# VENTOLIN NEBULES 2,5 mg

# VENTOLIN NEBULES 5 mg

**Salbutamol sulfate**

## QUALITATIVE AND QUANTITATIVE COMPOSITION

*VENTOLIN* Nebules 2.5 mg: contain a concentration of salbutamol of 0.1% (1 mg salbutamol, as the sulphate, in 1 ml). Each Nebule contains 2.5 ml of solution equivalent to 2.5mg salbutamol.

*VENTOLIN* Nebules 5 mg: contain a concentration of salbutamol of 0.2% (2 mg salbutamol, as the sulphate, in 1 ml). Each Nebule contains 2.5 ml of solution equivalent to 5.0 mg salbutamol.

## PHARMACEUTICAL FORM

Nebuliser solution.

*VENTOLIN* Nebules contain a clear, colourless liquid.

## CLINICAL PARTICULARS

### 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 *VENTOLIN*, treatment with inhaled corticosteroids is recommended to achieve and maintain control. Failing to respond to treatment with *VENTOLIN* may signal a need for urgent medical advice or treatment.

*VENTOLIN* Nebules are indicated for the routine management of chronic bronchospasm (unresponsive to conventional therapy) and treatment of acute severe asthma (status asthmaticus).

### Dosage and Administration

*VENTOLIN* 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 drug will be released in the local environment. *VENTOLIN* Nebules should therefore be administered in a well ventilated room, particularly in hospitals when several patients may be using nebulisers in the same space at the same time.

- **Adults and Children**

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.

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

## Contraindications

*VENTOLIN* Nebules are contraindicated in patients with a history of hypersensitivity to any of their components.

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

## Warnings and Precautions

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.

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

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 drugs.

*VENTOLIN* 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 *VENTOLIN* and ipratropium bromide. A combination of nebulised *VENTOLIN* 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.

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. *VENTOLIN* nebules should be discontinued, and if necessary a different fast-acting bronchodilator instituted for ongoing use.

In common with other beta-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 Adverse Reaction 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.

## Interactions

*VENTOLIN* and non-selective beta-blocking drugs, such as propranolol, should not usually be prescribed together.

*VENTOLIN* is not contraindicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

## Pregnancy and Lactation

### Fertility

There is no information on the effects of *VENTOLIN* on human fertility. There were no adverse effects on fertility in animals (*see Pre-clinical Safety Data*).

### Pregnancy

Administration of drugs 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.

As 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.

### Lactation

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.

## Effects on Ability to Drive and Use Machines

None reported.

## Adverse Reactions

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <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.

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

## Overdose

The most common signs and symptoms of overdose with *VENTOLIN* are transient beta agonist pharmacologically mediated events (see Warnings and Precautions and Adverse Reactions).

Hypokalaemia may occur following overdosage with *VENTOLIN*. 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.

# PHARMACOLOGICAL PROPERTIES

## Pharmacodynamics

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.

## Pharmacokinetics

### 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%.

### Metabolism

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.

### Elimination

Salbutamol administered intravenously has a half-life of four to six hours and is cleared partly renally 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. The majority of a dose of salbutamol given intravenously, orally or by inhalation is excreted within 72 hours.

## Pre-clinical 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 2.5 mg/kg, 4 times the maximum human oral. 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.

# PHARMACEUTICAL PARTICULARS

## List of Excipients

Sodium chloride.
Sulphuric acid.
Purified water.

## Incompatibilities

None reported.

## Shelf Life

The expiry date is indicated on the packaging.

## Special Precautions for Storage

*VENTOLIN* Nebules should be stored at a temperature below 25°C and protected from light.

Unused nebules must be discarded within three months after opening the foil.

Keep out of reach of children.

## Nature and Contents of Container

*VENTOLIN* nebules are plastic ampoules containing a solution of salbutamol sulphate in normal saline. Each Nebule contains 2.5ml of solution.

*VENTOLIN* nebules are available in strips of 5 overwrapped in printed foil, available in cartons containing 30 nebules.

Not all presentations are available in every country.

## Instructions for Use/Handling

Dilution:

*VENTOLIN* Nebules may be diluted with sterile normal saline.

Any unused solution in the chamber of the nebuliser must be discarded.

## Name and address of the holder of the certificate of registration

GlaxoSmithKline South Africa (Pty) Ltd

57 Sloane Street

Bryanston, 2021

South Africa

## Manufacturer

GlaxoSmithKline Australia (Pty) Ltd, 1061 Mountain Highway, Boronia, Victoria 3155, Australia

## Registration details

Botswana:

VENTOLIN NEBULES 2,5 mg - Reg No B9320760 S2

Namibia:

VENTOLIN NEBULES 2,5 mg - Reg No 04/10.2.1/0919 NS2

VENTOLIN NEBULES 5,0 mg - Reg No 04/10.2.1/0920 NS2

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