OF FIRST APPROVAL

18/03/2005

## 10 DATE OF REVISION

06/04/2022

## Summary Table of Changes

| Section Changed | Summary of New Information |
|---|---|
| **1 & 8** | Rebranding |
| **6.3** | Updated to include "Unopened ampoules should be used within 28 days of opening the pouch. Unused ampoules should be discarded." |



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