

PRODUCT INFORMATION

VENTOLIN ROTACAPS

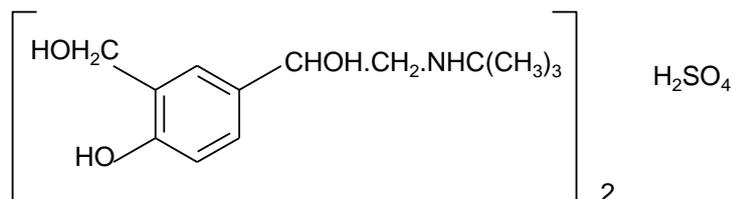
NAME OF THE MEDICINE:

Ventolin Rotacaps

Ventolin Rotacaps contain salbutamol (as sulfate) B.P.

The chemical name of salbutamol sulfate is 1-(4-hydroxy-3-hydroxymethylphenyl)-2-(tert-butylamino)ethanol sulfate

The structural formula is:



Molecular formula: $(\text{C}_{13}\text{H}_{21}\text{NO}_3)_2\text{H}_2\text{SO}_4$
Molecular Weight: 576.7
CAS Number: 51022-70-9

DESCRIPTION:

Salbutamol sulfate is a white or almost white odourless powder. It is soluble in 4 parts of water; slightly soluble in 95% alcohol, chloroform and solvent ether.

Ventolin Rotacaps contain microfined salbutamol sulfate and lactose (which contains milk protein) in a hard gelatin shell.

PHARMACOLOGY:

Salbutamol is a relatively selective beta-2 adrenoreceptor stimulant. It is more specific than both isoprenaline and orciprenaline for adrenergic beta-2 receptors.

After oral and parenteral administration, stimulation of the beta receptors in the body, both beta-1 and beta-2, occurs because (a) beta-2 selectivity is not absolute, and (b) higher concentrations of salbutamol occur in the regions of these receptors with these modes of administration. This results in the beta-1 effect of cardiac stimulation, though not so much as with isoprenaline, and beta-2 effects of peripheral vasodilatation and hypotension, skeletal muscle tremor and uterine muscle relaxation.

Metabolic effects such as hyperinsulinaemia and hyperglycaemia also may occur, although it is not known whether these effects are mediated by beta-1 or beta-2 receptors. The serum potassium levels have a tendency to fall.

Pharmacokinetics

Following inhalation, salbutamol acts topically on bronchial smooth muscle and initially the drug is undetectable in the blood. After 2 to 3 hours low concentrations are seen, due presumably to the portion of the dose which is swallowed and absorbed in the gut.

The elimination half-life of inhaled or oral salbutamol is between 2.7 and 5 hours.

Salbutamol is not metabolised in the lung but is converted to the 4'-o-sulfate ester in the liver. Salbutamol is excreted in the urine as free drug and as the metabolite. After oral administration 58-78% of the dose is excreted in the urine in 24 hours, approximately 60% as metabolites. A small fraction is excreted in the faeces.

Impairment of liver or renal function may necessitate a reduction in dosage (see **DOSAGE AND ADMINISTRATION**).

INDICATIONS:

For the relief of bronchospasm in patients with asthma or chronic obstructive pulmonary disease, and for acute prophylaxis against exercise-induced asthma or in other situations known to induce bronchospasm.

Ventolin Rotacaps are indicated for the above conditions in those patients unable to use a pressurised aerosol bronchodilator satisfactorily. Patients most likely to benefit from the use of Rotacaps are:

- 1) Children from 3 to 6 years of age who are too young to operate a metered aerosol.
- 2) Patients who have difficulty synchronising deep inhalation with actuation of a metered aerosol.
- 3) Patients who are sensitive to freon propellants.

CONTRAINDICATIONS:

Salbutamol dry powder inhaler formulations are contraindicated in patients with severe milk protein allergy or who have a history of hypersensitivity to salbutamol or any of its components (see **DESCRIPTION**).

Non-intravenous formulations of salbutamol must not be used to arrest uncomplicated premature labour or threatened abortion.

PRECAUTIONS:

The management of asthma should 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.

In the event of a previously effective dose of inhaled salbutamol failing to give relief for at least three hours, the patient should be advised to seek medical advice in order that any necessary additional steps may be taken.

If patients with an acute attack of asthma fail to respond to a dry powder inhaler of beta-2 agonist they should be advised to follow their personal asthma action plan. Failure to respond to beta-2 agonists in general can be due to various reasons related to drug administration or the disease itself. Particularly in children 5 years or younger, and exceptionally in other cases, inspiratory flow through a dry powder inhaler may not be sufficient for optimal drug delivery. If a non-response occurs, medical help should be sought while beta-2 agonist treatment is continued. In such a situation, and if available, a nebuliser or pressurised metered dose inhaler with spacer should be used.

Animal studies suggest that cardioneurotic effects may occur with high dosages of some sympathomimetic amines. On this evidence the possibility of the occurrence of myocardial lesions cannot be excluded subsequent to long term treatment with these drugs.

Care should be taken with patients who are known to have received large doses of salbutamol or other sympathomimetic drugs, or who are suffering from hypertension, hyperthyroidism, myocardial insufficiency, or diabetes mellitus.

Salbutamol should be administered cautiously to patients with thyrotoxicosis.

Excessive use may induce a non-responsive state leading to a worsening of hypoxaemia.

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 hypoxia. It is recommended that serum potassium levels are monitored in such situations.

The possibility of cardiac arrhythmias arising as a consequence of salbutamol induced hypokalaemia should be borne in mind, especially in digitalised patients, following the administration of Ventolin Injection.

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.

Effects on Fertility

There is no information on the effects of salbutamol on human fertility.

Use in Pregnancy

Pregnancy Category: A

Salbutamol is known to cross the placental barrier in humans. Safety for use in pregnancy has not been demonstrated, therefore the drug should not be used in pregnant women, or those likely to become pregnant, unless the expected benefit outweighs any potential risk.

Oral administration of salbutamol to rats and rabbits during pregnancy showed no teratogenic effects in offspring.

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.

Although intravenous salbutamol and occasionally salbutamol tablets are used in the management of uncomplicated premature labour, Ventolin presentations should not be used for threatened abortion during the first or second trimesters of pregnancy. Intravenous salbutamol is contra-indicated in cases of ante-partum haemorrhage because of the risk of further haemorrhage from an atonic uterus and there is the risk of the same problem arising inadvertently in asthmatics using salbutamol. Profuse uterine bleeding following spontaneous

abortion has been reported after the use of salbutamol. Special care is required in pregnant diabetic women.

Use in Lactation

It is not known whether salbutamol is excreted in breast milk nor whether it has a harmful effect on the newborn. Therefore it is not recommended for nursing mothers unless the expected benefits outweigh any potential risk.

INTERACTIONS WITH OTHER MEDICINES:

Beta adrenergic blocking drugs inhibit the bronchodilator action of salbutamol and other sympathomimetic bronchodilators. However, such drugs should not be used in asthmatic patients as they may increase airway resistance.

Care is recommended if it is proposed to administer salbutamol in concomitant therapy with other sympathomimetic amines as excess sympathetic stimulation may occur.

Animal studies have shown that large doses of salbutamol may interact with imipramine, chlordiazepoxide and chlorpromazine but any practical significance of these results in man remains to be established.

ADVERSE EFFECTS:

A fine tremor of skeletal muscle has been reported in some patients when salbutamol is administered orally or by inhalation, and in about 20% of patients receiving Ventolin Injection; the hands being the most obviously affected with a few patients feeling tense. These effects are dose related and are caused by a direct action on skeletal muscle and not by direct CNS stimulation.

With higher doses than those recommended, or in patients who are unusually sensitive to beta-adrenergic stimulants, dilatation of some peripheral arterioles may occur leading to a small reduction in arterial pressure; a compensatory increase in cardiac output may then occur.

Cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles) have been reported. Peripheral vasodilation and a compensatory small increase in heart rate may occur in some patients. Tachycardia may occur in some patients.

Other reactions which may occur are headaches, nausea, palpitations and sensations of warmth. Hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse have been reported very rarely. There have been very rare reports of muscle cramps. Mouth and throat irritation may occur with inhaled salbutamol.

Note: The incidence and severity of particular side effects depends on the dosage and route of administration. Ventolin does not cause difficulty in micturition because, unlike sympathomimetic drugs such as ephedrine, therapeutic doses have no alpha-adrenergic receptor stimulant activity.

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

As with other inhalation therapy, paradoxical bronchospasm may occur, resulting in an immediate increase in wheezing after dosing.

As with other beta-2 agonists, hyperactivity has been reported rarely in children.

DOSAGE AND ADMINISTRATION:

Ventolin Rotacaps are for inhalation use only using a Ventolin Rotahaler inhaler.

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.

Studies in asthmatics have shown that the use of one 200 mcg Ventolin Rotacap will produce bronchodilatation of a similar order to that produced by the use of one (100 mcg) puff of Ventolin Inhaler.

Adults: The contents of one or two Rotacaps (200-400 micrograms of salbutamol) to be inhaled 3 or 4 times daily.

Children to the age of 12 years: The contents of one Rotacap (200 micrograms of salbutamol) to be inhaled 3 or 4 times daily.

The total amount of salbutamol administered by Rotahaler in any 24 hour period should not exceed 12 Rotacaps for an adult or 6 Rotacaps for a child.

Note 1: Failure to obtain relief from Rotacaps may be a medical emergency. Other appropriate treatment must be instituted without delay.

Note 2: It is important that the patient be instructed in the proper use of the Rotahaler.

Geriatric

Initial doses of salbutamol in the elderly should be lower than the recommended adult dosage. The dose may then be gradually increased if sufficient bronchodilatation is not achieved.

In impaired liver function

As about 60% of orally administered salbutamol (this includes not only tablet and syrup preparations but also approximately 90% of an inhaled dose) is metabolised to an inactive form, impairment of liver function may result in accumulation of unchanged salbutamol.

In impaired renal function

About 60-70% of salbutamol administered by inhalation or intravenous injection is excreted in urine unchanged. Impairment of renal function may therefore require a reduction in dosage to prevent exaggerated or prolonged effects.

OVERDOSAGE:

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

The most common signs and symptoms of overdose with salbutamol are transient beta agonist pharmacologically mediated events (see **PRECAUTIONS** and **ADVERSE EFFECTS**). The signs of salbutamol overdose are significant tachycardia and/or significant muscle tremor.

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.

Consideration should be given to discontinuation of treatment and appropriate symptomatic treatment such as a cardio-selective beta-blocking agent given by intravenous injection, in patients presenting with cardiac symptoms (e.g. tachycardia, palpitations). Beta-blocking drugs should be used with caution as they may cause bronchospasm in sensitive individuals.

In treating overdose with Ventolin Rotacaps it is to be remembered that twenty 200 microgram Rotacaps contain as much salbutamol as one 4 milligram Ventolin tablet.

PRESENTATION:

Ventolin Rotacaps are hard capsules. Each Ventolin Rotacap contains the equivalent of 200 micrograms salbutamol. One half of each Rotacap is clear and the other half pale blue. Printed on each capsule is either "Ventolin 200" in light red once on the body and once on the cap or "Ventolin 200" in light red once on the cap and an arrow on the body. A 10% overage is included for wastage in the Rotahaler.

Ventolin Rotacaps are packed in foil in cartons of 100 and 128 Rotacaps.

Not all pack sizes may be available.

VENTOLIN ROTACAPS CONTAIN A POWDER FOR INHALATION AND SHOULD BE USED IN CONJUNCTION WITH THE VENTOLIN ROTAHALER. The Rotahaler breaks the Rotacap in halves. These halves are rotated and agitated to release the drug powder when the patient inhales.

The Rotacaps must only be inserted into the Rotahaler immediately prior to use. Failure to observe this instruction will affect the delivery of the drug.

Ventolin Rotacaps have a shelf-life of 3 years when stored below 30°C. Avoid storage areas of high humidity.

NAME AND ADDRESS OF THE SPONSOR:

GlaxoSmithKline Australia Pty Ltd
Level 4, 436 Johnston Street,
Abbotsford, Victoria 3067
Australia

POISON SCHEDULE OF THE MEDICINE:

Schedule 3 – Pharmacist Only Medicine

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG):

12 August 1999

DATE OF MOST RECENT AMENDMENT: 3 July 2017

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