1.3.1 Summary of Product Characteristics (SmPC)

Summary of Product Characteristics (SPC)

Azmasol® HFA Inhalation Aerosol

1. Name of the medicinal product

Azmasol® HFA Inhalation Aerosol

2. Qualitative and quantitative composition

Azmasol® HFA Inhalation Aerosol is a pressurised metered-dose inhaler delivering 100 micrograms of salbutamol (as Salbutamol Sulphate BP) per actuation. Azmasol® HFA Inhaler contains a new propellant (HFA 134a) and does not contain any chlorofluorocarbons.

3. Pharmaceutical form

Pressurized Inhalation Aerosol

4. Clinical particulars

4.1 Therapeutic indications

Azmasol® HFA Inhalation Aerosol is indicated in adults, adolescents and children aged 4 to 11 years. For babies and children under 4 years of age, see sections 4.2 and 5.1.

Azmasol® HFA Inhalation Aerosol provides short-acting (4 to 6 hour) bronchodilation with fast onset (within 5 minutes) in reversible airways obstruction.

It is particularly suitable for the relief and prevention of asthma symptoms. It 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® HFA Inhalation Aerosol 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.

4.2 Posology and method of administration

Azmasol® HFA Inhalation Aerosol is for oral inhalation use only. Azmasol® HFA Inhalation

Adults (including the elderly): For the relief of acute asthma symptoms including bronchospasm, one inhalation (100 micrograms) may be administered as a single minimum starting dose. This may be increased to two inhalations if necessary. To prevent allergen- or exercise-induced symptoms, two inhalations should be taken 10-15 minutes before challenge.

For chronic therapy, two inhalations up to four times a day.

Paediatric Population

Relief of acute bronchospasm

The usual dosage for children under the age of 12 years: one inhalation (100 micrograms). The dose may be increased to two inhalations if required.

Children aged 12 years and over: Dose as per adult population.

Prevention of allergen or exercise-induced bronchospasm

The usual dosage for children under the age of 12 years: one inhalation (100 micrograms) before challenge or exertion. The dose may be increased to two inhalations if required.

Children aged 12 years and over: Dose as per adult population.

Chronic therapy

The usual dosage for children under the age of 12 years: up to two inhalations 4 times daily.

Children aged 12 years and over: Dose as per adult population.

The spacer device may be used to facilitate administration to children under 5 years of age.

On-demand use of Azmasol® HFA Inhalation Aerosol should not exceed 8 inhalations in any 24 hours. Reliance on such frequent supplementary use, or a sudden increase in dose, indicates poorly controlled or deteriorating asthma (see section 4.4).

4.3 Contraindications

Although intravenous salbutamol, and occasionally salbutamol tablets, are used in the management of premature labour uncomplicated by conditions such as placenta praevia, ante-partum haemorrhage or toxaemia of pregnancy, inhaled salbutamol preparations are not appropriate for managing premature labour. Salbutamol preparations should not be used for threatened abortion.

Azmasol® HFA Inhalation Aerosol is contra-indicated in patients with a history of hypersensitivity to any of the components.

4.4 Special warnings and precautions for use

Patients inhaler technique should be checked to make sure that aerosol actuation is synchronised with inspiration of breath for optimum delivery of drug to the lungs. Patients should be warned that they may experience a different taste upon inhalation compared to their previous inhaler.

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 patients are at risk of severe attacks and even death. Physicians should consider using the maximum recommended dose of inhaled corticosteroid and/or oral corticosteroid therapy in these patients.

The dosage or frequency of administration should only be increased on medical advice. If a previously effective dose of inhaled salbutamol fails to give relief lasting at least three hours, the patient should be advised to seek medical advice.

Increasing use of bronchodilators, in particular short-acting inhaled β2-agonists, to relieve symptoms, indicates deterioration of asthma control. The patient should be instructed to seek medical advice if short-acting relief bronchodilator treatment becomes less effective, or more inhalations than usual are required. In this situation the patient should be assessed and consideration given to the need for increased anti-inflammatory therapy (e.g. higher doses of inhaled corticosteroid or a course of oral corticosteroid).

Severe exacerbations of asthma must be treated in the normal way.

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.

Salbutamol should be administered cautiously to patients with thyrotoxicosis.

Potentially serious hypokalaemia may result from β2-agonist therapy, mainly from parenteral and nebulised administration. Particular caution is advised in acute severe asthma as this effect may be potentiated by hypoxia and by concomitant treatment with xanthine derivatives, steroids and diuretics. Serum potassium levels should be monitored in such situations.

4.5 Interaction with other medicinal products and other forms of interaction

Salbutamol and non-selective β-blocking drugs such as propranolol, should not usually be prescribed together.

4.6 Pregnancy and lactation

Studies in animals have shown reproductive toxicity (see section 5.3). 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. Azmasol® HFA Inhalation Aerosol should not be used during pregnancy unless clearly necessary.

As salbutamol is probably secreted 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 is likely to outweigh any potential risk to the neonate.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

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) and very rare (<1/10,000) including isolated reports. Very common and common events were generally determined from clinical trial data. Rare, very rare and unknown events were generally determined from spontaneous data.

Immune system disorders

Very rare:

Hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse.

Metabolism and nutrition disorders

Rare:

Hypokalaemia.

Potentially serious hypokalaemia may result from beta2 agonist therapy.

Nervous system disorders

Common:

Tremor, headache.

Very rare:

Hyperactivity.

Cardiac disorders

Common:

Tachycardia.

Uncommon:

Palpitations.

Very rare:

Cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles).

Unknown:

Myocardial ischaemia* (see section 4.4)

Vascular disorders

Rare:

Peripheral vasodilatation.

Respiratory, thoracic and mediastinal disorders

Very rare:

Paradoxical bronchospasm.

As with other inhalation therapy, paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. This should be treated immediately with an alternative presentation or a different fast-acting inhaled bronchodilator. Azmasol® HFA Inhalation Aerosol should be discontinued immediately, the patient assessed, and, if necessary, alternative therapy instituted.

Gastrointestinal disorders

Uncommon:

Mouth and throat irritation.

Musculoskeletal and connective tissue disorders

Uncommon:

Muscle cramps.

* reported spontaneously in post-marketing data therefore frequency regarded as unknown

4.9 Overdose

The most common signs and symptoms of overdose with salbutamol are transient beta agonist pharmacologically mediated events, including tachycardia, tremor, hyperactivity and metabolic effects including hypokalaemia (see sections 4.4 and 4.8).

Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored.

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

5. Pharmacological properties

5.1 Pharmacodynamic properties

Salbutamol is a selective β2-adrenoceptor agonist. At therapeutic doses it acts on the β2-adrenoceptors of bronchial muscle providing short acting (4-6 hour) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction.

Special Patient Populations

Children < 4 years of age

Paediatric clinical studies conducted at the recommended dose (SB020001, SB030001, SB030002), in patients < 4 years with bronchospasm associated with reversible obstructive airways disease, show that Salbutamol HFA Inhalation Aerosol has a safety profile comparable to that in children ≥ 4 years, adolescents and adults.

5.2 Pharmacokinetic properties

Salbutamol administered intravenously has a half life of 4 to 6 hours and is cleared partly renally and partly by metabolism to the inactive 4'-O-sulphate (phenolic sulphate) which is also excreted primarily in the urine. The faeces are a minor route of excretion.

After administration by the inhaled route between 10 and 20% of the dose reaches the lower airways. The remainder is retained in the delivery system or is deposited in the oropharynx from where it is swallowed. 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 drug 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 drug and conjugate are excreted primarily in the urine. Most of a dose of salbutamol given intravenously, orally or by inhalation is excreted within 72 hours. Salbutamol is bound to plasma proteins to the extent of 10%.

5.3 Preclinical safety data

In common with other potent selective β2-agonists, salbutamol has been shown to be teratogenic in mice when given subcutaneously. In a reproductive study, 9.3% of fetuses were found to have cleft palate at 2.5mg/kg dose. In rats, treatment at the levels of 0.5, 2.32, 10.75 and 50mg/kg/day orally throughout pregnancy resulted in no significant fetal abnormalities. The only toxic effect was an increase in neonatal mortality at the highest dose level as the result of lack of maternal care. Reproductive studies in the rabbit at doses of 50mg/kg/day orally (i.e. much higher than the normal human dose) have shown fetuses with treatment related changes; these included open eyelids (ablepharia), secondary palate clefts (palatoschisis), changes in ossification of the frontal bones of the cranium (cranioschisis) and limb flexure. Reformulation of the Ventolin Evohaler has not altered the known toxicological profile of salbutamol.

The non-CFC propellant, HFA 134a, has been shown to have no toxic effect at very high vapour concentrations, far in excess of those likely to be experienced by patients, in a wide range of animal species exposed daily for periods of two years.

6. Pharmaceutical particulars

6.1 List of excipients

Oleic Acid (Vegetable Source)

Dehydrated Alcohol

1,1,1,2-Tetrafluoroethane (HFA 134a)

6.2 Incompatibilities

None reported.

6.3 Shelf life

24 months when stored below 30°C.

6.4 Special precautions for storage

Store below 30°C (86°F).

Protect from frost and direct sunlight.

As with most inhaled medications in aerosol canisters, the therapeutic effect of this medication may decrease when the canister is cold.

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

Replace the mouthpiece cover firmly and snap it into position.

6.5 Nature and contents of container

An inhaler comprising an aluminium alloy can sealed with a metering valve, actuator and dust cap. Each canister contains 200 metered actuations providing 100 micrograms of salbutamol (as Salbutamol Sulphate BP).

6.6 Special precautions for disposal and other handling

The aerosol spray is inhaled through the mouth into the lungs. After shaking the inhaler, the mouthpiece is placed in the mouth and the lips closed around it. The actuator is depressed to release a spray, which must coincide with inspiration of breath.

For detailed instructions for use refer to the Patient Information Leaflet in every pack.

7. Marketing authorisation holder

BEXIMCO PHARMACEUTICALS LTD.

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8. Manufacturer

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