

DATA SHEET

Volmax™

Salbutamol controlled release tablets.

Qualitative and quantitative composition

Volmax Tablets 4mg: White hexagonal controlled release biconvex tablets each containing 4mg salbutamol, as sulphate. Printed 4 on one side.

Volmax Tablets 8mg: White hexagonal controlled release biconvex tablets each containing 8mg salbutamol, as sulphate. Printed 8 on one side.

The tablet consists of an outer semi-permeable membrane and an inner core containing salbutamol sulphate. There is a hole in the outer coat which allows osmotically controlled release of the medicine.

Clinical particulars

Therapeutic indications

Salbutamol is a selective β_2 adrenoceptor agonist. At therapeutic doses it acts on the β_2 adrenoceptors of bronchial muscle, with little or no action on the β_1 adrenoceptors of the heart. Volmax tablets are a controlled-release formulation of salbutamol and are particularly suitable for nocturnal asthma.

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. >1mg/day beclomethasone dipropionate) or oral corticosteroid therapy. Sudden worsening of symptoms may require increased corticosteroid dosage which should be administered under urgent medical supervision.

The therapeutic indication of Volmax is the treatment of reversible airways obstruction of all types including bronchial asthma, chronic bronchitis and emphysema.

Posology and method of administration

Volmax Tablets must be swallowed whole with a glass of water and not chewed or crushed.

Increasing use of β_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.

Adults:-

One 8mg tablet twice daily.

Children (3 to 12 years):-

One 4mg tablet twice daily. There are insufficient data to recommend use in children under 3 years.

Special patient groups:-

There is no need to adjust the dose in the elderly.

Contra-indications

Volmax Tablets are contra-indicated in patients with a history of hypersensitivity to any of their components.

Although intravenous salbutamol and occasionally salbutamol tablets are used in the management of premature labour uncomplicated by conditions such as placenta praevia, ante-partum haemorrhage or toxemia of pregnancy, salbutamol presentations should not be used for threatened abortion.

Special warnings and special 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.

Increasing use of short-acting inhaled β_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.

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.

Salbutamol should be administered cautiously to patients with 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 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 β -adrenoceptor agonists, salbutamol 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 ketacidosis has been reported. Concurrent administration of corticosteroids can exaggerate this effect.

Interaction with other medicaments and other forms of interaction

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

Salbutamol is not contra-indicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

Pregnancy and lactation

Administration of medicines 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.

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.

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.

Undesirable effects

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

Immune system disorders

Very rare: Hypersensitivity.

Hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse have been reported very rarely.

Metabolism and nutrition disorders

Rare: Hypokalaemia.

Potentially serious hypokalaemia may result from beta₂ agonist therapy.

Nervous system disorders

Very common: Tremor.

Volmax Tablets may cause a fine tremor of skeletal muscle in some patients, usually the hands are most obviously affected. This effect is common to all beta-adrenergic stimulants. The incidence of tremor with this preparation is similar to that seen with standard salbutamol tablets.

Common: Headache.

Very rare: Hyperactivity.

As with other beta₂ agonists hyperactivity has been reported very rarely in children.

Cardiac Disorders

Common: Tachycardia.

Rare: Cardiac arrhythmias.

Cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles) have been reported, usually in susceptible patients.

Vascular disorders

Rare: Peripheral vasodilatation.

Peripheral vasodilatation and a compensatory small increase in heart rate may occur in some patients.

Musculoskeletal and connective tissue disorders

Common: Muscle cramps.

Very rare: Feeling of muscle tension.

A few patients experience a feeling of tension; this is also due to the effects on skeletal muscle and not to direct CNS stimulation.

Overdose

The preferred antidote for overdosage with salbutamol is a cardio-selective β -blocking agent, but β -blocking agents should be used with caution in patients with a history of bronchospasm.

Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored.

Pharmacological properties

Pharmacodynamic properties

Salbutamol is a selective β_2 adrenoceptor agonist. At therapeutic doses it acts on the β_2 adrenoceptors of bronchial muscle, with little or no action on the β_1 adrenoceptors of cardiac muscle.

Volmax tablets are a controlled release formulation of salbutamol.

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-sulphate (phenolic sulphate) which is also excreted primarily in the urine. The faeces are a minor route of excretion. 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 sulphate. Both unchanged drug and conjugate are excreted primarily in the urine. The bioavailability of orally administered salbutamol is about 50%.

Volmax tablets are designed to deliver 90% of their salbutamol content in vitro over 9 hours. This corresponds to a release rate of 0.8mg/h for the 8mg tablet, and 0.4mg/h for the 4mg tablet.

Pre-clinical safety data

In common with other potent selective β_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.

Pharmaceutical particulars

Shelf Life:-

36 months.

Storage Conditions:-

Volmax Tablets should be stored at a temperature not exceeding 30°C.

Volmax Tablets should not be removed from their foil pack until required for administration.

Package Quantities:-

Volmax Tablets 4mg and 8mg are supplied in double foil blisters of 14 in cartons of 56.

Medicines classification

Prescription Only Medicine

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Date of preparation

Issue date: 14 May 2003

Version: 1.0

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