SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

Ventolin Injection

2. Qualitative and Quantitative Composition

Ventolin Injection is presented as ampoules of 1 ml, each containing 500 micrograms (0.5mg) salbutamol as salbutamol sulfate BP in a sterile isotonic solution.

3. Pharmaceutical Form

A colourless to pale straw coloured solution for injection.

Clinical Particulars

4.1. Therapeutic Indications

Ventolin Injection is indicated in adults.

Ventolin Injection provides short-acting (4-6 hour) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction. It is indicated for the relief of severe bronchospasm.

4.2. Posology and Method of Administration

Ventolin Injection may be administered by the subcutaneous, intramuscular or intravenous route, under the direction of a physician.

Adults:

Subcutaneous route: 500 micrograms (8 micrograms/kg body weight) and repeated every four hours as required.

Intramuscular route: 500 micrograms (8 micrograms/kg body weight) and repeated every four hours as required.

Slow intravenous injection:
250 micrograms (4 micrograms/kg body weight) injected slowly. If necessary the dose may be repeated.

The use of Ventolin Injection 500 micrograms in 1ml (500 micrograms/ml, for intravenenous administration may be facilitated by dilution to 10 ml with Water for Injection (final concentration of 50 micrograms/ml) and 5 mls of the diluted preparation (250 micrograms/5 ml) administered by slow intravenous injection.

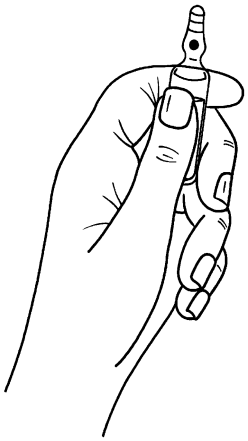
Paediatric Population

At present there is insufficient evidence to recommend a dosage regimen for routine use in children.

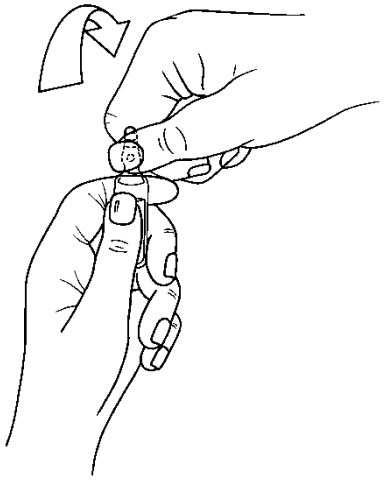
Instructions to open the ampoule

Ampoules are equipped with the OPC (One Point Cut) opening system and must be opened using the following instructions:
hold with one hand the bottom part of the ampoule as indicated in Picture 1 put the other hand on the top of the ampoule positioning the thumb above the coloured point and press as indicated in Picture 2

Picture 1



Picture 2



4.3. Contra-indications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4. Special Warnings and Special Precautions for Use

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma. Severe asthma requires regular medical assessment, including lung-function testing, as patients are at risk of severe attacks and even death. Physicians should consider using the maximum recommended dose of inhaled corticosteroid and/or oral corticosteroid therapy in these patients**.**

The dosage or frequency of administration should only be increased on medical advice.

Patients being treated with Ventolin Injection may also be receiving short-acting inhaled bronchodilators to relieve symptoms. Increasing use of bronchodilators, in particular short-acting inhaled β_2-agonists to relieve symptoms, indicates deterioration of asthma control.

The patient should be instructed to seek medical advice if short-acting relief bronchodilator treatment becomes less effective, or more inhalations than usual are required. In this situation the patient should be assessed and consideration given to the need for increased anti-inflammatory therapy (e.g. higher doses of inhaled corticosteroid or a course of oral corticosteroid).

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischaemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving salbutamol 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.

Salbutamol should be administered cautiously to patients suffering from thyrotoxicosis.

Potentially serious hypokalaemia may result from β_2-agonist therapy, mainly from parenteral and nebulised administration. Particular caution is advised in acute severe asthma as this effect may be potentiated by hypoxia and by concomitant treatment with xanthine derivatives, steroids and diuretics. Serum potassium levels should be monitored in such situations.

Severe exacerbations of asthma must be treated in the normal way.

The use of Ventolin Injection in the treatment of severe bronchospasm does not obviate the requirement for corticosteroid therapy as appropriate. When practicable, administration of oxygen concurrently with Ventolin Injection is recommended. In common with other β-adrenoceptor agonists, salbutamol can induce reversible metabolic changes such as hypokalaemia and increased blood glucose levels. Diabetic patients may be unable to compensate for the increase in blood glucose and the development of ketoacidosis has been reported. Concurrent administration of corticosteroids can exaggerate this effect. Diabetic patients and those concurrently receiving corticosteroids should be monitored frequently.

Lactic acidosis has been reported 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.

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

4.5. Interactions with other Medicaments and other forms of Interaction

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

4.6. 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.

As with the majority of drugs, there is little published evidence of the safety of salbutamol 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.

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. In such situations the use of the inhaled route may be preferable although it is not known whether salbutamol 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

Not applicable.

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 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10,000 and <1/1000) and very rare (<1/10,000). Very common and common events were generally determined from clinical trial data. Rare, very rare and unknown 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-agonist therapy.

Unknown: Lactic acidosis (see section 4.4)

Nervous system disorders

Very common: Tremor.

Common: Headache.

Very rare: Hyperactivity.

Cardiac disorders

Very common: Tachycardia.

Common: Palpitations.

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

Unknown: Myocardial ischaemia* (see section 4.4)

Vascular disorders

Rare: Peripheral vasodilatation.

Gastrointestinal disorders

Unknown: Nausea, vomiting *.

Musculoskeletal and connective tissue disorders

Common: Muscle cramps.

Injury, poisoning and procedural complications

Unknown: Slight pain or stinging on intramuscular use of undiluted injection*.

* reported 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.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il
Additionally, you should also report to GSK Israel (il.safety@gsk.com).

4.9. Overdose

The most common signs and symptoms of overdose with salbutamol are transient beta agonist pharmacologically mediated events, including tachycardia, tremor, hyperactivity and metabolic effects including hypokalaemia and lactic acidosis (see sections 4.4 and 4.8).

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.

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

Pharmacological Properties

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: Selective beta-2-adrenoreceptor agonists
ATC Code: R03CC02

Salbutamol is a selective beta-$_2$ adrenoceptor agonist. At therapeutic doses it acts on beta-$_2$ adrenoceptors of bronchial muscle providing short-acting (4-6 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 β2-agonists, salbutamol has been shown to be teratogenic in mice when given subcutaneously. In a reproductive study, 9.3% of fetuses were found to have cleft palate at 2.5mg/kg dose, 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 fetal abnormalities. The only toxic effect was an increase in neonatal mortality at the highest dose level as the result of lack of maternal care. Reproductive studies in the rabbit at doses of 50mg/kg/day orally (i.e. much higher than the normal human dose) have shown fetuses with treatment related changes; these included open eyelids (ablepharia), secondary palate clefts (palatoschisis), changes in ossification of the frontal bones of the cranium (cranioschisis) and limb flexure.

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

6.1. List of Excipients

Sodium chloride
Sodium hydroxide
Dilute sulfuric acid
Water for injections
Nitrogen

6.2. Incompatibilities

None stated

6.3. Shelf Life

The expiry date of the product is indicated on the label and packaging materials.

Shelf life after reconstitution: All unused admixtures of Ventolin Injection should be discarded 24 hours after preparation.

6.4. Special Precautions for Storage

Store below 30°C and keep the ampoule in the outer container in order to protect from light.

6.5. Nature and Contents of Container

Clear, neutral glass ampoules, packed in plastic trays with a cardboard sleeve over the trays.

Pack size: 1ml ampoules in plastic trays of 5.

6.6. Special precautions for disposal and other handling

The only recommended diluents for Ventolin Injection are water for injections, sodium chloride injection BP, sodium chloride and dextrose injection BP or dextrose injection BP.

All unused admixtures of Ventolin Injection should be discarded 24 hours after preparation.

Ventolin Injection should not be administered in the same syringe as any other medication.

7. Manufacturer

GlaxoSmithKline Manufacturing S.p.A., Parma, Italy

8. License Holder and Importer

GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.

9. License Number

027-64-21556-05

Revised in October 2023 according to MOHs guidelines

Ven Inj DR V4