# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Novolizer Salbutamol 100 micrograms/dose inhalation powder

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One delivered dose contains 100 micrograms of salbutamol equivalent to 120 micrograms of salbutamol sulphate.

The delivered dose is the dose which is available for the patient after passing the mouthpiece.

Excipient:
11.42 milligrams of lactose monohydrate/delivered dose.

## 3 PHARMACEUTICAL FORM

Inhalation powder.
White powder.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Novolizer Salbutamol is indicated in adults, adolescents and children aged 6 to 12 years.

Symptomatic treatment of conditions with associated reversible airway obstruction, e.g. asthma or chronic obstructive pulmonary disease with a substantial component of reversibility.

Prevention of asthma attacks induced by exercise or exposure to allergens.

### 4.2 Posology and method of administration

Posology
The dose depends on the type, severity, and course of the disorder.

*Asthma*
Adults (including older and adolescents)
For the relief of acute symptoms including bronchospasm a starting dose of one inhalation (100 micrograms) is recommended for adults.
For prevention of exercise-induced or allergen induced symptoms two inhalations (200 micrograms) should be taken 10-15 minutes prior to challenge.
The maximum on-demand use in any 24 hours should not exceed 8 inhalations (equivalent to 800 micrograms).

Children (aged 6 to 12 years)
For the relief of acute symptoms including bronchospasm a starting dose of one inhalation (100 micrograms) is recommended for children aged 6 years and above.
For prevention of exercise-induced or allergen induced symptoms one inhalation (100 micrograms) should be taken10-15 minutes prior to challenge and a further inhalation (to a total of 200 micrograms), if necessary.
The maximum on-demand use in any 24 hours should not exceed 4 inhalations (equivalent to 400 micrograms).

Children below 6 years of age
Novolizer Salbutamol is not recommended for use in children below age 6 due to insufficient data on safety and efficacy.

*COPD*
Adults (including older and adolescents)

For the relief of acute symptoms including bronchospasm a starting dose of one inhalation (100 micrograms) is recommended for adults.
The maximum on-demand use in any 24 hours should not exceed 8 inhalations (equivalent to 800 micrograms).

For all patients
When other salbutamol inhalers are replaced by Novolizer Salbutamol 100 micrograms inhalation powder the amount of salbutamol delivered to the lung may vary between different inhalers and therefore the posology may have to be adjusted.

*Method of administration*
There should be an interval of at least 1 minute between 2 inhalations.
For inhalation use
Usage and handling of the Novolizer device

Refilling

1. Lightly press together the ribbed surfaces on both sides of the lid, move the lid forwards and lift off.
2. Remove the protective aluminium foil from the cartridge box and take out the new cartridge.
3. Insert the cartridge into the Novolizer device with the dosage counter facing the mouthpiece.
4. Replace the lid into the side guides from above and push down flat towards the button until it snaps into place. The cartridge can be left in the Novolizer device until it has been used up, or for up to 6 months after insertion.

Note: Novolizer Salbutamol 100 micrograms cartridges may only be used in the Novolizer powder inhaler

Usage

1. When using the Novolizer device always keep it horizontal. First remove the protective cap.
2. Completely depress the coloured dosage button. A loud double click will be heard and the colour of the control window (lower) will change from red to green. Then release the coloured dosage button. The colour green in the window indicates that the Novolizer device is ready for use.
3. Exhale (but not into the powder inhaler).
4. Put the lips around the mouthpiece. Inhale the powder steadily, deeply and as rapidly as possible (to the maximum inhalation).. During this breath a loud click should be heard, indicating correct inhalation. Hold the breath for a few seconds and then continue with normal breathing.

Note: If the patient needs to take more than 1 inhalation at a time, steps 2 - 4 should be repeated.
5. Replace the protective cap on the mouth piece - the dosing procedure is now complete.
6. The number in the top window indicates the number of inhalations left.

Note: The coloured dosage button should onlybe pressed immediately before inhalation.

A double inhalation in error is not possible with the Novolizer device. The click sound and the change of colour in the control window indicate that inhalation has been performed correctly. If the colour of the control window does not change then inhalation should be repeated. If inhalation is not completed correctly after several attempts, then the patient should consult the doctor/physician.

Cleaning

The Novolizer device should be cleaned at regular intervals, but at least every time the cartridge is changed. Instructions on how to clean the device can be found in the 'Instructions for use' which is part of package leaflet.

Note: In order to ensure correct use of the inhaler, patients should receive thorough instructions on how to use the device. Children should only use this product under the supervision of an adult.

**4.3 Contraindications**

Hypersensitivity to the active substance salbutamol or to the excipient lactose monohydrate (which contains small amounts of milk proteins).

**4.4 Special warnings and precautions for use**

Treatment should be carried out stepwise according to the severity.

Bronchodilators should not be the only or main treatment in patients with persistent asthma. Severe asthma requires regular medical assessment as patients are at risk of severe attacks and even death.

For patients with asthma, use of Novolizer Salbutamol 100 micrograms inhalation powder should not delay the introduction and regular use of inhaled corticosteroid therapy.

In the following cases, salbutamol should only be used with caution and if strictly indicated:
- serious cardiac disorders, in particular recent myocardial infarction
- coronary heart disease, hypertrophic obstructive cardiomyopathy and tachyarrhythmia
- severe and untreated hypertension
- aneurysm
- hyperthyroidism
- diabetes which is difficult to control
- pheochromocytoma

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, tachyarrhythmia or severe heart failure) who are receiving salbutamol for respiratory disease, should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease.

Care should be taken when treating acute asthma attacks or exacerbation of severe asthma as increased serum lactate levels, and rarely, lactic acidosis have been reported after the use of high doses of salbutamol. This is reversible on reducing the dose of salbutamol.

Daily self assessment of asthma control following instructions regarding the use of Novolizer Salbutamol 100 micrograms and any other drugs required for the management of asthma is important in order that the course of the disease can be followed and the success of both bronchodilator and anti-inflammatory therapy monitored. The patient should be instructed in the regular measurement of peak expiratory flow rate (PEFR) using a portable peak flow meter.

If disease control does not improve satisfactorily or deteriorates, or if the short-acting relief bronchodilator treatment becomes less effective, or more inhalations than usual are required, medical advice must be sought in order that the clinical condition can be re-assessed and therapeutic management revised appropriately.
In this situation, for patients with asthma anti-inflammatory therapy may be required, the dose of anti-inflammatory therapy may need to be increased or a short course of oral glucocorticoids may be needed. For patients with chronic obstructive pulmonary disease regular treatment of one or more long-acting bronchodilators may be required, rehabilitation, use of inhaled corticosteroids or long term oxygen may be needed.
Increasing use of bronchodilators and in particular short-acting inhaled beta2 adrenergic agonists to relieve symptoms indicates deterioration of disease control.
A sudden and increasing deterioration of symptoms can be life-threatening. Therefore, medical assistance must be sought immediately.

The dose and frequency of inhalation of short-acting beta2 agonists should only be increased following medical advice and if a previously effective dose fails to give the expected relief the patient should be advised to seek medical advice. Exceeding the prescribed dose can be dangerous (see section 4.9). If acute asthma symptoms are not relieved or gets even worse following a second inhalation, or if patients are unable to trigger the Powder inhaler (= Novolizer) during an acute asthma attack, medical assistance should be sought immediately.

Potentially serious hypokalaemia may result from beta2-agonist therapy, mainly from parenteral and nebulised administration. Particular caution is advised in acute severe asthma as this effect may be potentiated by hypoxia.

Inhaled salbutamol preparations are not appropriate for the management of premature labour and should not be used for threatened abortion.

Lactose may contain milk protein. The amount of lactose contained in Novolizer Salbutamol does not normally cause problems in lactose intolerant people.
However, in patients with profound enzyme deficiency, lactose intolerance has been reported very rarely following inhalation of powder containing lactose.

Patients should be instructed in the proper use of the Novolizer device. The patient's inhaler technique should be checked to ensure that the patient is able to use the Novolizer device correctly.

**4.5 Interaction with other medicinal products and other forms of interactions**

Salbutamol and non-selective β-receptor blocking drugs should not usually be prescribed together. In patients with asthma administration of β-receptor blocking drugs is associated with a risk of severe bronchoconstriction.

When administering halogenated anaesthetics, e.g. halothane, methoxyflurane or enflurane, to patients treated with salbutamol an increased risk of severe dysrhythmia and hypotension must be expected.
If anaesthesia with halogenated anaesthetics is planned, care should be taken to ensure that salbutamol is not used for at least 6 hours before initiation of the anaesthesia.

Treatment with salbutamol can lead to hypokalaemia (see 4.4 Special warning and precautions for use and 4.8 Undesirable effects). This effect may be potentiated by the concomitant administration of other drugs, in particular xanthine derivatives, glucocorticoids, diuretics and cardiac glycosides (digoxin). Serum potassium levels should be monitored in these situations.

Monoamine oxidase inhibitors and tricyclic antidepressants may increase the risk of cardiovascular side-effects.

**4.6 Fertility, pregnancy and lactation**

*Pregnancy*
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. Ventilastin Novolizer should not be used during pregnancy unless clearly necessary.

*Breast-feeding*
As salbutamol is probably secreted in breast milk, its use in nursing mothers required 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.

*Fertility*
There is no information on the effects of salbutamol on human fertility. There were no adverse effects on fertility in animals (see section 5.3).

**4.7 Effects on ability to drive and use machines**

No studies on the effects on the ability to drive and use machines have been performed.

**4.8 Undesirable effects**

Up to approximately 10% of patients can be expected to experience adverse reactions. These depend upon the dose and the individual sensitivity. Most commonly reported are: taste alteration (bad, unpleasant and unusual taste) and application site reaction (mouth and throat irritation, burning sensation of the tongue), fine tremor (usually of the hands), nausea, sweating, restlessness, headache and dizziness.These undesirable effects may subside on continuation of treatment within 1-2 weeks.
As with other inhalation therapies, in rare cases paradoxical bronchospasm may occur, manifest by an immediate increase in wheezing after dosing. Paradoxical bronchospasm should be treated immediately with an alternative presentation or a different fast-acting inhaled bronchodilator. Novolizer Salbutamol 100 micrograms should be discontinued immediately, the patient should be assessed and, if necessary, alternative therapy instituted.

There are reports about stimulating effects on the central nervous system after inhalation of salbutamol which manifest themselves in hyperexcitability, hyperactive behaviour, sleeping disturbances and hallucinations. These observations were predominantly made in children up to 12 years of age.

*Adverse events are listed below by system organ class and frequency. Frequencies are defined as:*
*Very common (≥ 1/10); Common (≥ 1/100, < 1/10); Uncommon (≥ 1/1,000, < 1/100);*
*Rare (≥ 1/10,000, < 1/1,000); Very rare (< 1/10,000)*

| Organ System | Frequency | Adverse drug reaction |
|---|---|---|
| **Blood and lymphatic disorders** | ***Very rare*** | Thrombopenia |
| **Immune system disorders** | ***Very rare*** | Hypersensitivity reaction |
| **Metabolism and nutrition disorders** | ***Rare*** | Hypokalaemia, hyperglycaemia, increase of insulin, free fatty acids, glycerol and ketone bodies |
| **Psychiatric disorders** | ***Common*** | Restlessness |
| **Nervous system disorders** | ***Common*** | Fine tremor, dizziness |
| | ***Rare*** | Hyperactive behaviour |
| | ***Very rare*** | Hyperexcitability, sleeping disturbances, hallucinations |
| **Cardiac disorders** | ***Rare*** | Tachycardia, cardiac arrhythmia (atrial fibrillation, supraventricular tachycardia, extrasystoles), palpitations, angina pectoris, blood pressure effects (lowering or increase) |
| | ***Very rare*** | Myocardial ischaemia |
| **Vascular disorders** | ***Rare*** | Peripheral vasodilatation |
| | ***Very rare*** | Collapse |
| **Respiratory, thoracic and mediastinal disorders** | ***Rare*** | Cough<br>Paradoxical bronchospasm |
| **Gastrointestinal disorders** | ***Common*** | Nausea, taste alteration |
| **Skin and subcutaneous tissue disorders** | ***Common*** | Sweating |
| | ***Very rare*** | Pruritus, rash, erythema, urticaria, angioedema |
| **Musculoskeletal and connective tissue disorders** | ***Rare*** | Muscle cramps |
| **Renal and urinary disorders** | ***Very rare*** | Nephritis |
| **General disorders and administration site condition** | ***Common*** | Headache, application site reaction (mouth and throat irritation, burning sensation of the tongue) |

Lactose-monohydrate contains small amounts of milk proteins and can therefore cause allergic reactions.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued

monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions preferably through the online reporting option accessible from the IMB homepage. A downloadable report form is also accessible from the IMB website, which may be completed manually and submitted to the IMB via 'freepost', in addition to the traditional post-paid 'yellow card' option.

FREEPOST
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**4.9 Overdose**

*Symptoms of an overdose*
In the case of an overdose, the above-mentioned undesirable effects (see section 4.8) occur very quickly and with increased severity. Typical symptoms are: tachycardia, palpitations, arrhythmia, restlessness, sleep disturbances, chest pain and vigorous tremor, especially on hands but also on the whole body.
Occasionally, psychotic reactions were observed after excessive doses of salbutamol.
In the case of a salbutamol overdose there can increasingly be a shift of potassium into the intracellular space resulting in hypokalaemia, as well as hyperglycaemia, hyperlipidaemia and hyperketonaemia.

*Management of an overdose*
Treatment after an overdose of a beta-sympathomimetic is mainly symptomatic. The following measures may be considered, depending upon the individual circumstances:

- If large amounts of the drug are swallowed, irrigation of the stomach should be considered. Activated charcoal and laxatives can have favourable effects on the undesired absorption of the beta-sympathomimetic.
- For the cardiac symptoms of overdosage with salbutamol a cardioselective beta-blocking agent may be considered, but beta-blocking drugs should only be used with caution and be avoided as far as possible in patients with a history of bronchospasm. ECG monitoring is indicated in such patients.
- In the case of fairly pronounced lowering of the blood pressure, volume substitution (e.g. plasma expanders) is recommended.
- If hypokalaemia develops electrolyte balance should be monitored and, if appropriate, electrolytes may need to be administered.

**5 PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES, ADRENERGICS INHALANTS; Selective beta-2-adrenoreceptor agonists
ATC-Code: R03AC02

Salbutamol is a beta2-selective adrenoceptor agonist, which has a selective action on bronchial beta2-receptors and little effect on cardiac beta1-receptors at therapeutic doses. Following inhalation, salbutamol exerts a stimulating action on beta2–receptors on bronchial smooth muscle, and thus ensures rapid bronchodilatation which becomes significant within a few minutes and persists for 4 to 6 hours. The drug also causes vasodilatation leading to reflex chronotropic effect and metabolic effects, including hypokalaemia.

**5.2 Pharmacokinetic properties**

Absorption and metabolism of salbutamol in lungs and gastrointestinal tract differ. After inhalation, about 20-47 % of the active substance based on the delivered dose pass into the deeper bronchial paths, while the remainder deposits in the mouth

and the upper section of the respiratory tract and 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**

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction. Effects seen in toxicity studies were related to the beta-adrenergic activity of salbutamol.

In common with other potent selective beta2-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 2.5 mg/kg dose. In rats, treatment at the levels of 0.5, 2.32, 10.75 and 50 mg/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 50 mg/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.

In an oral fertility and general reproductive performance study in rats at doses of 2 and 50 /mg/kg/day, with the exception of a reduction in number of weanlings surviving to day 21 post partum at 50 mg/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**

Lactose monohydrate

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

o Medicinal product in the container
Shelf life before opening the container
3 years
Shelf life after first opening the container
6 months

o Novolizer device
Shelf life before first use
3 years
In-use shelf life
1 year

To note: The functioning of the Novolizer device has been demonstrated in tests for 2000 metered doses. Therefore a maximum of 10 cartridges containing 200 metered doses can be used with this device (within a single year) prior to replacement.

**6.4 Special precautions for storage**

Do not store above 30 °C.
Store in the original package.
When in use Novolizer Salbutamol 100 micrograms should be stored protected from moisture.

**6.5 Nature and contents of container**

Original sales packs and samples:
1 cartridge 200 metered doses (polystyrene / polypropylene) filled with not less than 2.308g of powder packed in a polypropylene container sealed by aluminium foil and 1 powder inhaler (mouthpiece in polycarbonate and device in acrylnitrilbutadienestyrol copolymer, polyoxymethylene)

Refill packs:
1 cartridge 200 metered doses (polystyrene / polypropylene) filled with not less than 2.308g of powder packed in a polypropylene container sealed by aluminium foil
2 cartridges each 200 metered doses (polystyrene / polypropylene) filled with not less than 2.308g of powder packed in a polypropylene container sealed by aluminium foil

Hospital pack:
Pack of 10 of original sales packs

Not all pack sizes may be marketed.

**6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

No special requirements.

**7 MARKETING AUTHORISATION HOLDER**

Mylan IRE Healthcare Limited
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**8 MARKETING AUTHORISATION NUMBER**

PA2010/033/001

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 30 September 2004
Date of last renewal: 17 January 2011

**10 DATE OF REVISION OF THE TEXT**

June 2018