PACKAGE INSERT FOR

ASTHAVENT ECOHALER

SCHEDULING STATUS:

S2

PROPRIETARY NAME (AND DOSAGE FORM):

ASTHAVENT ECOHALER (Metered dose inhaler)

COMPOSITION:

Each actuation contains salbutamol sulphate 100 µg.

The inhaler also contains the non-CFC propellant 1,1,1,2-tetrafluoroethane.

PHARMACOLOGICAL CLASSIFICATION:

A 10.2.1 Inhalants.

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Salbutamol is a direct-acting sympathomimetic agent, a highly selective β_2-adrenergic agonist that activates the pulmonary receptors to relax the bronchial smooth muscle and decrease airway resistance. Evidence suggests that salbutamol may inhibit the release of leukotrienes and histamines from the mast cells in the pulmonary tissue, that it may enhance mucociliary function, decrease microvascular permeability and inhibit phospholipase A_2. Bronchodilation is produced within 5 to 15

minutes after inhalation, with near maximal bronchodilatation occurring within five minutes, and with therapeutic effects lasting for 4 to 6 hours. In therapeutic doses, salbutamol has minimal effect on the cardiovascular system and less skeletal muscle tremor than that associated with oral therapy.

Pharmacokinetic properties:

Absorption and distribution:

The systemic absorption of inhaled salbutamol is low and it has been suggested that the majority of an inhaled dose is swallowed and absorbed from the gastrointestinal tract and excreted in the urine.

The therapeutic effect of inhaled salbutamol is dependent on direct stimulation of receptors in the lungs. After administration by the inhaled route between 10 and 20 % of the dose reaches the lower airways.

Salbutamol is bound to plasma proteins to the extent of 10 %.

Metabolism and elimination:

The fraction deposited in the airways is absorbed into the pulmonary tissues and circulation, but is not metabolised by the lung. On reaching the systemic circulation, it becomes accessible to hepatic metabolism and is excreted, primarily in the urine, as unchanged medicine and as the phenolic sulphate.

The swallowed portion of an inhaled dose is absorbed from the gastrointestinal tract

and undergoes considerable first-pass metabolism to the phenolic sulphate. Both unchanged salbutamol and conjugate are excreted primarily in the urine. Most of a dose of salbutamol given by inhalation is excreted within 72 hours.

INDICATIONS:

ASTHAVENT ECOHALER is indicated:

- For the treatment and prophylaxis of reversible obstructive pulmonary diseases, such as bronchial asthma, chronic bronchitis and emphysema.
- For the treatment of acute bronchospasm.
- For the prevention of exercise-induced bronchospasm.

CONTRAINDICATIONS:

ASTHAVENT ECOHALER is contraindicated in:

- Patients with hypersensitivity to salbutamol, or any of the components of **ASTHAVENT ECOHALER**.
- Combination with propranolol and other beta-adrenoceptor blocking agents, as these medicines antagonise the effects of salbutamol, as in **ASTHAVENT ECOHALER**, and should not be prescribed together (see **"INTERACTIONS"**).
- Patients receiving mono-amine oxidase inhibitors, or within 14 days after termination of such therapy.
- Pregnancy and lactation, as adequate and well-controlled studies have not been done (see **"PREGNANCY AND LACTATION"**).

WARNINGS:

If difficulty in breathing persists, or if the condition deteriorates, or if more inhalations than usual are needed to relieve an acute attack, a medical practitioner should be consulted immediately (see **"Special Precautions"**).

ASTHAVENT ECOHALER has been found to be suitable for the relief of bronchospasm in patients with co-existing heart disease, but caution is advised (see **"Special Precautions"**).

ASTHAVENT ECOHALER is not appropriate for managing premature labour. **ASTHAVENT ECOHALER** should not be used for threatened abortion.

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma. Severe asthma requires regular medical assessment as the condition is potentially life-threatening. Patients with severe asthma have constant symptoms and frequent exacerbations, with limited physical capacity, and PEF values below 60 % predicted at baseline with greater than 30 % variability, usually not returning entirely to normal after a bronchodilator. These patients will require high dose inhaled or oral corticosteroid therapy. With this primary background corticosteroid treatment, **ASTHAVENT ECOHALER** provides essential rescue medication for a severe asthmatic in treating acute exacerbations. Failure to respond promptly or fully to such rescue medication signals a need for urgent medical advice and treatment.

INTERACTIONS:

Extreme caution is advised when beta-adrenergic blocking agents, such as propranolol, are prescribed to patients using **ASTHAVENT ECOHALER**, as beta-blockage may antagonise the bronchodilating effect of **ASTHAVENT ECOHALER**, and may in fact induce bronchospasm (see **"CONTRAINDICATIONS"**).

The concomitant use of xanthine derivatives, steroids and diuretics may potentiate the possible hypokalaemic effect of **ASTHAVENT ECOHALER** in patients suffering from acute severe asthma (see **"Special Precautions"**). The risk of hypokalaemia may be increased in the presence of hypoxia and acidosis. The serum potassium levels should be monitored in such situations.

ASTHAVENT ECOHALER should be used with caution in patients undergoing anaesthesia with cyclopropane, halothane or other halogenated anaesthetics. The concurrent use of these medicines may cause ventricular fibrillation.

The risk of dysrhythmias may be increased with the concurrent use of cardiac glycosides, quinidine and tricyclic antidepressants.

Caution is advised when **ASTHAVENT ECOHALER** is prescribed to patients who have received large doses of other sympathomimetic agents.

ASTHAVENT ECOHALER should be used 5 minutes prior to the administration of adrenocorticoid or ipratropium inhalations, unless otherwise directed by a medical practitioner.

PREGNANCY AND LACTATION:

Safety during pregnancy and lactation has not been established (see **"CONTRAINDICATIONS"**).

DOSAGE AND DIRECTIONS FOR USE:

FOR ORAL INHALATION ONLY. SHAKE WELL BEFORE USE.

Read the instructions carefully.

Avoid contact with the eyes.

Do not exceed the recommended dose. The frequency and the dosage should only be increased if so advised by a medical practitioner.

Advise patients to rinse the mouth with water after each inhalation to help prevent dryness of the mouth and throat.

ASTHAVENT ECOHALER acts rapidly and may be used when necessary to relieve attacks of acute dyspnoea. Doses may be taken prophylactically before exertion to prevent exercise-induced asthma.

Adults:

Acute bronchospasm:	1 or 2 inhalations (100 – 200 µg salbutamol) as a single dose.

Chronic bronchospasm:	1 or 2 inhalations (100 – 200 µg salbutamol) 3 – 4 times daily.
Exercise-induced bronchospasm:	2 inhalations (200 µg salbutamol) 15 minutes before exercise.

Warning:

If more than one inhalation is needed per day, it is recommended that additional treatment with an inhaled corticosteroid be considered (see **"Special Precautions"**). Advise patients to consult a doctor if a previous inhalation is effective for less than 3 hours (see **"Special Precautions"**).

Children (over 12 years):

Acute bronchospasm:	1 inhalation (100 µg salbutamol) 3 or 4 times daily.
Episodic or exercise-induced asthma:	1 inhalation (100 µg salbutamol) 15 minutes before exercise.
Routine maintenance or prophylaxis:	1 inhalation (100 µg salbutamol) 3 or 4 times daily. Increase to 2 inhalations (200 µg salbutamol) 3 or 4 times daily if necessary.

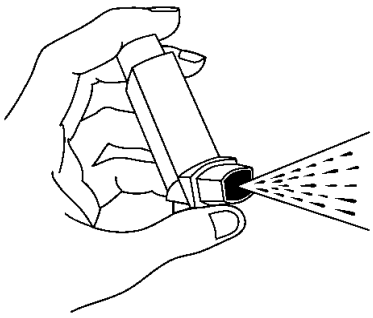
<u>How to use ASTHAVENT ECOHALER correctly:</u>

Important:

Follow instructions carefully.

Before using ASTHAVENT ECOHALER for the first time:

1. Remove the cap / cover from the mouthpiece and ensure that the mouthpiece is clean.
2. Hold the inhaler away from the face. Shake it well and release two puffs into the air.

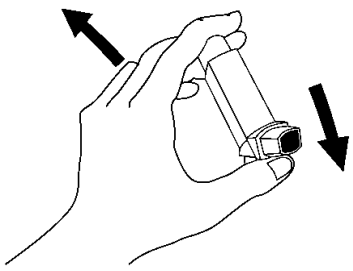


3. **ASTHAVENT ECOHALER** is now ready for use.

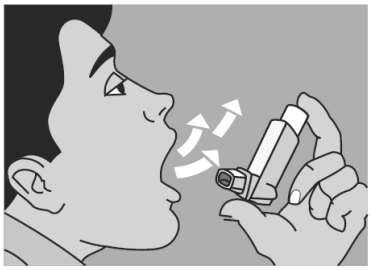
If the inhaler has not been used for a week or more, shake well and release one puff into the air.

Using ASTHAVENT ECOHALER:

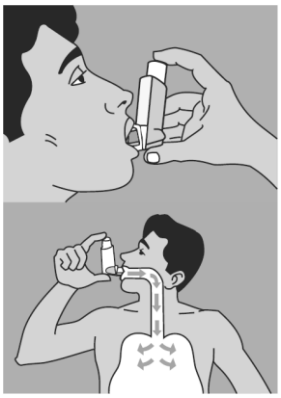
1. Sit or stand upright. Remove the mouthpiece cap / cover and shake **ASTHAVENT ECOHALER** well. Hold it upright as shown, with the thumb at the base below the mouthpiece. Place either one or two fingers on top of the canister.



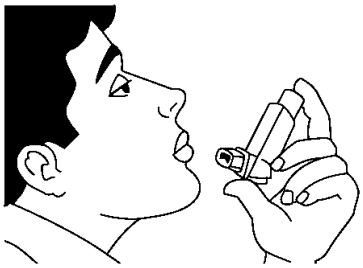
2. **Breathe out fully**, through the mouth.



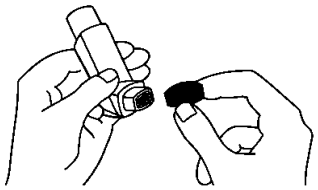
3. Place the mouthpiece of the inhaler in the mouth between the teeth and close the lips around it (do not bite it). **Start to breathe in slowly through the mouth. Press the canister down firmly and fully to release one spray while continuing to breathe in slowly and deeply.**



4. Remove **ASTHAVENT ECOHALER** from the mouth and hold the breath for at least 10 seconds, or as long as it is comfortable. Breathe out normally.

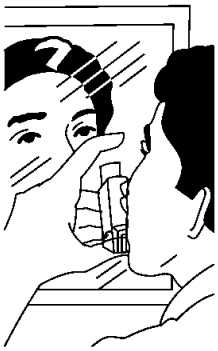


5. If another dose is required, wait for at least one minute. Shake **ASTHAVENT ECOHALER** well and repeat steps 2 to 4. After use, replace the mouthpiece cap / cover firmly and snap it into position.

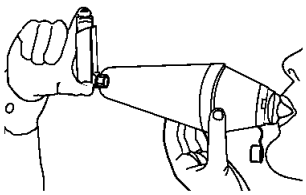


NOTE:

Do not rush stages 2, 3 and 4. It is important to breathe in slowly through the mouth, just before pressing the canister. To ensure proper use of **ASTHAVENT ECOHALER**, patients may initially practice these steps in front of a mirror until they are comfortable with the technique. If there is 'mist' escaping from the inhaler or the sides of the mouth, start again from step 1. This escaping mist indicates incorrect technique.

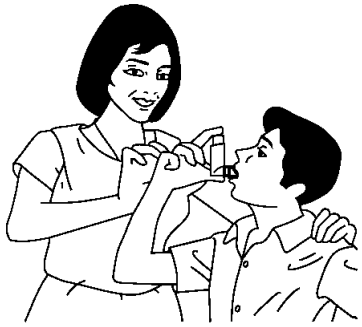


If the patient finds it difficult to use the device correctly, they may use a spacer device along with ASTHAVENT ECOHALER.

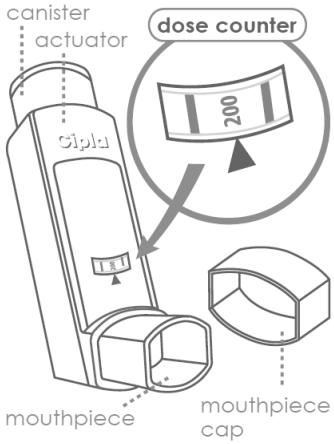


For children:

Parents must assist those children who need help in using the **ASTHAVENT ECOHALER** correctly with/without a spacer.



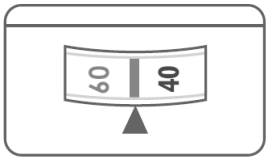
Dose counters:



ASTHAVENT ECOHALER containing 200 doses has a dose counter. It shows the number of puffs in the inhaler. As the patient uses the inhaler, the dose counter will countdown and indicate the number of remaining puffs.

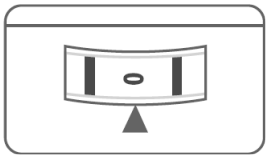
When the ASTHAVENT ECOHALER is nearly empty:

When there are 40 puffs remaining, the colour of the numbers will change from green to red.



This indicates that there are 40 or fewer puffs left in the **ASTHAVENT ECOHALER**. The patient should now obtain a new **ASTHAVENT ECOHALER**.

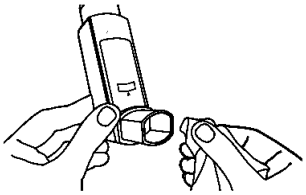
When the dose counter displays ‘0’, it means that there is no medicine left in the **ASTHAVENT ECOHALER** and the patient should discard it. The **ASTHAVENT ECOHALER** may not feel empty and it may continue to operate, but the patient will not receive the correct amount of medicine if he/she continues to use this canister.



Cleaning ASTHAVENT ECOHALER:

It is important to keep **ASTHAVENT ECOHALER** clean. Clean **ASTHAVENT ECOHALER** at least once a week.

1. Remove the mouthpiece cap / cover. **DO NOT take the metal canister out of the actuator.**
2. Wipe the inside and the outside of the mouthpiece with a clean, dry cloth.
3. Replace the mouthpiece cap / cover.
4. **DO NOT wash or soak any part of ASTHAVENT ECOHALER in water.**



DO NOT:

- Spray **ASTHAVENT ECOHALER** in the eyes.
- Exceed the recommended dose.
- Change / tamper with the numbers on the dose counter.
- Puncture or burn **ASTHAVENT ECOHALER**, even when empty, as it is pressurised.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Side-Effects:

Immune system disorders:

Less frequent:	Hypersensitivity reactions, including angioedema, urticaria, bronchospasm, hypotension, and collapse.

Metabolism and nutrition disorders:

Less frequent:	Hypokalaemia (see **"Special Precautions"**).
Frequency unknown:	Altered metabolism, reduced appetite, sweating.

Psychiatric disorders:

Less frequent:	Hyperactivity (in children).
Frequency unknown:	Nervousness, fear, insomnia, tenseness.

Nervous system disorders:

Frequent:	Tremor (see **"Special Precautions"**), headache.
Frequency unknown:	Dizziness, confusion, light-headedness.

Cardiac disorders:

Frequent:	Tachycardia.
Less frequent:	Palpitations, cardiac dysrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles).
Frequency unknown:	Myocardial ischaemia (see **"Special Precautions"**).

Vascular disorders:

Less frequent:	Peripheral vasodilatation (with compensatory small increase in heart rate).

Respiratory, thoracic and mediastinal disorders:

Less frequent:	Paradoxical bronchospasm (see **"Special Precautions"**).
Frequency unknown:	Dyspnoea, coughing.

Gastrointestinal disorders:

Less frequent: Dryness and irritation of the mouth and throat.

Frequency unknown: Hypersalivation, nausea and vomiting.

Musculoskeletal, connective tissue and bone disorders:

Less frequent: Muscle cramps.

Renal and urinary disorders:

Frequency unknown: Difficulty in micturition, urinary retention.

Special Precautions:

The excessive use of **ASTHAVENT ECOHALER** may lead to life-threatening cardiac arrest following the development of severe acute crisis and subsequent hypoxia. **It is important to avoid the excessive use of ASTHAVENT ECOHALER.**

Patients with underlying severe heart disease (e.g. ischaemic heart disease, dysrhythmia or severe heart failure) who are receiving **ASTHAVENT ECOHALER** 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.

If difficulty in breathing persists, or if the condition deteriorates, or if more inhalations than usual are needed to relieve an acute attack, a medical practitioner should be consulted (see **"WARNINGS"** and **"DOSAGE AND DIRECTIONS FOR USE"**).

Caution is advised when **ASTHAVENT ECOHALER** is prescribed to patients suffering from thyrotoxicosis.

The risk versus benefit should be considered when prescribing **ASTHAVENT ECOHALER** to patients suffering from cardiac dysrhythmias, coronary insufficiency, hypertension or ischaemic heart disease.

ASTHAVENT ECOHALER may cause a fine tremor of skeletal muscle, usually the hands are most obviously affected (see **"Side-Effects"**). This effect is dose-related.

Paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing (see **"Side-Effects"**). This should be treated immediately with an alternative presentation of salbutamol, or a different fast-acting inhaled bronchodilator. In this instance **ASTHAVENT ECOHALER** should be discontinued immediately, the patient assessed, and if necessary, alternative therapy instituted.

The management of asthma should normally follow a stepwise programme and patient response should be monitored clinically and by lung function tests. Increasing use of **ASTHAVENT ECOHALER** to control symptoms indicates deterioration of asthma control (see **"WARNINGS"** and **"DOSAGE AND DIRECTIONS FOR USE"**).

Under these conditions, the patient's therapy plan should be reassessed. Sudden and progressive deterioration in asthma control is potentially life-threatening and consideration should be given to starting or increasing corticosteroid therapy. In patients considered at risk, daily peak flow monitoring may be instituted.

In the event of a previously effective dose of **ASTHAVENT ECOHALER** failing to give relief for at least three hours, the patient should be advised to seek medical advice in order that any necessary additional steps may be taken (see **"DOSAGE AND DIRECTIONS FOR USE"**).

Patients' inhaler technique should be checked to make sure that aerosol actuation is synchronised with inspiration of breath for optimum delivery of the medicine to the lungs (see **"DOSAGE AND DIRECTIONS FOR USE"**).

Potentially serious hypokalaemia may result from **ASTHAVENT ECOHALER** therapy (see **"Side-Effects"**). 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 (see **"INTERACTIONS"**). It is recommended that serum potassium levels are monitored in such situations.

Overdosage may cause cardiac effects (see **"Side-Effects"**). High dosages may increase the risk of serious side-effects, including cardiac dysrhythmias. The risk is further aggravated if administered concomitantly with other medicines that cause

hypokalaemia and cardiac dysrhythmias, or in the presence of hypoxia and acidosis. The maximum dose should not be exceeded.

Although no geriatric specific problems have been reported to date, older patients may be more sensitive to the side-effects of **ASTHAVENT ECOHALER**.

Effects on ability to drive and operate machinery:

None reported.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

The most frequent signs and symptoms of overdose with salbutamol, as in **ASTHAVENT ECOHALER**, are transient beta-agonist pharmacologically mediated events, including tachycardia, tremor, hyperactivity and metabolic effects including hypokalaemia (see **"SIDE-EFFECTS AND SPECIAL PRECAUTIONS"**). Serum potassium levels should be monitored.

Consideration should be given to discontinuation of treatment and appropriate symptomatic therapy, such as cardioselective beta-blocking agents in patients presenting with cardiac symptoms (e.g. tachycardia, palpitations), but should be used with caution in patients with a history of bronchospasm.

IDENTIFICATION:

A white, homogenous suspension aerosol for inhalation, in propellant HFA-134a, supplied in an aluminium pressurised container fitted with a metered dispensing valve attached to a mouthpiece.

PRESENTATION:

Carton containing a metered dose inhaler with 200 or 300 doses of salbutamol 100 µg each, supplied in an aluminium pressurised container with 'SHAKE WELL BEFORE USE" embossed on the base, fitted with a metered dispensing valve attached to a mouthpiece.

The 200 MD ASTHAVENT ECOHALER is available with or without a dose counter.

STORAGE INSTRUCTIONS:

Store in well-closed containers at or below 30 °C, protected from direct sunlight. Do not freeze. Do not puncture, break or burn, even when apparently empty.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

34/10.2.1/0354

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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