# SALBUTAMOL SULPHATE 100 MICROGRAMS INHALER
**PL 36390/0034**
**UKPAR**

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted STD Chemicals Limited a Marketing Authorisation (licence) for the medicinal product Salbutamol Sulphate 100 micrograms Inhaler (PL 36390/0034) on 30 June 2011. This medicine is only available on prescription from your doctor and is used to:

- help relieve the symptoms of asthma, such as wheezing, shortness of breath, tightness in the chest and cough
- prevent symptoms of asthma that are brought on by exercise or allergens, such as house dust mites, pollen, cigarette smoke, cat and dog fur, etc.
- relieve symptoms, such as chest tightness, wheezing, shortness of breath and coughing, in some other chest diseases.

Salbutamol Sulphate 100 micrograms Inhaler is a pressurised inhalation suspension (inhaler), which contains the active ingredient salbutamol (as salbutamol sulphate). Salbutamol belongs to a group of medicines called short-acting β2 agonists, bronchodilators or “relievers”. Salbutamol acts directly on the muscles in the walls of the airways in the lung causing the muscles to relax. This widens or opens up your airways making it easier to breathe.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of using Salbutamol Sulphate 100 micrograms Inhaler outweigh the risks; hence a Marketing Authorisation has been granted.
SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted a Marketing Authorisation for the medicinal product Salbutamol Sulphate 100 micrograms Inhaler (PL 36390/0034) to STD Chemicals Limited on 30 June 2011. The product is available as a prescription-only medicine (POM) and is indicated for use in the management of asthma, for the relief of asthma symptoms (such as wheezing and shortness of breath), on an ‘as required’ basis. Salbutamol Sulphate 100 micrograms Inhaler should be used to relieve symptoms when they occur and to prevent symptoms in those circumstances recognised by the patient to precipitate an asthma attack, for example before exercise or unavoidable allergen exposure.

Salbutamol Sulphate 100 micrograms Inhaler can be used for the relief of symptoms in mild, moderate or severe asthma, providing that reliance on the inhaler does not delay the introduction and use of regular inhaled corticosteroid therapy.

The application was submitted as an abridged application according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Asmavent CFC-Free Inhaler 100 micrograms (PL 08137/0130), which was granted a Marketing Authorisation to Neolab Limited on 03 July 2009.

Salbutamol sulphate, the active ingredient belongs to the class of medicines known as selective β₂ adrenoceptor agonists. It acts on β₂ receptors to cause an increase in intracellular adenylate cyclase, the enzyme which catalyses the conversion of adenosine triphosphate (ATP) to cyclic -3’, 5’-adenosine monophosphate (c-AMP). At therapeutic doses salbutamol sulphate acts on the β₂-adrenoceptors of bronchial muscle providing short-acting (4-6 hours) bronchodilatation with a fast onset (within 5 minutes) in reversible airways obstruction

No new data were submitted nor were they necessary for this simple application, as the data are identical to those of the previously granted cross-reference product.
1. INTRODUCTION
This is an abridged application for Salbutamol Sulphate 100 micrograms Inhaler, submitted under Article 10c of Directive 2001/83/EC, as amended. The proposed Marketing Authorisation Holder is STD Chemicals Limited, Hillbrow House, Hillbrow Road, Esher, Surrey, KT10 9NW.

The application cross-references to Asmavent CFC-Free Inhaler 100 micrograms (PL 08137/0130) which was granted a Marketing Authorisation to Neolab Limited on 03 July 2009.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)
The proposed name of the product is Salbutamol Sulphate 100 micrograms Inhaler. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
Salbutamol Sulphate 100 micrograms Inhaler is a pressurised inhalation suspension (inhaler). The inhaler comprises of an aluminium canister sealed with a metering valve, which is inserted into a polypropylene actuator fitted with a removable polypropylene mouthpiece cover. Each metered dose (ex-valve) contains 100 micrograms salbutamol (as sulphate). Each canister contains 200 metered actuations.

The proposed shelf-life (2 years) and storage conditions (“Do not store above 30°C. The canister contains a pressurised liquid. Do not expose to temperatures higher than 50°C. Do not pierce the canister.”) are consistent with the details registered for the cross-reference product.

2.3 Legal status
On approval, the product will be available as a prescription-only medicine (POM).

2.4 Marketing Authorisation Holder/Contact Persons/Company
STD Chemicals Limited, Hillbrow House, Hillbrow Road, Esher, Surrey, KT10 9NW, United Kingdom

The Qualified Person (QP) responsible for pharmacovigilance is stated and his CV is included.
2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

2.6 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specification
The proposed finished product specification is in line with the details registered for the cross-reference product.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance
None of the excipients contain materials of animal or human origin. This is consistent with the cross-reference product.

2.11 Bioequivalence
No bioequivalence data are required to support this informed consent application, as the proposed product is manufactured to the same formula and utilising the same process as the reference product Asmavent CFC-Free Inhaler 100 micrograms (PL 08137/0130).

3. EXPERT REPORTS
The applicant cross-refers to the data for Asmavent CFC-Free Inhaler 100 micrograms (PL 08137/0130), to which it claims identicality. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed Summary of Product Characteristics is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
PIL
The patient information leaflet has been prepared in-line with the details registered for the cross-reference product.

Neolab Limited has previously submitted results of consultations with target patient groups (‘user testing’), in accordance with Article 59 of Council Directive 2001/83/EC, for the reference product Asmavent CFC-Free Inhaler 100 micrograms (PL 08137/0130). The
results indicate that the leaflet is well-structured and organised, easy to understand, and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

As the leaflets for Asmavent CFC-Free Inhaler 100 micrograms (PL 08137/0130) and this product are considered the same, no further user testing of the leaflet for this product is necessary.

**Carton and canister**
The proposed artwork is consistent with the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

**7. CONCLUSION**
The data submitted with the application are acceptable. The grant of a Marketing Authorisation is recommended.
NON-CLINICAL ASSESSMENT

As this is an abridged application submitted under Article 10c, no new non-clinical data have been supplied and none are required.

The grant of a Marketing Authorisation is recommended.
CLINICAL ASSESSMENT

As this is an abridged application submitted under Article 10c, no new clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that they have the services of a qualified person responsible for pharmacovigilance, and have the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

The grant of a Marketing Authorisation is recommended.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for this application are consistent with those previously assessed for the cross-reference product and as such have been judged to be satisfactory.

NON-CLINICAL
No new non-clinical data were submitted and none are required for an application of this type.

EFFICACY
This application is identical to a previously granted application for Asmavent CFC-Free Inhaler 100 micrograms (PL 08137/0130). No new or unexpected safety concerns arise from this application.

PRODUCT LITERATURE
The SmPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

BENEFIT/RISK ASSESSMENT
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with salbutamol sulphate is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.
SALBUTAMOL SULPHATE 100 MICROGRAMS INHALER
PL 36390/0034

STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the marketing authorisation application on 03 February 2011.
2. Following standard checks and communication with the applicant the MHRA considered the application valid on 17 February 2011.
3. Following assessment of the application the MHRA requested further information relating to the dossier on 15 April 2011.
4. The applicant responded to the MHRA’s request, providing further information on 29 June 2011.
5. The application was determined on 30 June 2011.
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Salbutamol Sulphate 100 micrograms Inhaler

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each metered dose (ex-valve) contains 100 micrograms salbutamol (as sulphate).

Each delivered dose (ex-actuator) contains 80 micrograms salbutamol (as sulphate).

For full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM
Pressurised inhalation, suspension.

The inhaler comprises an aluminium canister fitted with a metering valve, which is inserted into a light blue standard plastic actuator fitted with a removable blue plastic mouthpiece cover, marked with “SALBUTAMOL”, “100” and “STD Chemicals”.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Salbutamol Sulphate Inhaler is indicated in the management of asthma, for the relief of asthma symptoms such as wheezing and shortness of breath, on an as required basis. Salbutamol Sulphate Inhaler should be used to relieve symptoms when they occur and to prevent symptoms in those circumstances recognised by the patient to precipitate an asthma attack, for example before exercise or unavoidable allergen exposure.

Salbutamol Sulphate Inhaler can be used for the relief of symptoms in mild, moderate or severe asthma providing that reliance on the inhaler does not delay the introduction and use of regular inhaled corticosteroid therapy.

Salbutamol Sulphate Inhaler may also be used in the treatment of the reversible component of airways obstruction.

4.2 Posology and method of administration
For inhalation use.

ADULTS (including the elderly): For the relief of acute asthma symptoms including bronchospasm and for the relief of wheezing, shortness of breath and attacks of acute dyspnoea, one inhalation (100 micrograms) may be administered as a single minimum starting dose. This may be increased to two inhalations if necessary.

To prevent exercise-induced or allergen-induced symptoms two inhalations should be taken 10-15 minutes prior to exercise or allergen exposure.

CHILDREN: This product is not recommended for use in children 12 years of age and under.

For optimum results, Salbutamol Sulphate Inhaler should be used as required.

For all patients, the maximum recommended dose, when Salbutamol Sulphate Inhaler is used on demand as required for the relief of symptoms, should not exceed 8 inhalations in 24 hours. Each dose should not usually be repeated more often than every 4 hours. However reliance on such frequent supplementary use, or a sudden increase in dose, or if a dose appears to be less effective than usual, indicates poorly controlled or deteriorating asthma.

Salbutamol Sulphate Inhaler cannot be used with any spacing device at this time. If a patient needs a spacing device an alternative product, which can be used with such a device, will need to be prescribed instead of Salbutamol Sulphate Inhaler.
Instructions for Use

1. The mouthpiece cover should be removed and the patient should check inside and outside to make sure that the mouthpiece is clean and that there is no dust, dirt or foreign objects. If it needs cleaning the instructions for cleaning outlined below should be followed. If the inhaler gets very cold, patients should be instructed to take the metal canister out of the plastic actuator and warm it in their hands for a few minutes before use. Patients should never use anything else to warm it up. The inhaler should be shaken prior to use.

2. The inhaler should be held upright with the thumb on the base, below the mouthpiece. Patients should breathe out as far as is comfortable and then.

3. Immediately place the mouthpiece in the mouth between the teeth, and close their lips around it. Patients should be instructed to be careful not to bite the mouthpiece.

4. Breathe in slowly. Just after starting to breathe in through the mouth, patients should press down on the top of the inhaler to release a spray, while still breathing in steadily and deeply.

5. Patients should hold their breath, remove the inhaler from the mouth, and take their finger from the top of the inhaler. Patients should continue holding their breath for about 10 seconds, or as long as is comfortable, prior to breathing out slowly.

Patients should be instructed not to rush stages 3, 4 and 5.

It is important that patients breathe in as slowly as possible just before using the inhaler. Patients should be instructed to try practising in front of a mirror for the first few times. If patients see mist or spray coming from the inhaler or the sides of the mouth, they should start again from stage 2.

6. If patients are to take another spray, they should keep the inhaler upright, and wait about half a minute before repeating steps 2 to 5.

7. Once patients have finished using the inhaler, they should be instructed to always replace the mouthpiece cover to keep out dust and fluff and should make sure to replace the cover firmly and snap it into position.

People with weak hands may find it easier to operate the inhaler with both hands, by putting both forefingers on the top of the inhaler, and both thumbs on the bottom below the mouthpiece.

For detailed instructions for use, the patient should be referred to the Patient Information Leaflet included in each pack, with specific reference to the pictograms which accompany the instructions for use.

The inhaler should be cleaned at least once a week as described below, as it can become blocked, which will affect the way in which the inhaler works and will affect the amount of salbutamol which is inhaled.

1. First remove the metal can from the plastic actuator and take off the mouthpiece cover.

2. Rinse the plastic actuator, mouthpiece and mouthpiece cover in tap water; DO NOT place the metal can into water or clean the can using water. Make sure the water runs through the actuator from both ends to ensure that the actuator orifice is clear and not blocked.

3. The plastic components (actuator and mouthpiece cover) should be placed in a warm place to dry thoroughly before re-assembling the inhaler. Avoid drying near direct or excessive heat.

The patient should follow the cleaning instructions described in the Patient Information Leaflet carefully in order to ensure that the inhaler continues to work properly.

At first use of a new inhaler, or after a period when the inhaler has not been used (7 days or more), the inhaler should be shaken well and two sprays should be discharged prior to use, to prime the inhaler.
4.3 Contraindications
Hypersensitivity to salbutamol or any of the inactive ingredients in Salbutamol Sulphate Inhaler.

Unlike intravenous salbutamol and occasionally salbutamol tablets, inhaled salbutamol is not suitable for the treatment of uncomplicated premature labour and should not be used to treat threatened abortion.

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 or feel on inhalation compared with their previous inhaler.

Bronchodilators are rarely the only or main treatment in patients with asthma and should not be the only or main treatment in patients with moderate, severe or unstable asthma. Asthma requires regular medical assessment, including pulmonary function tests, as patients with asthma are at risk of severe attacks and even death. If symptoms persist following the introduction of a short-acting bronchodilator consideration must be given to the need for inhaled and/or oral corticosteroid therapy. Consideration may need to be given to using maximum recommended doses of inhaled corticosteroids and/or oral corticosteroids in patients with more severe disease.

The dose or frequency of administration of salbutamol should only be increased on medical advice. If a previously effective dose of inhaled salbutamol fails to give relief lasting for 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 inhaled corticosteroids or an increase in the dose of anti-inflammatory therapy (e.g. an increase in the dose of inhaled corticosteroids or a course of oral corticosteroids).

Salbutamol should be administered cautiously to patients with thyrotoxicosis.

Potentially serious hypokalaemia may result from β₂ agonist therapy, although 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, diuretics and long-term laxatives. Serum potassium levels should be monitored in such situations.

Unwanted stimulation of cardiac adrenergic receptors can occur in patients taking β₂ agonist therapy.

4.5 Interaction with other medicinal products and other forms of interaction
Salbutamol and beta-blockers should not usually be prescribed together.

Hypokalaemia occurring with β₂ agonist therapy may be exacerbated by treatment with xanthines, steroids, diuretics and long-term laxatives.

Because Salbutamol Sulphate Inhaler contains ethanol there is a theoretical potential for interaction in patients taking disulfiram or metronidazole. The amount of ethanol is small but it may be enough to precipitate a reaction in some sensitive patients.
4.6 Pregnancy and lactation

Salbutamol Sulphate Inhaler

There is no experience of this product in pregnancy and lactation in humans. An inhalation reproductive study with a salbutamol sulphate CFC-free formulation in rats did not exhibit any teratogenic effects. It should not be used in pregnancy and lactation unless the expected benefit to the mother is thought to outweigh any risk to the fetus or neonate.

Propellant HFA 134a

Studies of propellant HFA 134a administered to pregnant and lactating rats and rabbits have not revealed any special hazard.

Salbutamol

Pregnancy

The safe use of inhaled salbutamol during pregnancy has not been established. However, in animal studies there was evidence of some harmful effects on the fetus at very high dose levels. In mice and rabbits large doses of salbutamol have been shown to be teratogenic.

Lactation

As it is not known whether salbutamol is secreted in breast milk, the use of Salbutamol Sulphate Inhaler in mothers who are breast-feeding requires careful consideration. It is not known whether salbutamol has any harmful effects on the neonate, and so its use should be restricted to situations where it is felt that the expected benefit to the mother will outweigh any potential risk to the neonate.

4.7 Effects on ability to drive and use machines

No studies on effects on the ability to drive and use machines have been performed. On the basis of the pharmacodynamic profile of salbutamol, and the lack of reported relevant adverse drug reactions, salbutamol has no or negligible influence on the ability to drive and use machines.

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 and very rare 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 $\beta_2$ agonist therapy.

Nervous system disorders

Common: Fine skeletal muscle tremor most obviously affecting the hands, headache.

Very rare: Hyperactivity (in children).

Cardiac disorders

Common: Tachycardia with or without peripheral vasodilatation.

Uncommon: Palpitations, cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles)

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 and shortness of breath after dosing. This should be treated immediately with an alternative presentation or a different fast-acting inhaled bronchodilator. Salbutamol Sulphate Inhaler should be discontinued immediately, the patient should be assessed, and alternative therapy instituted, if necessary.
Gastrointestinal disorders
Uncommon: Mouth and throat irritation.

Musculoskeletal and connective tissue disorders
Uncommon: Muscle cramps.

4.9 Overdose
Overdosage may result in skeletal muscle tremor, tachycardia, tenseness, headache and peripheral vasodilatation. The preferred antidote for overdosage with salbutamol is a cardioselective β-blocker agent, but β-blocking drugs should be used with caution in patients with a history of bronchospasm. Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Selective β₂ adrenoceptor agonists.
ATC Code R03A C02.

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

5.2 Pharmacokinetic properties
Salbutamol administered intravenously has a half life of 4 to 6 hours and is cleared mainly via the renal route partly as unchanged drug 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
Salbutamol
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.

Propellant HFA 134a
In animal studies propellant HFA 134a has been shown to have no significant pharmacological effects other than at very high exposure concentrations, when narcosis and a relatively weak cardiac sensitising effect were found. The potency of the cardiac sensitisation was less than that of CFC-11 (trichlorofluoromethane).
In studies to detect toxicity, repeated high dose levels of propellant HFA 134a indicated that safety margins based on systemic exposure would be of the order 2200, 1314 and 381 for mouse, rat and dog with respect to humans.

There are no reasons to consider propellant HFA 134a as a potential mutagen, clastogen or carcinogen judged from in vitro and in vivo studies including long-term administration by inhalation in rodents.

**Salbutamol sulphate – a CFC-free formulation**

Safety studies with a salbutamol sulphate CFC-free formulation in rat and dog showed few adverse effects. These occurred at high doses and were consistent with the known effects of salbutamol inhalation.

### 6 PHARMACEUTICAL PARTICULARS

#### 6.1 List of excipients

Norflurane (HFA 134a) – this is a hydrofluoroalkane, non-chlorofluorocarbon (non-CFC) propellant; this product does not contain CFCs.

Ethanol

Oleic Acid

#### 6.2 Incompatibilities

Not applicable.

#### 6.3 Shelf life

2 years.

#### 6.4 Special precautions for storage

Do not store above 30°C.

The canister contains a pressurised liquid. Do not expose to temperatures higher than 50°C. Do not pierce the canister.

#### 6.5 Nature and contents of container

An inhaler comprising an aluminium canister sealed with a metering valve, inserted into a polypropylene actuator with a polypropylene mouthpiece cover. Each canister contains 200 metered actuations.

#### 6.6 Special precautions for disposal

As the canister is pressurised, it should not be punctured or disposed of by burning.

### 7 MARKETING AUTHORISATION HOLDER

STD Chemicals Ltd,

Hillbrow House,

Hillbrow Road,

Esher,

Surrey,

KT10 9NW

### 8 MARKETING AUTHORISATION NUMBER(S)

PL 36390/0034

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

30/06/2011

### 10 DATE OF REVISION OF THE TEXT

30/06/2011

### 11 DOSIMETRY (IF APPLICABLE)

### 12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)
PATIENT INFORMATION LEAFLET

SALBUTAMOL Sulphate 100 micrograms Inhaler

Read all of this leaflet carefully before you start using this medicine.
- The full name of this product is Salbutamol Sulphate 100 micrograms Inhaler.
- However this name will be shortened within the text of this leaflet to Salbutamol Sulphate Inhaler.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, asthma nurse or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Salbutamol Sulphate Inhaler is and what it is used for
2. Before you use Salbutamol Sulphate Inhaler
3. How to use Salbutamol Sulphate Inhaler
4. Possible side effects
5. How to store Salbutamol Sulphate Inhaler
6. Further information

1. WHAT SALBUTAMOL SULPHATE INHALER IS AND WHAT IT IS USED FOR

Salbutamol Sulphate Inhaler is a pressurised inhalation suspension (inhaler) which contains the active ingredient salbutamol (as salbutamol sulphate). Salbutamol belongs to a group of medicines called short-acting β₂ agonists, bronchodilators or "relievers". Salbutamol is used by patients with asthma as it helps to relieve the symptoms of asthma such as wheezing, shortness of breath, tightness in the chest and cough. Salbutamol is also used to prevent symptoms of asthma which are brought on by exercise or allergens such as house dust mite, pollen, cigarette smoke, cat and dog fur, etc.

Salbutamol can also be used to relieve symptoms such as chest tightness, wheezing, shortness of breath and coughing in some other chest diseases. Salbutamol acts directly on the muscles in the walls of the airways in the lung causing the muscles to relax. This relaxes or opens up the airways making it easier to breathe.

Salbutamol Sulphate Inhaler cannot be used with any spacing device at this time. If you need a spacing device, your doctor will need to prescribe another product, which can be used with a spacing device, instead of Salbutamol Sulphate Inhaler.

2. BEFORE YOU USE SALBUTAMOL SULPHATE INHALER

Do not use Salbutamol Sulphate Inhaler if you are:
- allergic to salbutamol sulphate or any of the other ingredients in the inhaler (see Section 6);
- in premature labour or have a threatened miscarriage.

Tell your doctor or pharmacist before starting to take this medicine if you:
- are pregnant, think you may be pregnant, or trying to become pregnant. Tell your doctor or pharmacist before using Salbutamol Sulphate Inhaler.
- are breast-feeding. Salbutamol may pass into your breast milk.
- are being treated for an overactive thyroid (hyperthyroidism);
- are being treated for thyroid cancer;
- are being treated for an irregular or very fast heartbeat / rhythm;
- are being treated for an irregular or very fast fast heartbeat / rhythm.

Taking other medicines
Tell your doctor, pharmacist or asthma nurse if you are taking, or have recently taken, any other medicines, including other inhalers, or any medicines and tablets obtained without a prescription.

Tell your doctor, pharmacist or asthma nurse if you are taking any of the following medicines before using Salbutamol Sulphate Inhaler:
- beta-blockers (used to treat high blood pressure)
- diuretics (used to treat high blood pressure)
- beta-blockers (used to treat heart problems)
- beta-blockers (used to treat heart problems)
- metronidazole (used to treat some bacterial infections)
- methotrexate (used for example in chemotherapy or to treat psoriasis)
- theophylline tablets and inhaled steroids or steroid tablets (also used in the treatment of asthma)
- diuretics (water tablets)
- long-term laxatives.

Xanthine derivatives, steroids, diuretics and laxatives can all cause the level of potassium in your blood to fall. Your doctor will wish to monitor this and therefore from time to time may need to carry out a blood test to check your potassium levels.

Pregnancy and breast-feeding
The safe use of salbutamol during pregnancy has not been established. Tell your doctor if you are pregnant, if you think that you may be pregnant or if you are trying to become pregnant. Your doctor will advise you as to whether you should use Salbutamol Sulphate Inhaler or not.

Do not breastfeed whilst your doctor advises you to.

Do not use Salbutamol Sulphate Inhaler if you are in premature labour or have a threatened miscarriage. Unlike salbutamol injection, occasional salbutamol tablets, inhaled salbutamol cannot be used to treat premature labour or threatened miscarriage.

Ask your doctor, asthma nurse or pharmacist for advice before taking any medicines, tablets or inhalers if you are pregnant of breast-feeding.

If you need to see another doctor or need to go into hospital, you should take all your medicines (including all your inhalers and any medicines or tablets bought without a prescription) with you, in the original packaging if possible.

Driving and using machines
It is unlikely that taking Salbutamol Sulphate Inhaler will have an effect on your ability to drive or operate machinery.

3. HOW TO USE SALBUTAMOL SULPHATE INHALER

Always use the inhaler exactly as your doctor or asthma nurse has told you to and take the recommended dose.

Make sure you know HOW, WHEN and HOW MANY puffs you need to take. This information should be on the pharmacist’s label on the carton in which you received your inhaler. If it is not, or you are not sure, ask your doctor, pharmacist or asthma nurse.

Salbutamol Sulphate Inhaler produces a fine mist, which must be inhaled through your mouth into your lungs. Make sure that you know how to use this inhaler properly, by reading the section “How to use your inhaler” later in this leaflet. If you have any problems ask your doctor, pharmacist or asthma nurse.

If you have changed to this inhaler, you may find that it tastes different from your previous inhaler.

Children
Salbutamol Sulphate Inhaler is not recommended for use in children 12 years of age and under.

Adults (including the Elderly)
For the relief of acute asthma symptoms (such as wheezing, shortness of breath or tightness in your chest):
Take one puff, as described in “How to use your inhaler”. This may be increased to 2 puffs if necessary.
For the prevention of symptoms due to exercise and due to allergens (e.g. house dust mite, pollen, cigarette smoke, animal fur etc.):
Take two puffs, as described in “How to use your inhaler”, 10 – 15 minutes before exercise or allergen exposure.

These are the usual doses. Your doctor may have told you to take a different dose, because all patients are different. It is very important that you follow your doctor’s instructions carefully.

Salbutamol Sulphate Inhaler should be used as required.

However, do not take more than 8 puffs in 24 hours and do not take more than 2 puffs in 4 hours. If you find that you need to use your Salbutamol Sulphate Inhaler regularly every day or if you need to take more puffs than usual or you find that the dose is becoming less effective than usual, it may mean that your asthma is not very well controlled or is getting worse. You should contact your doctor or your asthma nurse straightaway.

If you find that your Salbutamol/Sulphate Inhaler does not provide you with relief from your symptoms for at least 3 hours you should tell your doctor or your asthma nurse as soon as possible.

If your symptoms are getting worse, your doctor may tell you to take more puffs than usual as an emergency treatment. IT IS VERY IMPORTANT that you follow your doctor’s instructions on how, when and how many puffs to take. You should contact your doctor or asthma nurse immediately if your symptoms are getting worse.

If you need to go into hospital, remember to take your Inhaler with you. How to use your inhaler.
1. If your inhaler is new, or if you have not used your inhaler for a week or more, shake well, remove the mouthpiece cover and release two sprays into the air before using.

2. Remove the mouthpiece cover and check that the inside and outside of the mouthpiece is clear of dust, dirt or foreign objects (figure 1).

3. If the inhaler is very cold, the canister should be taken out of the plastic actuator and warmed in your hands for a few minutes before you use it. Do not use anything else to warm the canister. Shake the inhaler before each use (figure 2).

4. Hold the inhaler upright with a thumb on the base. Breathe out as far as is comfortable (it is important that you practice this before using the inhaler – see ‘Breathing technique’ (figure 3).

5. And then immediately place the mouthpiece in your mouth and close your lips around it (figure 4). Be careful not to bite the mouthpiece.

6. Breathe in slowly through your mouth. Just after starting to breathe in through your mouth, press firmly down on the top of the canister to release an actuation (puff). Carry on breathing in deeply and steadily (figure 4).

7. Hold your breath, take the inhaler from your mouth and take your finger away from the top of the canister. Continue holding your breath for about 10 seconds, or for as long as is comfortable (figure 5). Then breathe out slowly.

8. If you are taking another puff, keep the inhaler upright and wait for at least 30 seconds before repeating steps 3 - 7.

9. After use, replace the mouthpiece cover firmly, making sure it snaps into position.

**Breathing Technique**

You must breathe in as slowly as possible just before using the inhaler. Do not rush steps 5 to 7. You should practice a few times in front of a mirror. If you see “mist” coming from the canister or the sides of your mouth, then you need to start again from step 5.

People with weak hands may find it easier to hold the inhaler with both hands, with the two fingers/fingertips on the top of the canister and both thumbs on the bottom under the mouthpiece.

**Cleaning your Inhaler**

You should follow the cleaning instructions described below very carefully in order to ensure that your inhaler continues to work properly.

1. Clean your inhaler once a week, or if blocked.

2. First remove the canister from the plastic actuator and take off the mouthpiece cover.

3. Rinse the plastic actuator, mouthpiece and mouthpiece cover in tap water. DO NOT place the metal canister in water or clean the can using water. Make sure the water runs through the actuator from both ends to ensure that the actuator is free from dirt and any residue that can be seen through the mouthpiece is clear and not blocked.

4. The plastic components (actuator and mouthpiece cover) should be placed in a warm place to dry thoroughly before putting the inhaler back together. Avoid drying near direct or excessive heat.

If you use more of your Salbutamol Sulphate Inhaler than you should:

If you accidentally use too many puffs, you may feel shaky, have a fast heartbeat, headache, feel tense or experience flushing. These effects usually wear off within a few hours but if they do not wear off or are troublesome you must tell your doctor as soon as possible or go to your nearest hospital casualty department.

Low levels of potassium in the blood may also occur if you take too much salbutamol and therefore your doctor may want to do some blood tests to monitor your potassium levels.

Do not use more than 2 puffs in 4 hours and never use more than 8 puffs in 24 hours. If you have any further questions on the use of this product, ask your doctor, asthma nurse or pharmacist.

4. **POSSIBLE SIDE EFFECTS**

Like all medicines, Salbutamol Sulphate Inhaler can cause side effects, although not everybody gets them.

Side effects may include:

- Common (seen in less than 1 in 10 people and more than 1 in 100 people):
  - tremor (shakes – especially noticeable in your hands)
  - headache
  - rapid heartbeat (with or without flushing)

- Uncommon (seen in less than 1 in 100 people and more than 1 in 1000 people):
  - palpitations (faster or stronger heartbeats) or changes in your heartbeat (especially extra beats)
  - changes in the rate or rhythm of the heartbeat
  - mouth and throat irritation
  - muscle cramps

- Rare (seen in less than 1 in 1000 people and more than 1 in 10,000 people):
  - low potassium levels in blood. Since salbutamol can change the salt balance in your body, your doctor may occasionally need to take a blood sample to check the potassium levels.
  - flushing
  - Very rare (occurring in less than 1 in 10,000 people):
    - Allergic reactions, which might include any of the following:
      - rapid swelling of the mouth, lips, tongue, face, ears, neck or throat (angioedema)
      - itching, raised bumps and/or redness on the skin (urticaria)
      - constriction of the small air passages in the lungs (bronchoconstriction)
      - low blood pressure (hypotension)
      - collapse
      - Restlessness or excitability (hypersensitivity – particularly in children)

If your breathing or wheezing gets worse immediately after using your inhaler, then stop using it immediately and contact your doctor straightaway. You may need to use a different “reliever” inhaler to treat your symptoms.

If the relief of your symptoms is not as good as usual, or if it does not last as long as usual, tell your doctor as soon as possible. This might mean that your asthma is getting worse and your treatment needs to be changed.

6. **FURTHER INFORMATION**

What Salbutamol Sulphate Inhaler looks like and contents of the pack

The inhaler contains 100 micrograms of salbutamol (as sulphate).

The other ingredients are oleic acid, ethanol and norfarnate (HFA 134a; a CFC-free propellant).

**Marketing Authorisation Holder and Manufacturer:**

The Product Licence holder is SDD Pharmaceuticals Limited, Hillside House, Hillside Road, Esher, Surrey, KT10 9NW.

The manufacturer responsible for batch release is Nellcor Ltd, 57 High Street, Chilworth, Hants, RG26 1LF.

This leaflet was last revised in December 2010.
Salbutamol Sulphate 100 micrograms Inhaler

For administration by your doctor. Do not exceed the recommended dose.

This product is not recommended for use in children 12 years of age and younger.

Salbutamol Sulphate Inhaler cannot be used with any spacers or reducers.

Do not store above 30°C. The canister contains a pressurised liquid. Do not expose to temperatures higher than 50°C. Do not pierce the canister.

Keep out of the reach and sight of children.

POM

MHRA PAR – Salbutamol Sulphate 100 micrograms Inhaler (PL 36390/0034)