

# New Zealand Data Sheet

## 1 PRODUCT NAME

Salair

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Pressurised metered-dose inhaler (pMDI) containing Salbutamol sulphate (equivalent to 100mcg salbutamol base per actuation).

## 3 PHARMACEUTICAL FORM

Salair Inhaler is a pressurised metered-dose that delivers salbutamol sulphate equivalent to 100mcg per actuation into a specifically designed actuator.

Salair Inhaler consists of a pressurised aluminium canister filled with microcrystalline salbutamol sulphate suspended in the non-CFC, HFA-134a propellant, also known as norflurane. The aluminium canister has a metering valve. The aerosol canister is placed within a grey plastic actuator. One Salair Inhaler delivers 200 actuations of medicine. The actuator incorporates a nozzle that atomises the suspension and is fitted with a plastic actuator cap.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Salbutamol sulphate is indicated for the prevention and treatment of bronchospasm and acts on the  $\beta_2$  (beta-2) adrenoceptors of bronchial muscle at therapeutic doses, with little or no action on the  $\beta_1$  (beta-1) adrenoceptors of the heart. With its fast onset of action, it is particularly suitable for the management and prevention of attack in mild asthma and for the treatment of acute exacerbations in moderate and severe asthma.

**Patients with unstable or severe asthma should not rely on bronchodilators as the main or only form of treatment.**

Severe asthma requires regular medical assessment as death may occur. Patients with severe asthma have constant symptoms and frequent exacerbations, with limited physical capacity, and PEF values below 60% (predicted at baseline) with greater than 30% variability, usually not returning entirely to normal after a bronchodilator.

Together with corticosteroid treatment, Salair Inhaler provides essential rescue medication for severe asthmatics in treating acute exacerbations. Urgent treatment and medical advice is required immediately - if the patient fails to respond rapidly or fully to the rescue medication.

Salair provides short-acting (4-6 hours) bronchodilation with fast onset in reversible airways obstruction disease appropriate for emphysema, asthma and chronic bronchitis. It is suitable for long-term use in the relief and prevention of asthmatic symptoms.

Salair should be utilized to alleviate symptoms when they happen and to prevent them in those circumstances recognised by the patient to precipitate an asthmatic attack (e.g. before exercise or unavoidable allergen exposure).

Salair is particularly valuable as rescue medication in mild, moderate or severe asthma, provided that reliance on it does not delay the introduction and use of regular inhaled corticosteroid therapy.

## 4.2 Dose and method of administration

Salair is for oral inhalation only. Babies, children and individuals who find management of a pMDI difficult may use a spacer device with Salair. Ask your doctor or pharmacist to explain how to use it or follow the instructions provided with the spacer.

In most patients, the duration of action of inhaled salbutamol is 4–6 hours.

One of the features of worsening asthma control is the increased use of inhaled  $\beta_2$  (beta-2) agonists to alleviate symptoms. If the use of  $\beta_2$  (beta-2) agonists has increased, the patient should have their asthma therapy plan re-examined and concomitant glucocorticoid therapy considered.

Excessive dosing of Salair may lead to adverse effects; therefore, increases in frequency or dosage should only be performed on medical recommendation.

Approved dosing of Salair is tabulated below:

	<b>Adults</b>	<b>Children</b>
<b>Relief of acute bronchospasm</b>	100 or 200 micrograms	100 micrograms; increased to 200 micrograms if required
<b>Prevention of allergen- or exercise-induced asthma</b>	200 micrograms before challenge	100 micrograms before challenge; increased to 200 micrograms if required
<b>Chronic therapy</b>	Up to 200 micrograms four times per day	Up to 200 micrograms four times per day

Salair should not be used on demand more than four times per day. If the patient requires supplementary use of Salair or has an unexpected increase in dosage requirements, this may indicate deterioration in asthma control (see Warnings and Precautions).

## 4.3 Contraindications

Management of threatened abortion and premature labour is contraindicated with salbutamol formulations administered non intravenously.

Hypersensitivity to salbutamol or other sympathomimetics or any of the inactive ingredients in Salair (see Excipient List).

## 4.4 Special warnings and precautions for use

Asthma should be managed in a step by step manner and by clinically monitoring and reviewing patients using pulmonary function (lung function) tests. One of the features of the decline of asthma control is the increased use of inhaled short-acting  $\beta_2$  (beta-2) agonists (SABA's) to alleviate symptoms. If use of short-acting  $\beta_2$  (beta-2) agonists (SABA's) has increased, the patient should have their asthma therapy plan re-examined. Starting corticosteroids or increasing the existing corticosteroid dose should be considered in patients with sudden and continuous deterioration of asthma control, as this is potentially life threatening. Daily peak flow monitoring could be initiated in patients at risk of sudden loss of asthma control.

If a dose of Salair Inhaler that was previously effective, fails to provide symptomatic relief for three hours or more, medical assistance should be sought to determine if any changes or additions are required to their asthma management plan.

Patients should have their inhaler technique assessed to ensure that the actuation of the inhaler is synchronised with their inspiration such that the medicine is optimally delivered to the lungs.

Salbutamol should be used with caution with patients who have been diagnosed with thyrotoxicosis.

$\beta_2$  (beta-2) agonist therapy, mainly when administered via the parenteral route or by nebuliser, may cause potentially serious hypokalaemia. Considerable caution should be particularly exercised in patients with acute severe asthma, as the risk of serious hypokalaemia increases with diuretics, concomitant xanthine derivatives, and corticosteroids and by hypoxia. Serum potassium levels should be monitored in patients in these situations.

Consistent with other types of therapy given by inhalation, acute paradoxical bronchospasm may result in wheezing immediately after salbutamol is given by inhaler. In cases where paradoxical bronchospasm occurs, treatment should be started immediately via a different presentation or by inhalation of another fast-acting bronchodilator administered immediately, if available. The current salbutamol medication should be immediately discontinued and if required, another bronchodilator that is fast acting should be introduced for continued treatment.

#### 4.5 Interaction with other medicines and other forms of interaction

It is not recommended that non selective beta blocking agents for example propranolol is prescribed together with salbutamol.

Salbutamol should not be prescribed in patients that are undergoing treatment with monoamine oxidase inhibitors (MAOI's).

#### 4.6 Fertility, pregnancy and lactation

Salbutamol effects on fertility within humans is not known due to no information being available. The effects on animal fertility are reviewed in the Preclinical Safety data.

Salair Inhaler must only be considered during pregnancy if the likely advantage to the mother exceeds any potential threat to the foetus.

In children of patients treated with salbutamol during pregnancy there have been rare cases reported of cleft palate, limb defects and other congenital anomalies in post-marketing surveys. It should be noted that multiple medications were taken by some mothers during pregnancy. The rate of congenital abnormalities in the general population is 2–3% and no regular relationship of anomalies has been discerned with antenatal salbutamol exposure; therefore a causal relationship cannot be established with salbutamol use.

Salbutamol is likely to be excreted into breast milk and it is not recognised whether this has a damaging effect on the breast-feeding child. It is not recommended that lactating women use salbutamol unless the potential benefit to the mother exceeds any possible risk to the child.

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

There were no reported effects.

## 4.8 Undesirable effects

Adverse events are organised by system organ class in the table below and frequency category, with frequencies categorised as: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  and  $< 1/10$ ), uncommon ( $\geq 1/1000$  and  $< 1/100$ ), rare ( $\geq 1/10,000$  and  $< 1/1000$ ) and very rare ( $\geq 1/10,000$ ), including isolated reports.

Clinical data was generally used to determine the incidence of very common, common and uncommon events. Spontaneous reports were generally used to determine the incidence of rare and very rare events.

**Table. Frequency of adverse events with salbutamol.**

System organ class	Frequency category	Adverse reaction	Additional notes
Immune system disorders	Very Rare	Hypersensitivity reactions	Including urticaria, hypotension, angio-oedema, bronchospasm, and collapse
Cardiac disorders	Common	Tachycardia	
	Uncommon	Palpitations	
	Very rare	Cardiac arrhythmias	Including tachycardia, atrial fibrillation, supraventricular and extrasystoles
Metabolism and nutritional disorders	Rare	Hypokalaemia	$\beta_2$ (beta-2) agonist use can potentially cause serious hypokalaemia.
Nervous system disorders	Common	Tremor Headache	
	Very rare	Hyperactivity	
Vascular disorders	Rare	Peripheral vasodilatation	
Respiratory, thoracic and mediastinal disorders	Very rare	Paradoxical bronchospasm <sup>(1)</sup>	
Gastrointestinal disorders	Uncommon	Mouth and throat irritation	
Musculoskeletal and connective tissue disorders	Uncommon	Muscle cramps	

1. Similar to that seen with other inhalation therapy, paradoxical bronchospasm with an increase in wheezing (and tachycardia in some patients) may occur immediately after using Salair Inhaler. Salair Inhaler should be discontinued immediately and the patient should be treated with an alternative salbutamol presentation or an alternative fast-acting inhaled bronchodilator. The patient should then be assessed and an alternative therapy initiated if required.

### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>.

## 4.9 Overdose

Signs and symptoms of an overdose of salbutamol are consistent with adverse effects mediated by  $\beta$  agonists (see Warnings and Precautions and Adverse Effects).

In patients who have taken Salair Inhaler at dosages that exceed those approved, discontinuation of treatment should be considered. Patients presenting with cardiac symptoms such as tachycardia or palpitations may require appropriate symptomatic treatment (e.g. a cardioselective  $\beta$  antagonist); however,  $\beta$  antagonists should be used with caution in patients with a history of bronchospasm.

Salbutamol overdose may also precipitate hypokalaemia. It is recommended that serum potassium levels are monitored in patients who have taken Salair Inhaler in dosages exceeding those approved.

With overdose and elevated therapeutic doses of SABA's (short acting beta-agonists), reports of lactic acidosis have been reported. Therefore in situations of overdose, serum lactate and resultant metabolic acidosis should be monitored if elevated (particularly if tachypnea persists or gets worse despite improvement of bronchospasm i.e. wheezing).

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Andrenergics, inhalants. Selective beta-2-adrenoreceptor agonists: ATC code: R03AC02

Salbutamol acts on the  $\beta_2$  (beta-2) adrenoreceptors of the bronchial muscle at therapeutic doses and is a selective  $\beta_2$  (beta-2) adrenoceptor agonist. There is minor or no action on the  $\beta_1$  (beta-1) adrenoceptors of cardiac muscle.

### 5.2 Pharmacokinetic properties

Intravenous salbutamol has a half life of 4-6 hours and is partially cleared by the metabolism to the phenolic sulphate, also known as the inactive 4'-O-sulphate, and partially cleared renally.

When administered either intravenously, by inhalation, or orally, the majority of the dose of salbutamol is cleared within 72 hours. Approximately 10% of salbutamol is bound to plasma proteins.

When inhaled, approximately 10-20% of the salbutamol dose is deposited in the lower airways. The dose fraction that reaches the lower airways is not metabolised by the lung but absorbed in the circulation and the tissues of the lung.

The remainder of the dose remains in the oropharynx where it is swallowed, or left on the actuator and/or spacer if used. The gastrointestinal tract absorbs the swallowed salbutamol where it goes through extensive first-pass metabolism to the phenolic sulphate (4'-O-sulphate metabolite). The unchanged salbutamol and the phenolic sulphate are both primarily excreted in the urine.

Salbutamol once it reaches the systemic circulation is excreted after undergoing hepatic metabolism. Salbutamol is excreted predominantly in the urine as salbutamol that is

unchanged, along with the inactive 4'-O-sulphate metabolite (phenolic sulphate). Minor excretion is seen in the faeces.

### 5.3 Preclinical safety data

Salbutamol administered subcutaneously has been shown to be teratogenic in mice which is also frequent with other  $\beta_2$  (beta-2) selective agents. At four times the human maximum oral potent dose of 2.5mg/kg, during a reproductive study, cleft palates were found in 9.3% of mice fetuses. There were no abnormalities that were significant in rats dosed orally through pregnancy with 0.5mg/kg/day, 2.32mg/kg/day, 10.75mg/kg/day or 50mg/kg/day. In rats, due to a lack of maternal care at the highest dose (50mg/kg/day), neonatal mortality was the only toxic outcome. In rabbits during a reproductive study at 78x the maximum dose for humans or 50mg/kg/day, 37% of foetuses displayed cranial malformations.

In rats in a general reproductive study and study on oral fertility with the dose of 2mg/kg/day and 50mg/kg/day, there were no harmful fertility effects, or effects on the size of litter, rate of growth, birth weight or development of the embryo-foetus. The exception was at the highest dose (50mg/kg/day), where the number of surviving weanlings reduced post partum to day 21.

In a wide number of animal species, HFA-134A given for more than two years at doses much higher than those received by humans, has been shown to be non toxic even at extremely high "vapour" concentrations.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

HFA-134a (also known as CFC Free norflurane) ethanol, oleic acid.

### 6.2 Incompatibilities

None reported.

### 6.3 Shelf life

Shelf life is 36 months (3 years) from manufacture.

### 6.4 Special precautions for storage

When the Salair Inhaler is not in use, the plastic dust cap should be securely placed back on the mouthpiece of the actuator.

Store Salair Inhaler below 25°C.

The shelf life of Salair Inhaler is 24 months.

Avoid direct sunlight or heat and protect from frost. As the canister is pressurised, no attempt should be made to puncture or dispose of it by burning.

As for other medications that are inhaled from aerosol canisters, the effect of the medication may be reduced if the canister is very cold. If this is the case, warm the inhaler in your hands for a few minutes before use. Do not use anything else to assist with warming up the canister.

### Instructions for use

Usage instructions can also be found in the package insert.

Correct operation of the Salair Inhaler is essential for successful therapy.

Prior to using the Salair Inhaler for the first time, remove the plastic dust cap from the mouthpiece of the inhaler, shake the inhaler and depress the canister twice into the air to prime the inhaler. If the inhaler has not been used for more than one week, remove the plastic dust cap from the mouthpiece of the inhaler, shake the inhaler well and depress the canister once (into the air) to prime the inhaler.

Technique for proper administration of Salair Inhaler is described in the following steps:

1. Remove the plastic dust cap from the mouthpiece of the inhaler and check the mouthpiece is clean. Shake inhaler well and prime if necessary as described above.
2. Hold the inhaler, with the inhaler upright using either one or two fingers on the top of the canister and your thumb on the base. Breathe out deeply through your mouth. Place the mouthpiece of the actuator in your mouth taking care to not bite it and close your lips over the mouthpiece.
3. Start breathing in through your mouth. Then depress the canister to release one dose while continuing to breathe in deeply and steadily.
4. Remove the inhaler away from your mouth and hold your breath for 10 seconds or as long as comfortable. Breathe out slowly.
5. If another dose is required, wait for at least one minute with the inhaler in an upright position, and then repeat steps 2 to 4.
6. After use, replace the mouthpiece cover making sure the dust cap is secure.

#### IMPORTANT:

Do not rush steps 2, 3 and 4. It is essential that just before depressing the canister that you begin breathing in as slow as possible.

It is useful to complete this exercise using a mirror for the initial few doses. If you see "mist or vapour" from the sides of your mouth or top of the inhaler, begin again from step 2.

Provide feedback to your doctor if you have any concerns or issues when using your Salair Inhaler. If different directions have been provided by your doctor, please follow these instructions with care.

#### Children:

An adult may need to assist young children with operating their inhaler. The child should be instructed to breathe out then breathe in again slowly with the actuator in their mouth. As the child begins to breathe in, the adult should depress the canister. This technique may require practice. Older children or individuals with weak hands should use both hands to hold the inhaler, with two forefingers on top of the inhaler and two thumbs on the base below the mouthpiece.

#### **Cleaning**

The Salair Inhaler plastic actuator must be cleaned at least once a week to ensure that it functions correctly.

1. Gently pull the metal canister out of the plastic actuator of the inhaler and take off the mouthpiece dust cap.
2. Immerse the plastic actuator and the mouthpiece dust cap in warm water.
3. Rinse the plastic actuator and mouthpiece dust cap under running tap water.
4. Shake well to remove excess water. Leave to dry in a warm place. Avoid excessive heat.
5. Replace the aluminium canister and the plastic mouthpiece dust cap.

If soap or detergent is used, the mouthpiece should be thoroughly rinsed in clean water. It is suggested that the patient has a spare Salair so that it can be used if required while the other inhaler is drying.

## **6.5 Nature and contents of container**

200 actuations per canister

## **6.6 Special precautions for disposal**

No special requirements

## **7 MEDICINE SCHEDULE**

Prescription Medicine

## **8 SPONSOR**

REX Medical Limited

PO Box 18 119

Glen Innes

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Telephone: (09) 574 6060

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## **9 DATE OF FIRST APPROVAL**

26 January 2012

## **10 DATE OF REVISION OF THE TEXT**

19 April 2017



## SUMMARY TABLE OF CHANGES

Section changed	Summary of new information