VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION

SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINE:

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION

Salbutamol 1 mg/ml

2. QUALITATIVE AND QUANTITIVE COMPOSITION:

Ampoules of 5 ml, each of which contains salbutamol sulphate equivalent to 5 mg salbutamol (1 mg/ml).

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

Solution for Infusion.

The solution is colourless to very pale straw coloured and odourless. Its specific gravity and viscosity are similar to water.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

1. **Use in Asthma:**

   VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION is indicated for the relief of severe bronchospasm associated with asthma or bronchitis and for the treatment of status asthmaticus.

2. **Use in Obstetrics:**

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION is indicated to inhibit uncomplicated premature labour between 22 and 37 weeks of gestation in patients with no medical or obstetric contraindication to tocolytic therapy.

4.2 Posology and method of administration:

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION is to be used only under medical direction.

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION should not be administered in the same syringe or infusion as any other medication.

1. **Use in Asthma:**

   In status asthmaticus infusion rates of 3 to 20 µg/minute are generally adequate, but in patients with respiratory failure higher dosage has been used with success. A starting dose of 5 µg/minute is recommended with appropriate adjustments in dosage according to patient response.

NOTE:

If VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION must be given to an asthmatic patient in labour, it will inhibit uterine contractions. This effect can be counteracted by administration of natural or synthetic oxytocic drugs.

2. **Use in Obstetrics:**

   Treatment with VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION should only be initiated by medical practitioners experienced in the use of tocolytic agents. Ideally, it should be carried out in facilities adequately equipped to perform continuous monitoring of maternal and foetal health status.

   Duration of treatment should not exceed 48 hours as data show that the main effect of tocolytic therapy is a delay in delivery of up to 48 hours. No statistically significant effect on perinatal

mortality or morbidity has been observed in randomised, controlled trials. This delay may be used to administer glucocorticoids or to implement other measures known to improve perinatal health.

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION should be administered as early as possible after the diagnosis of premature labour and after evaluation of the patient to eliminate any contraindications to the use of VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION (see section 4.3). This should include an adequate assessment of the patient's cardiovascular status with continuous ECG monitoring throughout treatment (see section 4.4).

In premature labour infusion rates of 10 to 45 µg/minute are generally adequate to control uterine contractions. The infusion rate required varies according to the strength and frequency of contractions. A starting dose of 10 µg per minute is recommended, increasing the rate at 10-minute intervals until there is evidence of patient response shown by a diminution in strength, frequency or duration of contractions. Thereafter the infusion rate may be increased slowly until contractions cease. Careful attention should be given to cardio-respiratory function, including increases in pulse rate and changes in blood pressure, electrolytes, glucose and lactate levels and fluid balance monitoring. A maximum sustained maternal heart rate of 120 beats/min should not be exceeded. Use of an infusion pump will facilitate accurate adjustments and control of salbutamol infusion. Once uterine contractions have ceased the infusion rate should be maintained at the same level for one hour and then reduced by 50 % decrements at 6-hourly intervals.

Treatment should be discontinued, should signs and symptoms of pulmonary oedema or myocardial ischaemia develop (see section 4.4).

4.3 Contraindications:

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION is contraindicated in patients with a history of hypersensitivity to salbutamol sulphate or to any of the components of VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION (see section 6.1).

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION should not be used for threatened abortion.

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION, when used in the management of premature labour, is contraindicated in the following conditions:

- at a gestational age < 22 weeks
- intra-uterine foetal death, known lethal congenital or lethal chromosomal malformation
- any condition of the mother or foetus in which prolongation of the pregnancy is hazardous (including placenta praevia, antepartum haemorrhage, toxaemia of pregnancy)
- in patients with pulmonary hypertension, valvular heart disease, pre-existing ischaemic heart disease or those patients with significant risk factors for ischaemic heart disease.

4.4 Special warnings and precautions:

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION should be administered with caution in patients with thyrotoxicosis.

Increasing use of VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION to control symptoms of asthma, 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.

Potentially serious hypokalaemia may occur from VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION therapy.

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION and beta-blocking medicines should not be prescribed together.

Diabetic patients and those concurrently receiving corticosteroids should be monitored frequently during IV infusion of VENTOLIN.

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION can induce increased blood glucose levels. A diabetic patient may be unable to compensate for this and the development of keto-acidosis has been reported. Concurrent administration of corticosteroids can exaggerate this effect.

Diabetic patients and those concurrently receiving corticosteroids should be monitored frequently during IV infusion of VENTOLIN so that remedial steps (e.g. an increase in insulin dosage) can be taken to counter any metabolic change occurring. For these patients VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION should be diluted with Sodium Chloride Injection B.P., rather than Sodium Chloride and Dextrose Injection B.P.

The contents of the ampoule of VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION 5 mg in 5 ml must not be injected in the undiluted form.

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION should be administered with caution to patients with co-existing heart disease.

The use of VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION in the treatment of severe bronchospasm or status asthmaticus does not obviate the requirement for glucocorticoid steroid therapy as appropriate.

When practicable, administration of oxygen concurrently with VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION is recommended, particularly when it is given by IV infusion to hypoxic patients.

Particular caution is advised in acute severe asthma, as hypokalaemia may be potentiated by concomitant treatment with xanthine derivatives, corticosteroids, diuretics and by hypoxia. It is recommended that serum potassium levels are monitored in such situations.

Lactic acidosis has been reported in association with high doses of VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION mainly in patients being treated for an acute asthma exacerbation. 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 VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION treatment. It is therefore recommended

that patients are monitored for the development of elevated serum lactate and consequent metabolic acidosis in this setting.

In addition, in obstetric use: In the treatment of premature labour, before VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION is given to any patient with known or suspected heart disease, an adequate assessment of the patient's cardiovascular status should be made by a medical practitioner experienced in heart diseases (see section 4.3).

Tocolysis with VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION is not recommended when membranes have ruptured or the cervix has dilated beyond 4 cm.

Increases in maternal heart rate of the order 20 to 50 beats per minute usually accompany infusion. The maternal pulse rate should be monitored and not normally allowed to exceed a sustained rate of 120 beats per minute. The effect of infusion on foetal rate is less marked but increases of up to 20 beats per minute may occur.

Maternal blood pressure may fall slightly during the infusion; the effect being greater on diastolic than on systolic pressure. Falls in diastolic pressure are usually within the range of 10 to 20 mmHg.

As maternal pulmonary oedema and myocardial ischaemia have been reported during or following treatment of premature labour with VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION, careful attention should be given to fluid balance and cardio-respiratory function, including ECG, should be monitored continuously. If signs of pulmonary oedema or myocardial ischaemia develop, VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION should be discontinued.

4.5 Interaction with other medicines and other forms of interaction:

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION and beta-blocking medicines should not be prescribed together.

4.6 Fertility, pregnancy and lactation:

The safety of VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION in pregnancy and lactation has not been established.

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 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000) and very rare (< 1/10 000), including isolated reports.

Clinical trials data:

Nervous system disorders:

Very common: tremor

Common: headache

Cardiac disorders:

Very common: tachycardia, palpitations

Uncommon: myocardial ischaemia*

*In the management of pre-term labour

Respiratory, thoracic and mediastinal disorders:

Uncommon: pulmonary oedema

In the management of pre-term labour VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION has been associated with pulmonary oedema

Musculoskeletal and connective tissue disorders:

Common: muscle cramps.

Post marketing data:

Immune system disorders: anaphylactic reactions (hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse)

Metabolism and nutrition disorders: potentially serious hypokalaemia may occur, lactic acidosis

Lactic acidosis has been reported in patients receiving VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION for the treatment of acute asthma exacerbation.

Nervous system disorders: hyperactivity, agitation

Cardiac disorders: cardiac dysrhythmias including atrial fibrillation, superventricular tachycardia and extrasystoles

Vascular disorders: peripheral vasodilatation

Gastrointestinal disorders: nausea, vomiting.

In the management of premature labour, VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION has been associated with nausea and vomiting

Injury, poisoning and procedural complications: slight pain or stinging on i.m. use of undiluted injection.

Reporting of side effects:

If you get side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form",** found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION.

4.9 Overdose:

The most common signs and symptoms of overdose with VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION are beta agonist pharmacologically mediated events (refer to section 4.8).

Agitation, hallucination and irritability have been reported.

Hypokalaemia may occur following overdose with VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION. Serum potassium levels should be monitored.

Nausea, vomiting and hyperglycaemia have been reported, predominantly in children and when salbutamol overdose has been taken via the oral route.

Consideration should be given to discontinuation of treatment and appropriate symptomatic therapy.

5. PHARMACOLOGICAL PROPERTIES:

A 10.2 Bronchodilator

5.1 Pharmacodynamic properties:

Salbutamol is a beta-adrenergic stimulant which has a selective action on the B_2-adrenoceptors throughout the body.

5.2 Pharmacokinetic properties:

Salbutamol administered intravenously has a half-life of 4-6 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. Salbutamol is bound to plasma proteins to the extent of 10 %.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients:

Excipients: a sterile isotonic solution consisting of sodium chloride, sulphuric acid, sodium hydroxide, nitrogen and water for injections.

6.2. Incompatibilities:

Not applicable.

6.3 Shelf life:

36 months

6.4 Special precautions for storage:

Store at or below 30 °C and protect from light.

Keep out of reach of children.

6.5 Nature and contents of container:

5 ml ampoules in boxes of 10.

6.6 Special precautions for disposal and other handling:

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION must not be used undiluted.

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION MUST be diluted with one of the following: Dextrose Injection B.P., Sodium Chloride Injection B.P. or Sodium Chloride and Dextrose Injection B.P. before administration. These are the only recommended diluents and it is inadvisable to administer VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION in a syringe or an infusion containing any other medication.

A suitable solution for infusion may be prepared by diluting VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION (5 mg in 5 ml) in 500 ml of a suitable infusion solution (see above), to provide a salbutamol concentration of 10 µg/ml of solution (see section 4.2).

All unused admixtures of VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION with infusion fluids should be discarded 24 hours after preparation.

7. HOLDER OF REGISTRATION CERTIFICATE:

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

Epping Industria 1, 7460

8. REGISTRATION NUMBER:

H/10.2.2/119

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:

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