SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Salbulin MDPI Novolizer 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

Salbulin MDPI Novolizer 100 micrograms is indicated in adults, adolescents and children aged 6 to 12 years.

Salbulin MDPI Novolizer 100 micrograms is recommended for use in patients with reversible airways obstruction such as asthma for relief and prevention of bronchospasm. It should be used to relieve asthma symptoms when they occur and to prevent symptoms in circumstances known by the patient to precipitate symptoms, for example prior to exercise or allergen exposure.

Salbulin MDPI Novolizer 100 micrograms is particularly useful for the relief of symptoms of asthma, providing it does not delay the introduction and regular use of inhaled corticosteroid therapy.

In asthma, short acting beta-2 agonists including Salbulin MDPI Novolizer should not be the main or only treatment. It is recommended that short acting

beta-2 agonists should be prescribed with concomitant inhaled corticosteroid (anti-inflammatory).

4.2 Posology and method of administration

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

Adults (including older people and adolescents)
For the relief of acute asthma symptoms including bronchospasm a starting dose of one inhalation (100 micrograms) is recommended for adults; this dose may be increased to two inhalations if necessary.
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).

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

Children (aged 6 to 12 years)
For the relief of acute asthma symptoms including bronchospasm a starting dose of one inhalation (100 micrograms) is recommended for children aged 6 years and above; this dose may be increased to two inhalations if necessary.
For prevention of exercise-induced or allergen induced symptoms one inhalation (100 micrograms) should be taken 10-15 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).

Chronic therapy:
The usual dosage for children under the age of 6-12 years: up to two inhalations 4 times daily.
Children below 6 years of age
Salbulin MDPI Novolizer is not recommended for use in children below age 6 due to insufficient data on safety and efficacy.

For all patients:
When other salbutamol inhalers are replaced by Salbulin MDPI Novolizer 100 micrograms, it may be necessary to adjust the dosage regimen as the amount of salbutamol delivered to the lung may vary between different inhalers.

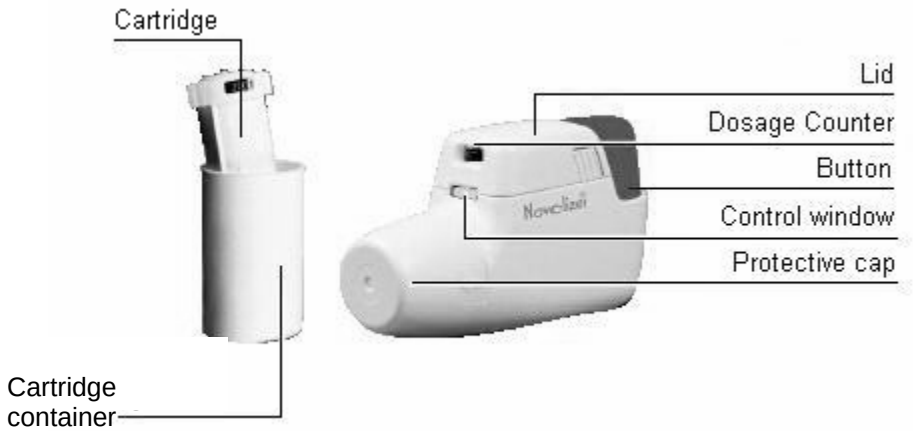
Reliance on such frequent supplementary use, or a sudden increase in dose, indicates poorly controlled or deteriorating asthma (see section 4.4).

Method of administration

Salbulin MDPI Novolizer 100 micrograms is for oral inhalation use only. There should be an interval of at least 1 minute between 2 inhalations.

Instructions for using the Novolizer device (Powder inhaler device)

Figure



Refilling

1. Lightly press together the ribbed surface of both sides of the lid, move the lid forwards, and lift off.
2. Remove the protective aluminium foil from the cartridge container 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 is empty, but it must be replaced with a new cartridge within 6 months of removal from its sealed container.

Note: Salutamol MDPI Novolizer 100 micrograms cartridges may only be used in the Novolizer Powder inhaler.

Usage

1. The Novolizer device must be kept horizontal when it is being used.
2. Remove the protective cap.
3. Prime the Novolizer device by completely depressing the large coloured button. A loud double click will be heard and the colour of the control window will change from red to green. The coloured button should then be released. The colour green in the window indicates that the Novolizer device is primed and ready for use.

4. The patient should exhale (not into the powder inhaler).
5. The lips should be placed around the mouthpiece and the powder inhaled steadily, deeply and as rapidly as possible (to the maximum inhalation). During this breath a loud click should be heard, indicating that the inhalation was sufficiently strong. The patient should hold their breath for a few seconds and then continue breathing normally. If the patient needs to take more than 1 inhalation, steps 2 - 5 should be repeated.
6. The protective cap should be replaced.
7. The number of inhalations left is indicated by the dosage counter.

Note: The large coloured button should only be pressed immediately before inhalation.

It is not possible for the patient to administer a double inhalation in error using the Novolizer device. The clicking 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. The Novolizer device cannot be primed a second time unless the inhalation has been performed correctly. If inhalation is not completed correctly after several attempts, then the patient should consult their doctor/physician.

Cleaning

The Novolizer device should be cleaned at regular intervals; at a minimum at least every time the cartridge is changed. Instructions for the patient on how to clean the Novolizer device can be found in the Patient Information Leaflet.

Note: In order to ensure correct use of the Novolizer device, patients should receive thorough instructions on how to use the Novolizer device and their inhaler technique checked to ensure that they are able to use it correctly. 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

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.

The use of brochodilators such as Salbulin MDPI Novolizer 100 micrograms should not delay the introduction and regular use of inhaled corticosteroid therapy. Daily patient self-assessment of asthma control following instructions on the use of Salbulin MDPI Novolizer 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 asthma 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 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.

Failing to respond to treatment with salbutamol may signal a need for urgent medical advice or treatment.

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 MDPI Novolizer.

Increasing use of bronchodilators and in particular short-acting inhaled $beta_2$ adrenergic agonists to relieve symptoms indicates deterioration of asthma control, and patients should be warned to seek medical advice as soon as possible. Under these conditions, the patient's therapy plan should be reassessed.

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.

Patients should be advised that a sudden and increasing deterioration of asthma symptoms can be life-threatening. Therefore, medical assistance must be sought immediately.

The dose and frequency of inhalation of short-acting $beta_2$ agonists should only be increased following medical advice and if a previously effective dose of inhaled salbutamol no longer provides relief for a duration of three hours following administration, the patient should be advised to promptly 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 Novolizer device during an acute asthma attack, medical assistance should be sought immediately.

Potentially serious hypokalaemia may result from beta $_2$-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 derivates, steroids, and diuretics. Serum potassium levels should be monitored in such situations.

Inhalation of high doses of salbutamol can increase the blood glucose level. Therefore, blood glucose levels in diabetic patients should be monitored closely.

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.

This medicinal product contains lactose. The amount of lactose contained in Salbulin MDPI Novolizer 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.

Inhaled salbutamol preparations are not indicated for threatened abortion.

4.5 Interaction with other medicinal products and other forms of interaction

Salbutamol and non-selective beta -receptor blocking drugs should not usually be prescribed together. Administration of beta-receptor blocking drugs to patients with asthma may cause severe bronchoconstriction.

When administering halogenated anaesthetics, e.g. halothane, methoxyflurane or enflurane, to patients treated with salbutamol there is an increased risk of severe dysrhythmia and hypotension. Salbutamol should not be used for at least 6 hours prior to the use of halogenated anaesthetics.

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. Salbutamol MDPI 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 10% of patients may experience adverse reactions. These reactions are dose-dependent.

The most commonly reported adverse reactions are: taste alteration (bad, unpleasant and unusual taste), mouth and throat irritation, 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, with an immediate increase in wheezing after dosing. Paradoxical bronchospasm should be treated immediately with an alternative fast-acting inhaled bronchodilator and Salbulin MDPI Novolizer 100 micrograms discontinued immediately. The patient should be assessed and, if necessary, alternative therapy instituted.

Hypersensitivity reactions such as rash, urticaria, dermatitis, pruritus and erythema have been observed. There have been very rare reports of angioedema (oedema of the face, lips, eyes and throat), bronchospasm, hypotension, collapse, thrombopenia and nephritis.

Tachycardia, with or without peripheral vasodilatation, may occur. In common with other β2 agonists, cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles), palpitations, angina pectoris, and blood pressure effects have been reported in association with the use of salbutamol, usually in susceptible patients.

There are also reports of the stimulating effects on the central nervous system after inhalation of salbutamol which manifest themselves in 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)), Not known (cannot be estimated from the available data)

Organ System	Frequency	Adverse drug reaction
Blood and lymphatic system 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
	Rare	Paradoxical bronchospasm
Gastrointestinal disorders	***Common***	Nausea, taste alteration
Skin and subcutaneous tissue disorders	***Common***	Sweating
	Very rare	Pruritus, rash, erythema, urticaria, angioedema
Musculoskeletal 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 via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms of an overdose
In the case of an overdose, the above-mentioned undesirable effects (see 4.8, Undesirable effects) occur very quickly and with increased severity. Typical symptoms include: tachycardia, palpitations, arrhythmia, restlessness, sleep disturbances, chest pain and vigorous tremor, especially the hands.

Occasionally, psychotic reactions were observed after excessive doses of salbutamol.

In the case of a salbutamol overdose there can 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 salbutamol is mainly symptomatic. The following measures may be considered, depending upon individual circumstances:

- If large amounts of the drug are swallowed, irrigation of the stomach should be considered. Activated charcoal and laxatives may reduce absorption.
- Cardiac symptoms can be treated with a cardioselective beta-blocker. However, attention should be given to an increased risk of bronchospasm in patients with asthma. ECG monitoring is indicated in such patients.
- If blood pressure is markedly reduced, volume substitution (e.g. plasma expanders) is recommended.
- If hypokalaemia develops electrolyte balance should be monitored and electrolytes administered if necessary.

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 beta $_2$-selective adrenoceptor agonist, which has a selective action on bronchial beta $_2$-receptors and little effect on cardiac beta $_1$-receptors at therapeutic doses. Following inhalation, salbutamol exerts a stimulating action on beta $_2$-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

After inhalation, 20-47 % of the active substance based on the delivered dose passes into the deeper bronchial airways, 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 well 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. Approximately 10% of the salbutamol is bound to plasma proteins.

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, embryo fetal 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

- Medicinal product (Salbutamol inhalation powder) in the container
  Shelf life before opening the container:
  3 years
  Shelf life after first opening the container:
  6 months
- Novolizer Device
  Shelf life before first use:
  3 years
  In-use shelf life:
  1 year or 10 cartridges

The Novolizer device has been shown to function for at least 2000 metered doses. Therefore a maximum of 10 cartridges containing 200 metered doses can be used with this Novolizer device (within a single year) prior to replacement.

6.4 Special precautions for storage

Do not store above 30ºC.

Store in the original package.

When in use Salbulin MDPI Novolizer 100 micrograms should be stored protected from moisture.

6.5 Nature and contents of container

Original sales packs and samples:

1 cartridge containing 200 metered doses filled with not less than 2.308 g of powder packed in a container sealed by aluminium foil and 1 Novolizer device.

Refill packs:

1 or 2 cartridges each containing 200 metered doses packed in a container sealed by aluminium foil

Hospital pack:

Pack of 10 of original sales packs

All components are made of plastic materials (the cartridge is made of acrylonitrile butadiene styrene (ABS) / polypropylene, the Novolizer device is made of acrylnitrilbutadienestyrol copolymer / polyoxymethylene and the mouthpiece of polycarbonate).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Viatris Products Limited,
Station Close,
Potters Bar,
EN6 1TL,
United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03/01/2008 / 31/12/2011

10 DATE OF REVISION OF THE TEXT

20/05/2026