



New Zealand Data Sheet

APO-IPRAVENT NASAL SPRAY

Ipratropium bromide 0.03% and 0.06%

Presentation

APO-IPRAVENT NASAL SPRAY 0.03% is a clear colourless solution and contain 300mcg/mL or ipratropium bromide. The solution is filled into a white opaque plastic bottle, closed with a white plastic pump and activator.

APO-IPRAVENT NASAL SPRAY 0.06% is a clear colourless solution and contain 600mcg/mL or ipratropium bromide. The solution is filled into a white opaque plastic bottle, closed with a white plastic pump and activator.

Uses

Actions

Ipratropium bromide, a quaternary ammonium derivative of atropine, is an anticholinergic drug. Ipratropium bromide administered intranasally has a localized parasympathetic blocking action which reduces watery hypersecretion from mucosal glands in the nose.

Nasal provocation trials in perennial rhinitis patients (n=44) using ipratropium bromide nasal spray showed a dose-dependent increase in inhibition of methacholine-induced nasal secretion with an onset of action within 15 minutes. The duration of action of ipratropium bromide nasal spray was also dose-dependent.

Controlled clinical trials showed that intranasal ipratropium bromide is effective for controlling the severity and duration of rhinorrhoea in patients with allergic and non-allergic perennial rhinitis or the common cold.

Ipratropium bromide administration via nasal aerosol had no marked effect on sense of smell, nasal mucociliary transport, ciliary beat frequency, or the air-conditioning capacity of the nose.

Pharmacokinetics

Ipratropium bromide is a quaternary amine that is rapidly absorbed from the nasal mucosa, however to a low extent. In normal volunteers, in patients with an experimentally-induced cold or in perennial rhinitis patients less than 10% of a nasally given dose (single or multiple administration) is absorbed, as estimated from the renal excretion of ipratropium bromide over 24 hours. This corresponds to a systemic bioavailability of less than 20% (range: 7-18%).

The systemic absorption of ipratropium bromide across inflamed nasal mucosa due to experimentally-induced cold was not altered. After a single dose or QID dosing 6-8% of ipratropium bromide was excreted unchanged in healthy as well as in infected volunteers. Following chronic dosing in rhinitis patients the amount of unchanged ipratropium bromide excreted in the urine over a 24-hour period at steady state was 4-6% of the dose.

Kinetic parameters describing the disposition of ipratropium bromide were calculated from plasma concentrations after i.v. administration.

A rapid biphasic decline in plasma concentrations is observed. The volume of distribution (V_z) is 338 l (\approx 4.6 l/kg). The drug is minimally (less than 20%) bound to plasma proteins. The ipratropium ion does not cross the blood-brain barrier, consistent with the ammonium structure of the molecule.

The half-life of the terminal elimination phase is about 1.6 hours.



APO-IPRAVENT NASAL SPRAY

Ipratropium bromide 0.03% and 0.06%

The mean total clearance of the drug is determined to be 2.3 L/min. The major portion of approximately 60% of the systemic available dose is eliminated by metabolic degradation, probably in the liver. The main urinary metabolites bind poorly to the muscarinic receptor and have to be regarded as ineffective.

A portion of approximately 40% of the systemic available dose is cleared via urinary excretion corresponding to an experimental renal clearance of 0.9 L/min. (After oral dosing less than 1% of the dose is renally excreted indicating an insignificant absorption of ipratropium bromide from the gastro-intestinal tract.)

In excretion balance studies after intravenous administration of a radioactive dose less than 10% of the drug-related radioactivity (including parent compound and all metabolites) are excreted via the biliary-faecal route. The dominant excretion of drug-related radioactivity occurs via the kidneys.

Indications

APO-IPRAVENT NASAL SPRAY is indicated for the treatment and management of perennial rhinitis, allergic rhinitis and vasomotor rhinitis when characterised by watery rhinorrhoea.

APO-IPRAVENT NASAL SPRAY is also indicated for the symptomatic relief of rhinorrhoea associated with the common cold.

Dosage and Administration

Priming of pump is required before first use.

For the treatment and management of perennial rhinitis, allergic rhinitis and vasomotor rhinitis when characterised by watery rhinorrhoea:

Regular Therapy

Adults: Two sprays up each nostril 2 - 3 times a day. Some patients may need 3 - 4 sprays up each nostril during early therapy to obtain maximum benefit during early treatment.

Children: 2 sprays up each nostril 2 times a day.

Optimal dosage varies with the response of the individual patient.

Intermittent Therapy

Patients with occasional episodes of watery rhinorrhoea triggered by provoking factors, e.g. temperature changes, food and exercise, should administer 2 - 4 sprays up each nostril prior to exposure.

For the symptomatic relief of rhinorrhoea associated with the common cold

Adults

0.03% strength: Initial dose: Two sprays into each nostril, followed by two further sprays five minutes after the first spray. Subsequent doses (2-3 times per day) two sprays into each nostril.

0.06% strength: Two sprays per nostril 3 or 4 times a day

Treatment in the common cold has only been studied up to four days. Efficacy and safety of treatment beyond four days have not been established, although there has been no evidence of adverse safety effects with longer treatment in perennial rhinitis patients.

APO-IPRAVENT NASAL SPRAY

Ipratropium bromide 0.03% and 0.06%

Contraindications

Known hypersensitivity to atropine-like substance or any of the inactive excipients.

Warnings and Precautions

Isolated cases of ocular complications (i.e. angle-closure glaucoma, eye pain, increased ocular pressure, and mydriasis) have been reported when aerosolised ipratropium bromide either alone or in combination with adrenergic beta-2-agonist has escaped into the eyes. Eye pain or discomfort, blurred vision, visual halos or coloured images in association with red eyes from conjunctival or corneal congestion may be signs of acute angle-closure glaucoma. If any combinations of these symptoms arise, treatment with miotic eye drops should be initiated and specialist advice sought immediately.

Patients must be instructed on the correct administration of the nebuliser solution and be warned not to allow the solution or mist to enter their eyes.

APO-IPRAVENT NASAL SPRAY should be used with caution in patients predisposed to narrow-angle glaucoma, or with prostatic hypertrophy or bladder-neck obstruction.

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

Immediate hypersensitivity reactions may occur after administration of APO-IPRAVENT NASAL SPRAY, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm and oropharyngeal oedema.

Ability to drive or operate machinery:

APO-IPRAVENT NASAL SPRAY is presumed to be safe or unlikely to produce an effect on the ability to drive or use machinery.

Use in Pregnancy and Lactation

Category B1

Even though pre-clinical studies have shown no hazard, safety during human pregnancy is not yet established. Preclinical studies showed no embryotoxic or teratogenic effects following inhalation at doses considerably higher than those recommended in man. As with all medicines, ipratropium bromide should not be used in pregnancy, especially in the first trimester, unless the expected benefit is thought to outweigh any possible risk to the fetus.

It is not known whether ipratropium bromide is excreted into human milk. Although lipid-insoluble quaternary cations pass into breast milk, it is unlikely that ipratropium bromide would reach the infant to an important extent, when taken intranasally. However, because many drugs are excreted into human milk, caution should be exercised when APO-IPRAVENT NASAL SPRAY is administered to nursing mothers.

Adverse Effects

The most frequent local undesirable effects of APO-IPRAVENT NASAL SPRAY are nasal reactions including epistaxis, dryness of the nose and nasal irritation.

Headache, nausea and local irritation (e.g. burning sensation) may occur as non-specific reactions in association with use of APO-IPRAVENT NASAL SPRAY.

Potential systemic anticholinergic effects are dry mouth and dry throat. Ocular side effects, increase of heart rate and palpitations, urinary retention and gastrointestinal motility disturbances have been reported in isolated patients in association with use of ipratropium bromide either intranasally or after oral inhalation.

APO-IPRAVENT NASAL SPRAY

Ipratropium bromide 0.03% and 0.06%

Allergic-type reactions such as skin rash, angio-oedema of tongue, lips and face, urticaria, laryngospasm and anaphylactic reactions may occur.

After oral inhalation of ipratropium bromide in patients suffering from COPD/Asthma supraventricular tachycardia and atrial fibrillation have been reported.

Interactions

There is no evidence that the concomitant use of APO-IPRAVENT NASAL SPRAY with other drugs commonly prescribed for common cold i.e. decongestants increases the incidence of side effects.

APO-IPRAVENT NASAL SPRAY is minimally absorbed into the systemic circulation; nonetheless, there is some potential for additive interaction with other concomitantly administered anti-cholinergic medications, including ipratropium bromide containing aerosols for oral inhalation.

Overdosage

No symptoms specific to overdose have been encountered. In view of the wide therapeutic range and topical administration of APO-IPRAVENT NASAL SPRAY, no serious anticholinergic symptoms are to be expected. Minor systemic manifestation of anticholinergic action, including dry mouth, visual accommodation disturbances and increase of heart rate may occur.

Pharmaceutical Precautions

Store in a safe place out of the reach of children.

Store at or below 25°C. Avoid freezing.

Medicine Classification

Pharmacy Only Medicine

Package Quantities

APO-IPRAVENT NASAL SPRAY 0.03% comes in a 30ml pump activated, metered dose container.

APO-IPRAVENT NASAL SPRAY 0.06% comes in a 15ml pump activated, metered dose container.

Further Information

Instructions for Use

1. Remove the clear plastic dust cap and the safety clip from the nasal spray pump. The safety clip prevents the accidental discharge of the spray in your pocket or purse.
2. The nasal spray pump must be primed before APO-IPRAVENT NASAL SPRAY is used for the first time. To prime the pump, hold the bottle with your thumb at the base and your index and middle fingers on the white shoulder area. Make sure the bottle points upright and away from your eyes. Press your thumb firmly and quickly against the bottle seven times. The pump is now primed and can be used. Your pump should not have to be reprimed unless you have not used the medication for more than 24 hours; repriming the pump will only require one or two sprays.
3. Before using APO-IPRAVENT NASAL SPRAY, blow your nose gently to clear your nostrils, if necessary.
4. Close one nostril by gently placing your finger against the side of your nose, tilt your head slightly forward and, keeping the bottle upright, insert the nasal tip into the other nostril. Point the tip toward the back and outer side of the nose.



APO-IPRAVENT NASAL SPRAY

Ipratropium bromide 0.03% and 0.06%

5. Press firmly and quickly upwards with the thumb at the base while holding the white shoulder portion of the pump between your index and middle fingers. Following each spray, sniff deeply and breathe out through your mouth.
6. After spraying the nostril and removing the unit, tilt your head backwards for a few seconds to let the spray spread over the back of the nose.
7. Repeat steps 4 through 6 in the other nostril.
8. Replace the clear plastic dust cap and safety clip.
9. When the amount of APO-IPRAVENT NASAL SPRAY begins to run low, the amount of medication in each spray cannot be assured. Therefore, at some time before the medication is completely used up, you should consult your physician or pharmacist to determine whether a refill is needed. You should not take extra doses of APO-IPRAVENT NASAL SPRAY without consulting your physician.

TO CLEAN

If the nasal tip becomes clogged, remove the clear plastic dust cap and safety clip. Hold the nasal tip under running, warm tap water for about a minute. Dry the nasal tip, reprime the nasal spray pump (step 2 above), and replace the plastic dust cap and safety clip.

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