AZMASOL 100MCG/DOSE HFA METERED DOSE INHALER

FORMULATION

Each actuation delivers: Salbutamol sulfate BP (equivalent to Salbutamol) ..... 100 mcg

PRODUCT DESCRIPTION

It is a homogenous suspension aerosol for inhalation, supplied in a pressurized container.

PHARMACODYNAMICS

Salbutamol is a selective ß2-adrenergic receptor agonist. The pharmacological effects of salbutamol are at least in part attributable to stimulation through beta-adrenergic receptors of intracellular adenyl cyclase, the enzyme that catalyses the conversion of adenosine triphosphate (ATP) to cyclic-3',5',-adenosine monophosphate (cyclic AMP). Increased cyclic AMP levels are associated with relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells. Salbutamol also stimulates mucous secretion and mucociliary transport in the respiratory tract. Bronchial effects of inhaled salbutamol can be detected after a few minutes and duration of action is normally 4-6 hours.

Like other ß2-adrenoceptor agonists salbutamol also has cardiovascular effects in some patients as measured by changes in pulse rate, blood pressure, symptoms and ECG changes. These effects can especially be detected after oral and intravenous administration of salbutamol. Furthermore, oral and intravenous salbutamol causes reduction in uterine tonicity which has been associated with pain relief in pregnancy. In addition, salbutamol has some metabolic effects. Especially intravenous and nebulised salbutamol decreases serum potassium concentrations although the effect is generally mild and transient. Salbutamol has also lipolytic effects and it has been shown to cause increases in blood glucose and insulin probably by stimulating glycogenolysis and having a stimulatory effect on ß2-receptors in pancreas cells.

PHARMACOKINETICS

<u>Absorption</u>

Orally administered salbutamol is well absorbed with peak plasma concentrations occurring 1 to 4 hours after administration.

Distribution

The major proportion of inhaled Salbutamol is swallowed. The fraction that is distributed to the lung (approx. 10-25%) is rapidly seen in the circulation as free unmetabolized drug. The remainder is retained in the delivery system or is deposited in the oropharynx from where it is swallowed. The swallowed portion of an inhaled dose is absorbed from the gastrointestinal tract and undergoes considerable first-pass metabolism.

Elimination

The plasma concentrations of inhaled Salbutamol are, however, lower than those produced by usual oral doses. Salbutamol and its metabolites are rapidly excreted in the urine and faeces with about 80% of dose being recovered in urine within 24 hours. The elimination half-life of Salbutamol is 2.7-5.5 hours after oral and inhaled administration.

INDICATION

Azmasol provides short-acting (4 to 6 hours) bronchodilation with fast onset (within 5 minutes) in reversible airway obstruction. It is particularly suitable for the relief and prevention of asthma symptoms. Azmasol should be used to relieve symptoms when they occur, and to prevent them in those circumstances recognised by the patient to precipitate an asthma attack (e.g. before exercise or unavoidable allergen exposure).
Azmasol is particularly valuable as relief medication in mild, moderate or severe asthma, provided that reliance on it does not delay the introduction and use of regular inhaled corticosteroid therapy.

RECOMMENDED DOSE

Azmasol has a duration of action of 4 to 6 hours in most patients.

Increasing use of beta-2 agonists may be a sign of worsening asthma. Under these conditions a reassessment of the patient's therapy plan may be required and concomitant corticosteroid therapy should be considered.

As there may be adverse effects associated with excessive dosing, the dosage or frequency of administration should only be increased on medical advice.

Azmasol is administered by the oral inhaled route only.
In patients who find co-ordination of a pressurised metered-dose inhaler difficult a spacer may be used with Azmasol inhaler.

Babies and young children using the Azmasol may benefit from the use of a paediatric spacer device with a face mask (See Clinical Studies).

RELIEF OF ACUTE BRONCHOSPASM

- Adults
  100 or 200 micrograms.
- Children
  100 micrograms. The dose may be increased to 200 micrograms if required.

PREVENTION OF ALLERGEN OR EXERCISE-INDUCED BRONCHOSPASM

- Adults
  200 micrograms before challenge or exertion.
- Children
  100 micrograms before challenge or exertion. The dose may be increased to 200 micrograms if required.

CHRONIC THERAPY

- Adults
  Up to 200 micrograms 4 times daily.
- Children
  Up to 200 micrograms 4 times daily.

On demand use of Azmasol should not exceed four times daily. Reliance on such supplementary use or a sudden increase in dose indicates deteriorating asthma (see Warnings and Precautions).

CONTRAINDICATIONS

Hypersensitivity to salbutamol or to the excipient listed in section 6.1 (lactose monohydrate, which contains small amounts of milk proteins).

Salbutamol inhalation is contraindicated in treatment of threatened abortion or premature labour.

WARNINGS AND PRECAUTIONS

Patients who are prescribed regular anti-inflammatory therapy (e.g., inhaled corticosteroids) should be advised to continue taking their anti-inflammatory medication even when symptoms decrease, and they do not require Salbutamol.

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma.

Severe asthma requires regular medical assessment including lung function testing as the patients are at risk of severe attacks and even death. Physicians should consider using oral corticosteroid therapy or the maximum use of inhaled corticosteroids. Increasing use of bronchodilators, particularly short-acting inhaled ß 2-agonists to relieve symptoms indicates deteriorating asthma control (especially if the peak expiratory flow rate value falls and/or becomes irregular), and patients should be warned to seek medical advice as soon as possible.

Overuse of short-acting beta-agonists may mask the progression of the underlying disease and contribute to deteriorating asthma control, leading to an increased risk of severe asthma exacerbations and mortality.

Patients who take more than twice a week "as needed" salbutamol, not counting prophylactic use prior to exercise, should be re-evaluated (i.e., daytime symptoms, night-time awakening, and activity

limitation due to asthma) for proper treatment adjustment as these patients are at risk for overuse of salbutamol.

In the event of a previous effective dose of inhaled salbutamol failing to give relief for at least three hours or if they need more inhalations than usual, the patient should be advised to seek medical advice as soon as possible. In this situation patients should be reassessed and consideration given to an increase in their anti-inflammatory therapy, (e.g. higher doses of inhaled corticosteroids or a course of oral corticosteroids). A regular anti-inflammatory controller medication taken on a daily basis is required as soon as the patient needs inhaled ß 2-agonists more than twice a week. Severe episodes of asthma must be treated in the normal way.

As there may be adverse effects associated with excessive dosing, the dosage and frequency of administration should only be increased on medical advice.

Salbutamol should be administered with caution in patients with thyrotoxicosis, cardiac insufficiency, hypokalaemia, myocardial ischaemia, tachyarrhythmia and hypertrophic obstructive cardiomyopathy.

Potentially serious hypokalaemia may result from ß 2 agonist therapy, mainly from parenteral and nebulised therapy. Particular caution is advised in acute severe asthma, as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids, diuretics and by hypoxia. It is recommended that serum potassium levels are monitored in such situations.

Rarely inhalation therapy may cause bronchospasm after dosing. In this event, treatment with Salbutamol must be immediately discontinued and, if need be, replaced with another therapy.

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischaemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving salbutamol should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin.

In common with other beta-adrenoceptor agonists, salbutamol can induce reversible metabolic changes such as increased blood glucose levels. Diabetic patients may be unable to compensate for the increase in blood glucose and the development of ketoacidosis has been reported. Concurrent administration of glucocorticoids can exaggerate this effect.

One dose contains less than 10 mg lactose, which probably does not cause symptoms in lactose intolerant patients. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

INTERACTIONS WITH OTHER MEDICAMENTS

If additional adrenergic drugs are administered to patients using Azmasol they should be used with caution to avoid deleterious cardiovascular effects.

Concomitant administration of salbutamol and non-selective ß -blocking drugs such as Propranolol is not recommended.

Patients treated with monoamine oxidase inhibitors or tricyclic antidepressants should be followed clinically in the beginning of salbutamol treatment, because the action of salbutamol on the vascular system may be potentiated.

The simultaneous administration of xanthines, corticosteroids or potassium excreting diuretics may increase hypokalaemia.

PREGNANCY AND LACTATION

Pregnancy

Safety in pregnant women has not been established. No controlled clinical trials with salbutamol have been conducted in pregnant women. Rare reports of various congenital anomalies following intrauterine exposure to salbutamol (including cleft palate, limb defects and cardiac disorders) have been received. Some of the mothers were taking multiple medications during their pregnancies. Administration of drugs during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus.

Breast-feeding

As salbutamol is excreted in breast milk, its use in nursing mothers requires careful consideration. It is not known whether salbutamol has a harmful effect on the neonate, and so its use should be restricted to situations where it is felt that the expected benefit to the mother outweighs any potential risk to the neonate.

Fertility

There is no information on the effects of salbutamol on human fertility.

SIDE EFFECTS

The undesirable effects caused by normally used inhaled doses of salbutamol are mild, typical for sympathomimetic agents, and they usually disappear with continued treatment.

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10), common, (≥ 1/100 and <1/10), uncommon (≥ 1/1000 and <1/100), rare (≥ 1/10,000 and <1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data).

	Common	Uncommon	Rare	Very Rare
Immune System disorders		hypersensitivity reactions (angioedema, urticaria, hypotension and collapse)		
Metabolism and nutrition disorders			hypokalaemia	

Nervous system disorders:		Headache	hyperactivity, restlessness, dizziness	
Cardiac disorders	palpitations			myocardial ischaemia Cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles
Vascular disorders	peripheral vasodilatation, and as a result small increase in heart rate			
Respiratory, thoracic and mediastinal disorders			bronchospasm (see section 4.4), cough, irritation of mouth and throat which may be prevented by rinsing the mouth after inhalation.	
Musculoskeletal and connective tissue and bone disorders:	tremor		muscle cramps,	

SYMPTOMS AND TREATMENTS OF OVERDOSE

Excess repeat use of inhalations may produce adverse effects such as tachycardia, CNS stimulation, tremor, hypokalaemia and hyperglycaemia.

Lactic acidosis has been reported in association with high therapeutic doses as well as overdoses of short-acting beta-agonist therapy, therefore monitoring for elevated serum lactate and consequent metabolic acidosis (particularly if there is persistence or worsening of tachypnea despite resolution of other signs of bronchospasm such as wheezing) may be indicated in the setting of overdose.

Treatment consists of discontinuation of salbutamol together with appropriate symptomatic therapy. The preferred antidote for overdosage with salbutamol is a cardioselective beta-blocking agent, but beta-blocking drugs should be used with caution in patients with a history of bronchospasm. Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored. If hypokalaemia occurs potassium replacement via the oral route should be given. In patients with severe hypokalaemia intravenous replacement may be necessary.

EFFECTS OF ABILITY TO DRIVE AND USE MACHINE

Azmasol inhaler has no or negligible influence on the ability to drive and use machines.

STORAGE CONDITIONS

Store at temperature not exceeding 30°C.

Replace the mouthpiece cover firmly and snap it into position.

Protect from frost and direct sunlight.

The container should not be broken, punctured or burnt, even when apparently empty.

Keep away from eyes. Avoid spraying in eyes.

Do not Puncture.

Do not use or store near heat or open flame.

Never throw canister into fire or incinerator.

Keep all medicines out of reach of children.

SHELF LIFE

2years

MANUFACTURED BY

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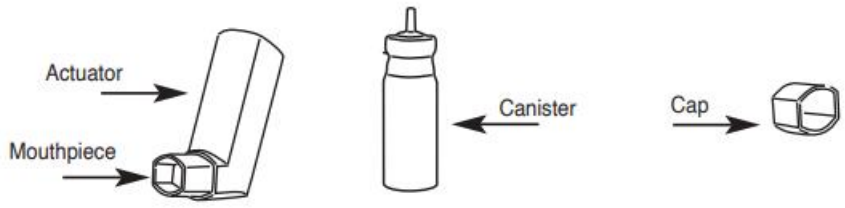
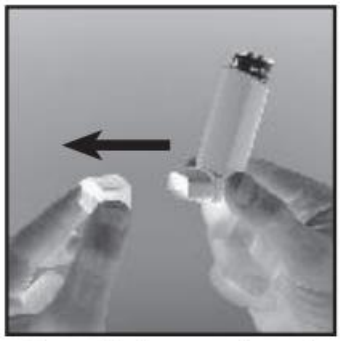
HOW TO USE YOUR INHALER CORRECTLY





1. Remove the mouthpiece cover by gently squeezing the sides of the cover.

2. Check inside and outside of the inhaler including the mouthpiece for the presence of loose objects.

3. Shake the inhaler well to ensure any loose objects are removed and the contents of the inhaler are evenly mixed.

4. Hold the inhaler upright between fingers and thumb with your thumb on the base, below the mouthpiece.

5. Breathe out as far as is comfortable and then place the mouthpiece in your mouth between your teeth and close your lips around it but do not bite it.

6. Just after starting to breathe in through your mouth press down on the top of the inhaler to release AZMASOL while still breathing in steadily and deeply.

7. While holding your breath, take the inhaler from your mouth and take your finger from the top of the inhaler. Continue holding your breath for as long as is comfortable.

8. If you are to take further puffs keep the inhaler upright and wait about half a minute before repeating steps three to seven.

9. Replace the mouthpiece cover by firmly pushing and snapping the cap into position.

Cleaning your Inhaler

Keeping the plastic actuator clean is very important to prevent medicine build up and blockage. The actuator should be washed, shaken to remove excess water and air-dried thoroughly at least once a week. The inhaler may stop spraying if not properly cleaned.

Shake well the inhaler before each use

A handy tip for Children

Children and others who have weaker hands may have difficulty pressing down on the top of the can with just one hand. They can use both hands to make their Inhaler work.

How to clean your Inhaler?

1. Remove the metal canister from the plastic casing of the inhaler and remove the mouth piece cover.
2. Rinse the actuator thoroughly with warm water.
3. Dry the actuator thoroughly inside and outside.
4. Replace the metal canister and the mouth piece cover
5. Do not put the metal canister in water.

Your Inhaler should be cleaned at least once a week