NATIONAL AGENCY FOR FOOD &

DRUG ADMINISTRATION & CONTROL

(NAFDAC)

Registration & Regulatory Affairs

(R&R)

Directorate

Product Name

AEROLINE INHALER
(Salbutamol 100mcg/actuation as Salbutamol Sulfate BP)

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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1. Name of Medicinal Product

Aeroline Inhaler

2. Qualitative and Quantitative Composition

Each actuation contains:

Salbutamol Sulfate, micronized (Eq. to Salbutamol base 100mg)	120.5mcg
Ethanol	4.165mg
Oleic acid	11.25mcg
Norflurane	71.54mg

No overages are used for this product. But considering when the product is close to use up, the residual liquid in the container cannot be delivered out, we overfill about 40 deliveries in addition to the labeled 200 deliveries per container, so as to ensure the labeled number of the product can be realized. The concentration of drug substance in each actuation won't be affected though the number of delivers per inhaler is designed as 240 doses.

3. Pharmaceutical Form

Oral Inhalation Aerosol

4. Clinical Particulars

4.1 Therapeutic indications

AEROLINE Inhaler is used to treat acute bronchospasm in asthma, prevent asthma (bronchospasm prophylaxis) following exercise or induced by allergies, relief wheezing and shortness of breath caused by certain other chest diseases, and also treat bronchospasm associated reversible obstructive airway disease including emphysema and chronic bronchitis. Aeroline Inhaler is known as a 'reliever'. You may be using another medicine such as regular inhaled corticosteroids to prevent you from having an asthma attack (a 'preventer'). You can safely use your preventer with your AEROLINE Inhaler.

4.2 Posology and method of administration

Aeroline inhaler is for oral inhalation use only. The patient should always use this medicine as advice by the doctor. Reliance on frequent supplementary use above 8 inhalations in any 24 hours, or sudden increase in dose, indicates poorly controlled or deteriorating asthma. The patient should inform the doctor if this medicine does not seem to be working as well as usual, as the chest problem may be getting worse and s/he may need a different medicine.

<u>Adults (including elderly) and adolescents aged 12 years and over:</u>

- To relieve asthma - One or two puffs.
- To prevent asthma - Two puffs 10-15 minutes before exercise or exposure to a "trigger".

~ For regular treatment - Two puffs up to 4 times a day.
~ The maximum dose is 8 puffs in a 24 hour period.

Children under 12 years of age:

~ To relieve asthma - One puff. Two puffs if required.
~ To prevent asthma - One puff 10-15 minutes before exercise or exposure to a "trigger". Two puffs if required.
~ For regular treatment - Two puffs up to 4 times a day.
~ The maximum dose is 8 puffs in a 24 hour period.
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4.3 Contraindications

Hypersensitivity to salbutamol sulfate and/or any of the listed excipients. Aeroline Inhaler must not be used to manage uncomplicated premature labour or threatened abortion.

4.4 Special warnings and precautions for use

The doctor, nurse or pharmacist should be informed before taking Aeroline inhaler if the patient:

~ Has active or severe asthma (e.g. frequent symptoms or flare ups or limited physical ability). There may be a need to start or increase a medicine to control your asthma such as an inhaled corticosteroid.
~ Has high blood pressure
~ Has an overactive thyroid gland
~ Has a history of heart problems or disease such as an irregular or fast heartbeat or angina,
~ Have heart problems (poor blood flow to the heart, high blood pressure, heart failure, etc)
~ Is taking xanthine derivatives (such as theophylline) or steroids to treat asthma.
~ Is taking water tablets (diuretics), sometimes used to treat high blood pressure or a heart condition
~ Have diabetes

Aeroline Inhaler should not be stopped without informing a doctor.

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 with Aeroline inhaler. Other drugs known to interact with this medication include:

~ Medicines used to treat high blood pressure known as guanethidine and methyldopa;
~ Reserpine (used to treat psychosis or high blood pressure);
~ Antidepressants known as monoamine oxidase inhibitors (MAOIs) such as moclobemide;
~ Medicines for depression known as tricyclic antidepressants;
~ Medicine used to treat heart problems known as digoxin;
~ Medicines known as xanthines e.g. aminophylline or theophylline;
~ Steroids;

- ~ Water tablets (diuretics);
- ~ Laxatives.
- ~ Some anesthetics

4.6 Fertility, pregnancy and lactation

No adverse effects on fertility of animals have been reported. Also, there is no information on the effects of salbutamol in human fertility. Salbutamol is secreted in breast milk. Harmful effects on neonates have not been reported. Also, safety in pregnant women has not been established as no controlled clinical trials with salbutamol have been conducted in pregnant women. Rare reports of congenital abnormalities including cleft palate, limb defects and cardiac disorders have been reported though some of the mothers were taking multiple medications during pregnancy. Because no consistent pattern of defects can be discerned, a relationship between salbutamol use and congenital anomalies has not been established. Aeroline inhaler use should be restricted to situations where it is felt that the expected benefit to the nursing mother or pregnant woman is likely to outweigh any potential risk to the neonate or fetus.

4.7 Effects on ability to drive and use machines

None reported

4.8 Undesirable effects

Adverse experiences reported with Salbutamol includes an allergic reaction (swelling of the lips, face or neck leading to severe difficulty in breathing; low blood pressure leading to collapse; skin rash or hives) which is a very serious but rare side effect that may need urgent medical attention or hospitalization. Chest pain or symptoms of your heart disease worsening is possible if a patient is suffering from a heart disease which may require urgent report to the nearest hospital. Common (affecting more than one person in one hundred but fewer than one person in ten) include mild tremor (shaking), headache, dizziness, and tenseness (in the beginning of treatment). Rare (affecting more than one person in ten thousand but fewer than one person in one thousand) include throat irritation, mouth irritation or sore mouth, tachycardia (fast heart rate) or palpitations, muscle cramps, hyperactivity in children, being or feeling sick or vomiting, widening of blood vesssels, low potassium levels or increased serum lactate levels in your blood. A doctor may wish to run regular blood tests to check the blood potassium levels. Very rare side effects (affecting fewer than one person in ten thousand) include trouble sleeping and changes in the way the heart beats.

4.9 Overdose

The expected symptoms with overdosage are those of excessive beta-adrenergic stimulation and/or occurrence or exaggeration of any of the symptoms listed of adverse reactions, e.g., seizures, angina, hypertension or hypotension, tachycardia with rates up to 200 beats per minute, arrhythmias, nervousness, headache, tremor, dry mouth, palpitation, nausea, dizziness, fatigue, malaise, and insomnia.

Hypokalemia may also occur. As with all sympathomimetic medications, cardiac arrest and even death may be associated with abuse of salbutamol. Treatment consists of discontinuation of salbutamol together with appropriate symptomatic therapy. The judicious use of a cardio-selective beta-receptor blocker may be considered, bearing in mind that such medication can produce bronchospasm. There is insufficient evidence to determine if dialysis is beneficial for overdosage of salbutamol

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.

If more puffs are accidentally taken than advised by the doctor (and symptoms appear), then the nearest hospital casualty department or doctor should be contacted immediately.

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Salbutamol is a selective β_2-adrenoceptor agonist which at therapeutic doses acts on the β_2-adrenoceptors of the bronchial muscles providing short acting (4-6 hours) bronchodilation with a fast onset (1-5minutes) in reversible airways obstruction. The mechanism of the antiasthmatic action of salbutamol is linked to the direct relaxation of airway smooth muscle and consequent bronchodilation. Salbutamol has an onset of action within 1 to 5 minutes and produces bronchodilation that lasts for about 2 to 6. The safety profile is comparable across all ages.

5.2 Pharmacokinetic properties

Following administration by the oral inhalation 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 metabolized by the lungs. On reaching the systemic circulation it becomes accessible to hepatic metabolism and is excreted, primarily in the urine, as unchanged drug and as the inactive 4'-O-sulphate (phenolic sulfate). The swallowed portion of the inhaled dose is absorbed from the gastrointestinal tract and undergoes considerable first-pass metabolism to the phenolic sulfate. Both unchanged drug and conjugate are excreted primarily in the urine. The faeces are a minor route of excretion. Most of the dose of salbutamol given by the oral inhalation route is excreted within 72hours. Salbutamol is bound to plasma proteins to the extent of 10% and has a half-life of 4 to 6 hours.

5.3 Preclinical safety data

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 the result of lack of maternal care. Reproductive studies in rabbit at doses of 50mg/kg/day (i.e. much higher than the normal human dose) have shown fetuses with treatment related changes; these include open eyelids, secondary palate clefts, changes in ossification of the frontal bones of the cranium, and limb flexure. In an oral fertility and general reproductive performance study in rats at doses of 2 and 50mg/kg/day, with the exception of a reduction in number of weanlings surviving to day 21 post partum at 52mg/kg/day, there were no adverse effects on fertility , embryofetal development , litter size, birth weight or growth rate.

6. Pharmaceutical Particulars

6.1 List of excipients

Ethanol
Oleic acid
Norflurane

6.2 Incompatibilities

None reported

6.3 Shelf life

36 months when stored below 30^{o}C

6.4 Special precautions for storage

Store below 30oC, protected from frost and direct sunlight. Cold may decrease the therapeutic effect of this drug product. The aluminium canister should not be broken, punctured or burnt, even when apparently empty.

6.5 Nature and contents of container

This product is contained in an aluminium canister with a metered-dose valve system. Each canister contains at least 200 metered actuations providing 100 micrograms of salbutamol (as albutamol sulfate BP). Each canister is further packed in a paper carton.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorisation Holder

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8. Marketing Authorisation Number(s)

To be allocated

9. Date of First Authorisation/Renewal of the Authorisation

To be allocated

10. Date of Revision of the Text

To be allocated