

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Ventolin 1mg/ml Concentrate for Solution for Intravenous Infusion

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml ampoule contains 5 mg salbutamol as salbutamol sulphate (1mg/ml).

*For a full list of excipients, see section 6.1.*

## 3 PHARMACEUTICAL FORM

Concentrate for solution for infusion.

A clear colourless to pale straw coloured sterile aqueous solution.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Ventolin Concentrate for Solution for Intravenous Infusion is indicated in adults and adolescents (children aged 12 years and over).

Ventolin Concentrate for Solution for Intravenous Infusion should be administered under the direction of a physician. It is indicated for two distinct clinical situations:

1. For the management of severe bronchospasm. It provides short acting bronchodilation in reversible airways obstruction due to asthma and chronic obstructive pulmonary disease (COPD) such as chronic bronchitis and emphysema.
2. For the short-term management of uncomplicated premature labour. To arrest 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

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

Ventolin parenteral preparations are to be used under the direction of a physician.

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.

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

Ventolin parenteral preparations should not to be administered in the same syringe or infusion as any other medication.

The contents of the ampoules of Ventolin Concentrate Solution for Intravenous Infusion must not be injected undiluted. The concentration should be reduced by 50% before administration.

### **Adults and Adolescents (children aged 12 years and over):**

*In bronchospasm and status asthmaticus:*

#### **Intravenous slow injection:-**

Infusion rates of 3 to 20 micrograms per minute are generally adequate but in patients with respiratory failure, higher dosage has been used with success. A starting dose of 5 micrograms per minute is recommended with appropriate adjustment in dosage according to patient response.

A suitable solution for infusion may be prepared by diluting 5ml of Ventolin Concentrate Solution for Intravenous Infusion in 500ml of an infusion solution such as sodium chloride and dextrose injection BP to provide a salbutamol dose of 10 mcg/ml of solution.

**In the short term management of uncomplicated premature labour.**

Treatment with Ventolin Infusion should only be initiated by obstetricians/physicians experienced in the use of tocolytic agents. It should be carried out in facilities adequately equipped to perform continuous monitoring of maternal and foetus 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 short term delay may be used to administer glucocorticoids or to implement other measures known to improve perinatal health.

Ventolin Infusion should be administered as early as possible after the diagnosis of premature labour, and after evaluation of the patient to eliminate any contra-indications to the use of salbutamol (see section 4.3). This should include an adequate assessment of the patient's cardiovascular status with supervision of cardiorespiratory function and ECG monitoring throughout treatment (see section 4.4).

**Intravenous Infusion:-**

Infusion rates of 10-45 micrograms per minute are generally adequate. A starting rate of 10 micrograms per minute is recommended, increasing the rate until there is evidence of patient response.

Special cautions for infusion: The dose must be individually titrated. 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. These parameters should be carefully monitored during treatment. A maximum maternal heart rate of 120 beats per min should not be exceeded.

Careful control of the level of hydration is essential to avoid the risk of maternal pulmonary oedema (see section 4.4). The volume of fluid in which the drug is administered should thus be kept to a minimum. A controlled infusion device should be used, preferably a syringe pump.

Treatment should be discontinued should signs of pulmonary oedema or myocardial ischaemia develop. (see section 4.4 and section 4.8 )

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.

**Paediatric Population:**

The safety and efficacy of Ventolin Concentrate for Solution for Intravenous Infusion in children under the age of 12 years has not been established. From the available data no recommendation on posology can be made.

**4.3 Contraindications**

Ventolin parenteral preparations are contraindicated in patients with a history of hypersensitivity to any of their components.

Ventolin Infusion is contra-indicated in the following conditions:

- Any condition at a gestational age < 22 weeks
- as a tocolytic agent in patients with pre-existing ischaemic heart disease or those patients with significant risk factors for ischaemic heart disease.
- threatened abortion during the 1st and 2nd trimester
- any condition of the mother or foetus in which prolongation of the pregnancy is hazardous, e.g. severe toxemia, intrauterine infection, vaginal bleeding resulting from placenta praevia, eclampsia or severe preeclampsia, placental abruption, or cord compression.
- intrauterine foetal death, known lethal congenital or lethal chromosomal malformation.

Ventolin Infusion is also contraindicated in any pre-existing medical conditions with which a betamimetic would have an untoward effect e.g., pulmonary hypertension and cardiac disorders such as hypertrophic obstructive cardiomyopathy or any type of obstruction of the left ventricular outflow tract, e.g. aortic stenosis.

#### 4.4 Special warnings and 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.

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

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.

The use of Ventolin parenteral preparations 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 parenteral Ventolin is recommended particularly when it is given by intravenous infusion to hypoxic patients.

In common with other beta-adrenoceptor agonists, Ventolin can induce reversible metabolic changes such as reversible hypokalaemia and increased blood glucose levels. The diabetic patient may be unable to compensate for this and the development of ketoacidosis has been reported. Concurrent administration of corticosteroids can exaggerate this effect.

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.

Diabetic patients and those concurrently receiving corticosteroids should be monitored frequently during intravenous 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 Concentrate Solution for Intravenous Infusion should be diluted with Sodium Chloride Injection BP, rather than Sodium Chloride and Dextrose Injection BP.

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 section 4.8). 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.

Salbutamol causes peripheral vasodilation which may result in reflex tachycardia and increased cardiac output. Caution should be used in patients with angina, severe tachycardia or thyrotoxicosis.

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature of myocardial ischaemia associated with salbutamol.

#### Tocolysis

Any decision to initiate therapy with Ventolin Infusion should be undertaken after careful consideration of the risks and benefits of treatment. In the treatment of premature labour, before salbutamol parenteral preparations are given to any patient with known or suspected heart disease, an adequate assessment of the patient's cardiovascular status should be made by a physician experienced in cardiology.

Treatment should only be carried out in facilities adequately equipped to perform continuous monitoring of maternal and foetal health status. Tocolysis with salbutamol parenteral preparations is not recommended when membranes have ruptured or the cervix dilation is beyond 4 cm.

Ventolin Infusion should be used with caution in *tocolysis* and supervision of cardiorespiratory function and ECG monitoring, should be performed throughout treatment.

The following monitoring measures must be constantly applied to the mother and, when feasible/appropriate, to the foetus:

- blood pressure and heart rate
- ECG
- electrolyte and fluid balance – to monitor for pulmonary oedema
- glucose and lactate levels – with particular regard to diabetic patients
- potassium levels– beta-agonists are associated with a decrease in serum potassium which increases the risk of arrhythmias (see section 4.5)

Treatment should be discontinued if signs of myocardial ischaemia (such as chest pain or ECG changes) develop.

Ventolin Infusion should not be used as a tocolytic agent in patients with significant risk factors for, or a suspicion of any kind of pre-existing heart disease (e.g. tachyarrhythmias, heart failure, or valvular heart disease; see section 4.3).

#### *Pulmonary oedema*

As maternal pulmonary oedema and myocardial ischaemia have been reported during or following treatment of premature labour with beta-2 agonists, careful attention should be given to fluid balance and cardio-respiratory function, including ECG, should be monitored. Patients with predisposing factors including multiple pregnancies, fluid overload, maternal infection and pre-eclampsia may have an increased risk of developing pulmonary oedema. Administration with a syringe pump as opposed to i.v. infusion will limit risk of fluid overload. If signs of pulmonary oedema or myocardial ischaemia develop, discontinuation of treatment should be considered (see section 4.2 and 4.8).

#### *Blood pressure and heart rate*

In the treatment of premature labour by i.v. infusion of salbutamol increases in maternal heart rate of the order 20 to 50 beats per minute usually accompany the infusion. The maternal pulse rate should be monitored and the need to control such increases by dose reduction or drug withdrawal should be evaluated on a case by case basis. Generally maternal pulse rate should not be allowed to exceed a steady rate of 120 beats per minute. The effect of infusion on foetal heart 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 20mmHg.

In order to minimise the risk of hypotension associated with tocolytic therapy, special care should be taken to avoid caval compression by keeping the patient in the left or right lateral positions throughout the infusion.

#### *Diabetes*

Administration of beta agonists is associated with a rise of blood glucose. Therefore blood glucose and lactate levels should be monitored in mothers with diabetes and diabetic treatment adjusted accordingly to meet the needs of the diabetic mother during tocolysis (see section 4.5).

#### *Hyperthyroidism*

Ventolin Infusion should only be administered cautiously to patients suffering from thyrotoxicosis after careful evaluation of the benefits and risks of treatment.

#### *Respiratory indications*

Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving salbutamol for respiratory disease, should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin.

This medicine contains less than 1 mmol sodium (23 mg) per 5ml ampoule, that is to say essentially 'sodium free'.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

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

Salbutamol is not contra-indicated in patients under treatment with monoamine oxidase inhibitors (MAOIs), however the effects of salbutamol may be altered by guanethidine, reserpine, methyldopa and tricyclic antidepressants.

The use of the drug will inhibit the effects of oxytocic drugs.

Salbutamol will inhibit the effects of non-selective beta-adrenoceptor blockers.

##### *Halogenated anaesthetics*

Owing to the additional antihypertensive effect, there is increased uterine inertia with risk of haemorrhage; in addition, serious ventricular rhythm disorders due to increased cardiac reactivity, have been reported on interaction with halogenated anaesthetics. Treatment should be discontinued, whenever possible, at least 6 hours before any scheduled anaesthesia with halogenated anaesthetics.

##### *Corticosteroids*

Systemic corticosteroids are frequently given during premature labour to enhance foetal lung development. There have been reports of pulmonary oedema in women concomitantly administered with beta-agonists and corticosteroids. Corticosteroids are known to increase blood glucose and can deplete serum potassium, therefore concomitant administration should be undertaken with caution with continuous patient monitoring owing to the increased risk of hyperglycaemia and hypokalaemia (see section 4.4).

##### *Anti-diabetics*

The administration of beta-agonists is associated with a rise of blood glucose, which can be interpreted as an attenuation of anti-diabetic therapy; therefore individual anti-diabetic therapy may need to be adjusted (see section 4.4).

##### *Potassium depleting agents*

Owing to the hypokalaemic effect of beta-agonists, concurrent administration of serum potassium depleting agents known to exacerbate the risk of hypokalaemia, such as diuretics, digoxin, methyl xanthines and corticosteroids, should be administered cautiously after careful evaluation of the benefits and risks with special regard to the increased risk of cardiac arrhythmias arising as a result of hypokalaemia (see section 4.4).

#### **4.6 Fertility, pregnancy and lactation**

##### 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.

Salbutamol has been in widespread use for many years in human beings without apparent ill consequence; this indicates its well established use in the management of premature labour. However, as with the majority of drugs, there is little published evidence of its safety in the early stages of human pregnancy, but in animal studies there was evidence of some harmful effects on the foetus at very high dose levels.

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).

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

None reported.

**4.8 Undesirable effects**

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $< 1/10$ ), uncommon ( $\geq 1/1000$  to  $< 1/100$ ), rare ( $\geq 1/10,000$  to  $< 1/1000$ ) and very rare ( $< 1/10,000$ ) including isolated reports. Very common and common reactions were generally determined from clinical trial data. Rare and very rare reactions were generally determined from spontaneous data.

The most common undesirable effects of Ventolin Infusionare correlated with the betamimetic pharmacological activity and may be limited or avoided by a close monitoring of hemodynamic parameters, such as blood pressure and heart rate, and an appropriate adjustment of the dose.They normally recede upon therapy discontinuation.

Unless otherwise indicated the following undesirable effects have been reported for Ventolin Infusion in the management of severe bronchospasm associated with asthma or bronchitis and for the treatment of status asthmaticus.

**Immune system disorders**

Very rare: Hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse.

**Metabolism and nutrition disorders**

Common \*\*Hypokalaemia.

Potentially serious hypokalaemia may result from beta-2 agonist therapy.

Rare: \*Hyperglycaemia.

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**

Very common: Tremor.

Common: Headache.

Very rare: Hyperactivity.

**Cardiac disorders**

Very common: \*\*Tachycardia, \*\*palpitations.

Common \*Decrease in diastolic pressure.

Uncommon \*\*\*Myocardial ischaemia (see section 4.4)

Rare: \*Cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles.

**Vascular disorders:**

Common: \*Hypotension (see section 4.4)

Rare: \*\*Peripheral vasodilatation.

**Respiratory, thoracic and mediastinal disorders:**

Uncommon: \*Pulmonary oedema.

In the management of pre-term labour, salbutamol injection/solution for infusion have uncommonly been associated with pulmonary oedema. Patients with predisposing factors including multiple pregnancies, fluid overload, maternal infection and pre-eclampsia may have an increased risk of developing pulmonary oedema.

**Gastrointestinal disorders**

Very rare: Nausea, vomiting.

In the management of premature labour, intravenous infusion of salbutamol has very rarely been associated with nausea and vomiting.

**Musculoskeletal and connective tissue disorders**

Common: Muscle cramps.

**Injury, poisoning and procedural complications**

Very rare: Slight pain or stinging on i.m. use of undiluted injection.

\* These reactions have been reported in association with the use of short acting beta-agonists in obstetric indications and are considered class effects (see section 4.4)

\*\* These reactions have been reported for Ventolin Infusion in the management of severe bronchospasm associated with asthma or bronchitis and for the treatment of status asthmaticus, and for short acting beta-agonists used in obstetric indications.

\*\*\* Myocardial ischaemia has been reported uncommonly with salbutamol injection/solution for infusion in the management of pre-term labour, rarely in association with the use of short acting beta-agonists in obstetric indications, and spontaneously in post-marketing data therefore frequency regarded as unknown.

Reporting of suspected adverse reactions.

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRC Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

**4.9 Overdose**

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

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

*Treatment*

Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

**5 PHARMACOLOGICAL PROPERTIES****5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Selective beta-2 -adrenoceptor agonist  
ATC code: R03A C02

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 in reversible airways obstruction.

**5.2 Pharmacokinetic properties**

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

### 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.

Reproduction studies in rats demonstrated no evidence of impaired fertility at oral doses of salbutamol up to 50 mg/kg.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Sodium chloride  
Dilute sulphuric acid (for pH adjustment)  
Sodium hydroxide (for pH adjustment)  
Water for injections

### 6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

### 6.3 Shelf life

Unopened: 48 months.  
Once opened and diluted: Use immediately. Discard any unused contents.

Chemical and physical in-use stability has been demonstrated for 24 hours at 20-25°C.

From a microbiological point of view, the product should be used immediately.

If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

### 6.4 Special precautions for storage

Do not store above 30°C. Keep the ampoules in the outer carton to protect from light.

### 6.5 Nature and contents of container

Ventolin Concentrate for Solution for Intravenous Infusion is presented in a 5 ml colourless, neutral Type I glass ampoule and is available in boxes of 5 or 10 ampoules.  
Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

To open the ampoule:

- Flick down any liquid in the ampoule neck.
- Hold ampoule upright.
- Break off the top tag in one quick turn.
- Attach syringe direct to ampoule or insert syringe.
- Withdraw contents using firm consistent pressure.

□

Dilute before use.  
For single use only.  
Discard any unused contents.

The following infusion fluids are compatible with Ventolin Concentrate Solution for Intravenous Infusion:

5% w/v Dextrose Injection BP  
0.9% w/v Sodium Chloride Injection BP  
0.18% Sodium Chloride and  
4% w/v Dextrose Intravenous Infusion BP

Chemical and physical in-use stability has been demonstrated for 24 hours at 20-25°C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

## **7 MARKETING AUTHORISATION HOLDER**

GlaxoSmithKline (Ireland) Limited  
12 Riverwalk  
Citywest Business Campus  
Dublin 24  
Ireland

## **8 MARKETING AUTHORISATION NUMBER**

PA1077/049/002

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorization: 10 November 1975

Date of last renewal: 5 August 2008

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

March 2024