NEW ZEALAND DATA SHEET

1. PRODUCT NAME
Ventolin Nebules 2.5 mg/2.5 mL
Ventolin Nebules 5 mg/2.5 mL

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Ventolin nebules 2.5mg are a plastic ampoule presentation containing a sterile, aqueous colourless solution of salbutamol sulfate in normal saline. The concentration of salbutamol is 0.1% (1mg salbutamol, as the sulfate, in 1mL). Each Nebule contains 2.5mL of solution equivalent to 2.5mg salbutamol.

Ventolin nebules 5.0mg are a plastic ampoule presentation containing a sterile, aqueous colourless solution of salbutamol sulfate in normal saline. The concentration of salbutamol is 0.2% (2mg salbutamol, as the sulfate, in 1mL). Each Nebule contains 2.5mL of solution equivalent to 5.0mg salbutamol.

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

3. PHARMACEUTICAL FORM
Solution for inhalation.

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

4.2 Dose and method of administration

Method of administration
Salbutamol has a duration of action of 4 to 6 hours in most patients.
Ventolin Nebules are intended to be used undiluted. However, if prolonged delivery time is desirable (more than 10 minutes) dilution using sterile normal saline as a diluent may be required.

Ventolin Nebules are to be used with a nebuliser, under the direction of a physician.

The solution must not be injected or swallowed.

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.

Delivery of the aerosol may be by facemask, 'T' piece or via an endotracheal tube. Intermittent positive pressure ventilation may be used but is rarely necessary. When there is a risk of anoxia through hypoventilation, oxygen should be added to the inspired air.

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

As many nebulisers operate on a continuous flow basis, it is likely that nebulised agent will be released in the local environment. Ventolin nebulie should therefore be administered in a well ventilated room, particularly in hospitals when several patients may be using nebulisers at the same time.

**Dose**

**Adults** A suitable starting dose of salbutamol by wet inhalation is 2.5 milligrams. This may be increased to 5 milligrams. Treatment may be repeated four times daily.

In adults higher dosing, up to 40 milligrams per day, can be given under strict medical supervision in hospital for the treatment of severe airways obstruction.

**Paediatric Population**

A suitable starting dose of salbutamol by wet inhalation is 2.5 milligrams. This may be increased to 5 milligrams. Treatment may be repeated four times daily.

Clinical efficacy of nebulised salbutamol in infants under 18 months is uncertain. As transient hypoxaemia may occur, supplemental oxygen therapy should be considered.

**4.3 Contra-indications**

Ventolin Nebules are contra-indicated in patients with a history of hypersensitivity to any of their components (see 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

Ventolin Nebules must only be used by inhalation, to be breathed in through the mouth, and must not be injected or swallowed.

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.

Patients receiving treatment at home with Ventolin Nebules must be warned that if either the usual relief is diminished or the usual duration of action reduced, they should not increase the dose or its frequency of administration, but should seek medical advice.

Ventolin Nebules should be used with caution in patients known to have received large doses of other sympathomimetic agents.

Salbutamol should be administered cautiously to patients with thyrotoxicosis.

A small number of cases of acute angle closure glaucoma have been reported in patients treated with a combination of nebulised salbutamol and ipratropium bromide. A combination of nebulised salbutamol with nebulised anticholinergics should therefore be used cautiously. Patients should receive adequate instruction in correct administration and be warned not to let the solution or mist enter the eye.

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.

In common with other -adrenoceptor agonists, Ventolin can induce reversible metabolic changes, for example increased blood sugar levels.

The diabetic patient may be unable to compensate for this and the development of ketacidosis has been reported. Concurrent administration of corticosteroids can exaggerate this effect.

Lactic acidosis has been reported very rarely in association with high therapeutic doses of intravenous and nebulised short-acting beta-agonist therapy, mainly in patients being treated for an acute asthma exacerbation (see Undesirable Effects section). Increase in lactate levels may lead to dyspnoea and compensatory hyperventilation, which could be misinterpreted as a sign of asthma treatment failure and lead to inappropriate intensification of short-acting beta-agonist treatment. It is therefore recommended that patients are monitored for the development of elevated serum lactate and consequent metabolic acidosis in this setting.

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 medicaments and other forms of interaction

Salbutamol and non-selective beta-blocking medicines, 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 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 beta2 agonist therapy.

Very rare: Lactic acidosis

Lactic acidosis has been reported very rarely in patients receiving intravenous and nebulised salbutamol therapy for the treatment of acute asthma exacerbation.

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.

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—adrenoreceptor 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 drug 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 drug 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 beta-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 2.5mg/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, embryo foetal development, litter size, birth weight or growth rate.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

- Sodium chloride
- Sulfuric acid
- Water for injection

**6.2 Incompatibilities**

None reported.
6.3 Shelf Life

36 months

6.4 Special precautions for storage

Ventolin Nebules should be stored at a temperature below 30°C and protected from light.

6.5 Nature and contents of container

Ventolin Nebules 2.5mg and 5.0mg are each available in boxes containing 20 Nebules in strips of 5.

6.6 Special precautions for disposal and other handling

Ventolin Nebules may be diluted with sterile normal saline. Any unused solution in the chamber of the nebuliser must be discarded.

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: 5 August 1981

10. DATE OF REVISION OF THE TEXT

29 May 2017
## Summary Table of changes

<table>
<thead>
<tr>
<th>Section changed</th>
<th>Summary of new information</th>
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</table>
| 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 |
| 3               | Addition of Pharmaceutical form section |
| 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 |
| 4.7             | Addition of Effects on ability to drive and use machines |
| 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 |
| 6.2             | Addition of Incompatibilities 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: 4.0

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