



VENTOLIN SYRUP

Salbutamol sulfate

QUALITATIVE AND QUANTITATIVE COMPOSITION

VENTOLIN Syrup contains 2 mg salbutamol, as sulfate, in each 5 mL of syrup.

PHARMACEUTICAL FORM

Syrup.

CLINICAL PARTICULARS

Indications

VENTOLIN is a selective beta₂-adrenoceptor agonist. At therapeutic doses it acts on the beta₂-adrenoceptors of bronchial muscle, with little or no action on the beta₁-adrenoceptors of the heart.

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma. Severe asthma requires regular medical assessment as death may occur. Patients with severe asthma have constant symptoms and frequent exacerbations, with limited physical capacity, and PEF values below 60% predicted at baseline with greater than 30% variability, usually not returning entirely to normal after a bronchodilator. These patients will require high dose inhaled (e.g., >1 mg/day beclomethasone dipropionate) or oral corticosteroid therapy. Sudden worsening of symptoms may require increased corticosteroid dosage which should be administered under urgent medical supervision.

Relief of bronchospasm in bronchial asthma of all types, chronic bronchitis and emphysema.

VENTOLIN Syrup is suitable oral therapy for children or those adults who prefer liquid medicines.

Dosage and Administration

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

Increasing use of beta₂-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.

- Adults

The usual effective dose is 10 mL salbutamol (4 mg of salbutamol) 3 or 4 times per day.

If adequate bronchodilation is not obtained each single dose may be gradually increased to as much as 20 mL of syrup (8 mg salbutamol).

Some patients obtain adequate relief with 5 mL of syrup (2 mg salbutamol) 3 or 4 times daily.

- Children

2-6 years : 2.5 to 5 mL of syrup (1 to 2 mg salbutamol) 3 or 4 times daily.

6-12 years : 5 mL of syrup (2 mg salbutamol) 3 or 4 times daily.

Over 12 years : 5 to 10 mL of syrup (2 to 4 mg salbutamol) 3 or 4 times daily.

- Special patient groups

In elderly patients or in those known to be unusually sensitive to beta-adrenergic stimulant drugs, it is advisable to initiate treatment with 5 mL of syrup (2 mg salbutamol) 3 or 4 times per day.

Contraindications

VENTOLIN is contraindicated in patients with a history of hypersensitivity to any of its 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 beta₂-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.

Patients should 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 should be administered cautiously to patients with thyrotoxicosis.

Potentially serious hypokalaemia may result from beta₂-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.

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 ketoacidosis has been reported. Concurrent administration of corticosteroids can exaggerate this effect.

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 salbutamol 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 to 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 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 ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$) 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.

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 beta₂-agonist therapy.

Nervous system disorders

Very common: Tremor.
Common: Headache.
Very rare: Hyperactivity.

Cardiac disorders

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

Vascular disorders

Rare: Peripheral vasodilatation.

Musculoskeletal and connective tissue disorders

Common: Muscle cramps.
Very rare: Feeling of muscle tension.

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 overdose 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.

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.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

Salbutamol is a selective beta₂-adrenoceptor agonist. At therapeutic doses it acts on the beta₂-adrenoceptors of bronchial muscle providing short-acting (4 to 6 hour) bronchodilation in reversible airways obstruction.

Pharmacokinetics

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%.

After oral administration, salbutamol is absorbed from the gastrointestinal tract and undergoes considerable first-pass metabolism to the phenolic sulfate. Both unchanged drug and conjugate are excreted primarily in the urine. The bioavailability of orally administered salbutamol is about 50%.

Pre-clinical Safety Data

In common with other potent selective beta₂-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 dose. In rats, treatment at the levels of 0.5, 2.32, 10.75 and 50 mg/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 50 mg/kg/day, 78 times the maximum human oral dose.

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

PHARMACEUTICAL PARTICULARS

List of Excipients

Citric acid monohydrate
Hydroxypropylmethyl cellulose
Sodium benzoate
Sodium citrate dihydrate
Sodium chloride
Orange flavour liquid
Sodium saccharin dihydrate

Incompatibilities

Sugar free formulation:

Dilution of *VENTOLIN* Syrup with syrup BP or sorbitol solution is not recommended as this may result in precipitation of the cellulose thickening agent.

Shelf Life

The expiry date is indicated on the packaging.

Special Precautions for Storage

Store below 30°C.

Store in a dry place and replace cap securely.

Protect from light.

Nature and Contents of Container

Amber plastic bottles with plastic child resistant caps.

Instructions for Use/Handling

Dilution:

Sugar free formulation:

VENTOLIN Syrup may be diluted with purified water BP (50% v/v). The resulting mixture should be protected from light and used within 28 days.

A 50% v/v dilution of *VENTOLIN* Syrup has been shown to be adequately preserved against microbial contamination. However, to avoid the possibility of introducing excessive microbial contamination, the purified water used for dilution should be recently prepared or alternatively it should be boiled and cooled immediately before use.

Admixture of *VENTOLIN* Syrup with other liquid preparation is not recommended.

Package Quantities and Registration Number

Box, bottle @ 100 mL

Reg. No. DKL9232000537A1

HARUS DENGAN RESEP DOKTER

Manufactured by

PT Sterling Products Indonesia

Jakarta, Indonesia

For

PT Glaxo Wellcome Indonesia

Jakarta, Indonesia

PI based on GDS22/IPI06 (29 April 2016) + remove tablet.

Trademarks are owned by or licensed to the GSK group of companies.

©2022 GSK group of companies or its licensor.

FAW_1eaVENSyr_RINJANI+newGSK+tabremoval_circ2_17Nov22 - for implementation