NEW ZEALAND DATA SHEET

1. PRODUCT NAME

Ventolin Inhaler (CFC-Free) 100 micrograms

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ventolin Inhaler (CFC-Free) is a pressurised metered-dose inhaler which delivers 100μg salbutamol (as sulfate) per actuation, into the mouthpiece of a specially designed actuator. The inhaler also contains the CFC-free propellant HFA134a.

For the full list of excipients, see section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Inhaler, aerosol, metered

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Salbutamol is a selective beta-$_2$ adrenoceptor agonist indicated for the treatment or prevention of bronchospasm. It provides short acting (four hours) bronchodilation in reversible airways obstruction due to asthma, chronic bronchitis and emphysema. For patients with asthma salbutamol may be used to relieve symptoms when they occur and to prevent them prior to a known trigger.

Bronchodilators should not be the only or main treatment in patients with persistent asthma. In patients with persistent asthma unresponsive to salbutamol, treatment with inhaled corticosteroids is recommended to achieve and maintain control. Failure to respond promptly or fully to such rescue medication signals a need for urgent medical advice and treatment.

4.2 Dose and method of administration

Method of administration

Ventolin Inhaler (CFC-Free) is administered by the oral inhaled route only, to be breathed in through the mouth.

Salbutamol has a duration of action of 4 to 6 hours in most patients.

Increasing use of beta-$_2$ agonists may be a sign of worsening asthma. Under these conditions a reassessment of the patient's therapy plan may be required and concomitant glucocorticosteroid therapy should be considered.

In patients who find co-ordination of a pressurised metered-dose inhaler difficult a spacer device may be used with the Ventolin Inhaler (CFC-Free).

Babies and young children may benefit from use of a spacer device with the Ventolin Inhaler (CFC-Free).

As there may be adverse effects associated with excessive dosing, the dosage or frequency of administration should only be increased on medical advice.

Dose

Adults

Relief of acute bronchospasm

100 or 200 micrograms. On demand use of Ventolin should not exceed four times daily. Reliance on such supplementary use or a sudden increase in dose indicates deteriorating asthma (see section 4.4 Special Warnings and Special Precautions for Use).

Prevention of allergen or exercise-induced bronchospasm

200 micrograms before challenge.

Chronic therapy

Up to 200 micrograms four times daily.

Paediatric Population

Relief of acute bronchospasm

100 micrograms, the dose may be increased to 200 micrograms if required.

On demand use of Ventolin should not exceed four times daily. Reliance on such supplementary use or a sudden increase in dose indicates deteriorating asthma (see section 4.4 Special Warnings and Special Precautions for Use).

Prevention of allergen or exercise-induced bronchospasm

100 micrograms before challenge, the dose may be increased to 200 micrograms if required.

Chronic therapy

Up to 200 micrograms four times daily.

4.3 Contraindications

Ventolin Inhaler (CFC-Free) is contraindicated in patients with a history of hypersensitivity to any of its components (see section 6.1 List of excipients).

Non-i.v. formulations of salbutamol must not be used to arrest uncomplicated premature labour or threatened abortion.

4.4 Special Warnings and Special Precautions for Use

The management of asthma should normally follow a stepwise programme, and patient response should be monitored clinically and by lung function tests.

Increasing use of short-acting inhaled beta-$_2$ agonists to control symptoms indicates deterioration of asthma control. Under these conditions, the patient's therapy plan should be reassessed. Sudden and progressive deterioration in asthma control is potentially life-threatening and consideration should be given to starting or increasing corticosteroid therapy. In patients considered at risk, daily peak flow monitoring may be instituted.

In the event of a previously effective dose of inhaled salbutamol failing to give relief for at least three hours, the patient should be advised to seek medical advice in order that any necessary additional steps may be taken.

Patients' inhaler technique should be checked to make sure that aerosol actuation is synchronised with inspiration of breath for optimum delivery of the drug to the lungs.

Salbutamol should be administered cautiously to patients with thyrotoxicosis.

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 concomitant treatment with xanthine derivatives, steroids, diuretics and by hypoxia. It is recommended that serum potassium levels are monitored in such situations.

As with other inhalation therapy, paradoxical bronchospasm may occur, resulting in an immediate increase in wheezing after dosing. This should be treated immediately with an alternative presentation or a different fast-acting inhaled bronchodilator, if immediately available. The specific salbutamol presentation should be discontinued, and if necessary a different fast-acting bronchodilator instituted for ongoing use.

4.5 Interaction with other medicines and other forms of interaction

Salbutamol and non-selective beta-blocking agents, such as propranolol, should not usually be prescribed together.

Salbutamol is not contra-indicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

4.6 Fertility, pregnancy and lactation

Pregnancy

Administration of medicines during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus.

During worldwide marketing experience, rare cases of various congenital anomalies, including cleft palate and limb defects have been reported in the offspring of patients being treated with salbutamol. Some of the mothers were taking multiple medications during their pregnancies.

Because no consistent pattern of defects can be discerned, and baseline rate for congenital anomalies is 2-3%, a relationship with salbutamol use cannot be established.

Breast-feeding

As salbutamol is probably secreted in breast milk its use in nursing mothers is not recommended unless the expected benefits outweigh any potential risk. It is not known whether salbutamol in breast milk has a harmful effect on 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 Preclinical safety data).

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

Tabulated list of adverse reactions

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: Tremor, headache.

Very rare: Hyperactivity.

Cardiac disorders
Common: Tachycardia.

Uncommon: Palpitations.

Very rare: Cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles.

Vascular disorders
Rare: Peripheral vasodilatation.

Respiratory, thoracic and mediastinal disorders
Very rare: Paradoxical bronchospasm.

Gastrointestinal disorders
Uncommon: Mouth and throat irritation.

Musculoskeletal and connective tissue disorders
Uncommon: Muscle cramps.

*Tachycardia may occur in some patients.

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 via: https://nzphvc.otago.ac.nz/reporting.

4.9 Overdose

The most common signs and symptoms of overdose with salbutamol are transient beta agonist pharmacologically mediated events (see section 4.4 Special Warnings and Special Precautions for Use and section 4.8 Undesirable Effects).

Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored.

Lactic acidosis has been reported in association with high therapeutic doses as well as overdoses of short-acting beta-agonist therapy, therefore monitoring for elevated serum lactate and consequent metabolic acidosis (particularly if there is persistence or worsening of tachypnea despite resolution of other signs of bronchospasm such as wheezing) may be indicated in the setting of overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Andrenergics, inhalants. Selective beta-2—andrenoreceptor agonists

ATC code: R03AC02.

Salbutamol is a selective beta-$_2$ adrenoceptor agonist. At therapeutic doses it acts on the beta-$_2$ adrenoceptors of bronchial muscle providing short acting (4 to 6 hour) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction.

5.2 Pharmacokinetic properties

Absorption

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.

Distribution

Salbutamol is bound to plasma proteins to the extent of 10%.

Biotransformation

On reaching the systemic circulation it becomes accessible to hepatic metabolism and is excreted, primarily in the urine, as unchanged salbutamol and as the phenolic sulfate.

The swallowed portion of an inhaled dose is absorbed from the gastrointestinal tract and undergoes considerable first-pass metabolism to the phenolic sulfate. Both unchanged salbutamol and conjugate are excreted primarily in the urine.

Elimination

Salbutamol administered intravenously has a half-life of 4 to 6 hours and is cleared partly renally and partly by metabolism to the inactive 4'-O- sulfate (phenolic sulfate) which is also excreted primarily in the urine. The faeces are a minor route of excretion. The majority of a dose of salbutamol given intravenously, orally or by inhalation is excreted within 72 hours.

5.3 Preclinical safety data

In common with other potent selective □$_2$ receptor agonists, salbutamol has been shown to be teratogenic in mice when given subcutaneously. In a reproductive study, 9.3% of foetuses were found to have cleft palate, at 2.5 mg/kg, 4 times the maximum

human oral 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 foetal abnormalities. The only toxic effect was an increase in neonatal mortality at the highest dose level as the result of lack of maternal care. A reproductive study in rabbits revealed cranial malformations in 37% of foetuses at 50mg/kg/day, 78 times the maximum human oral dose.

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.

HFA 134a has been shown to be non-toxic at very high vapour concentrations, far in excess of those likely to be experienced by patients, in a wide range of animal species exposed daily for periods of two years.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Norflurane

6.2 Incompatibilities

None reported.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Replace the mouthpiece cover firmly and snap it into position.

Ventolin Inhaler (CFC-Free) should be stored below 30°C.

Protect from frost and direct sunlight.

As with most inhaled medications in aerosol canisters, the therapeutic effect of this medication may decrease when the canister is cold.

The canister should not be broken, punctured or burnt, even when apparently empty.

6.5 Nature and contents of container

Ventolin Inhaler (CFC-Free) comprises a suspension of salbutamol sulfate in the non-CFC propellant HFA 134a. The suspension is contained in an aluminium alloy can, sealed with a metering valve. Each canister is fitted with a plastic actuator incorporating an atomising nozzle and fitted with a dustcap. Ventolin Inhaler (CFC-Free) delivers 100□g of salbutamol (as sulfate) per actuation.

Each canister contains at least 200 actuations.

6.6 Special precautions for disposal and other handling

Testing your inhaler:

Before using for the first time remove the mouthpiece cover by gently squeezing the sides of the cover, shake the inhaler well, and release two puffs into the air to make sure that it works. If it has not been used for 5 days or more, shake it well and release two puffs into the air to make sure that it works.

Using your inhaler:

1. Remove the mouthpiece cover by gently squeezing the sides of the cover.

2. Check inside and outside of the inhaler including the mouthpiece for the presence of loose objects.

3. Shake the inhaler well to ensure that any loose objects are removed and that the contents of the inhaler are evenly mixed.

4. Hold the inhaler upright between fingers and thumb with your thumb on the base, below the mouthpiece.

5. Breathe out as far as is comfortable and then place the mouthpiece in your mouth between your teeth and close your lips around it but do not bite it.

6. Just after starting to breathe in through your mouth press down on the top of the inhaler to release salbutamol while still breathing in steadily and deeply.

7. While holding your breath, take the inhaler from your mouth and take your finger from the top of the inhaler. Continue holding your breath for as long as is comfortable.

8. If you are to take further puffs keep the inhaler upright and wait about half a minute before repeating steps 2 to 6.

9. Replace the mouthpiece cover by firmly pushing and snapping the cap into position.

<u>IMPORTANT:</u>

Do not rush Stages 5, 6 and 7. It is important that you start to breathe in as slowly as possible just before operating your Inhaler.

Practise in front of a mirror for the first few times. If you see 'mist' coming from the top of the inhaler or the sides of your mouth you should start again from stage 2.

If your doctor has been given you different instructions for using your inhaler, please follow them carefully. Tell your doctor if you have any difficulties.

Cleaning your inhaler:

Your inhaler should be cleaned at least once a week.

1. Remove the metal canister from the plastic casing of the inhaler and remove the mouthpiece cover.

2. Rinse the actuator thoroughly under warm running water.

3. Dry the actuator THOROUGHLY inside and out.

4. Replace the metal canister and mouthpiece cover.

DO NOT PUT THE METAL CANISTER INTO WATER.

7. MEDICINE SCHEDULE

Prescription Only Medicine

8. SPONSOR

GlaxoSmithKline NZ Limited
Private Bag 106600
Downtown
Auckland
NEW ZEALAND

Phone: (09) 367 2900
Facsimile: (09) 367 2910

9. DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:
9 July 1998

10. DATE OF REVISION OF THE TEXT

29 May 2017

Summary Table of changes

Section changed	Summary of new information
All	Update to the DS format in accordance with the new SPC style format Minor editorial and formatting updates to correct spacing including changing the spelling of the word 'sulphate' to 'sulfate'
1	The registered symbol has been removed to as part of GSK's global trade mark requirements
4.2	The dosing information for children has been separated out from the Adult sub-group into a Paediatric population sub-group as per the NZ SPC Data Sheet requirements
4.6	Updated Pharmacokinetics section to align with NZ SPC
4.8	Added reporting of suspected adverse reactions information
5.1	Added Pharmacotherapeutic group and ATC code information
5.2	Updated Pharmacokinetics section to align with NZ SPC
6.1	Addition of List of excipients section to align with NZ SPC
9	Added date of first approval
10	Addition of Summary table of changes Update the GSK trade mark statements

Version: 5.0