SM PHARMACEUTICALS SDN. BHD.

BREATHNINE (SALBUTAMOL SULPHATE) SYRUP 2 MG / 5 ML

DESCRIPTION:
A clear, red coloured liquid with sweet taste and raspberry flavour.

COMPOSITION:
Salbutamol Sulphate equivalent to 2mg / 5ml Salbutamol.

ACTIONS AND MODE OR MECHANISMS OF ACTION:
A direct-acting sympathomimetic amine. Acts relatively selectively on beta 2 adrenergic receptors in the lungs to relax bronchiol smooth muscle, thereby relieving bronchospasm and reducing airway resistance. Also relaxes smooth muscle of the uterus and vascular supply to the skeletal muscle. These actions are believed to result from increased production of cyclic adenosine 3'5' monophosphate (cylic 3'5' -AMP) caused by activation of the enzyme adenyl cyclase.

PHARMACOLOGY (SUMMARY OF PHARMACODYNAMICS AND PHARMACOKINETICS):
Absorption - Well absorbed from the gastrointestinal tract.
Metabolism - Hepatic, primarily to salbutamol 4'-0 sulfate which has little or no beta-adrenergic blocking activity..
Half life - (plasma) 2.7 to 5 hours.
Onset of action - within 30 minutes
Time to peak plasma concentration - within 2 to 3 hours following a 6 mg of tritiated salbutamol sulphate.
Time to peak effect – 2 to 3 hours.
Duration of action – 6 hours or longer.
Excretion - Renal; approximately 76% of oral dose excreted over 3 days in the urine, the majority of dose being excreted within the first 24 hours, consisting of 60% as metabolites. Faecal; About 4% of oral dose may be excreted in the faeces.

INDICATIONS:
a. Relief of broncial asthma
b. Chronic bronchitis
c. Emphysema
d. Acute dyspnea

CONTRAINDICATIONS:
Use of this medication should be carefully considered when the following medical problems exist (reasons given where appropriate).
Cardiovascular disorders, including coronary insufficiency and hypertension.

Diabetes mellitus, Enlarged prostate, Hyperthyroidism.

SIDE EFFECTS / ADVERSE REACTIONS:
Fine tremor (usually hands), nervous tension, headache, peripheral vasodilation, tachycardia (seldom trouble-some when given by aerosol inhalation); hypokalemia after high doses.

PRECAUTIONS / WARNINGS:
Hyperthyroidism, ischaemia heart disease, hypertension, pregnancy, elderly patients, intravenous administration to diabetics (monitor blood glucose).
Pregnancy / Reproduction
Fertility – Animal (rat) reproduction studies with salbutamol have shown no evidence of impaired fertility.
Pregnancy – Although adequate and well-controlled studies in humans have not been done, risk-benefit must be considered since some studies in CD-1 mice have shown that salbutamol cause cleft palate formation where given subcutaneously in doses of 0.25mg and 2.5 mg per kg (corresponding to 0.4 times and 4 times the maximum human oral dose respectively).
Another study in CD – 1 mice has shown that salbutamol causes malformations when given orally in doses of 25 and 50 mg per kg (corresponding to at least 32 times the maximum human oral daily dose). Also a reproduction study in rabbits has shown that salbutamol causes cranioshisis when given in doses of 50 mg per kg (corresponding to 78 times the maximum human oral dose).
Labour – Salbutamol administration intravenously or orally reportedly inhibits uterine contractions. Although salbutamol administered orally has been reported to delay pre-term labour, there are no well-controlled studies which show that it will stop pre-term labour or prevent labour at term
Breast feeding
Although it is not known whether salbutamol is excreted in breast milk and problems in humans have not been documented, risk-benefit must be considered since some animal studies have shown salbutamol to be potentially tumorigenic.

INCOMPATIBILITIES / DRUG INTERACTIONS:
Be alert for the possible drug interactions with:
Adrenocorticoids, glucocorticoid, oral inhalation aerosols.
(inhalation aerosol dosage forms of both glucocorticoid adrenocorticoids and salbutamol contain fluorocarbon propellants, use of both medications in rapid sequence may increase the risk of fluorocarbon toxicity, patient should be advised to allow a 15 minute interval between using the 2 inhalation aerosols).
Anesthetics, hydrocarbon inhalations.
(administration of high doses of salbutamol prior to or shortly after anesthesia with chloroform, cyclopropane, halothane, or trichloroethylene may increase the risk of severe

ventricular arrhythmias, in patients with pre-existing heart disease, because these anesthetics greatly sensitize the myocardium to the effects of sympathomimetics).
(enflurane, isoflurane, or methoxyflurane may also cause some sensitization of the myocardium effects of sympathomimetics, caution is recommended during concurrent use with salbutamol.

Antihypertensives or Diuretics used as antihypertensives
(antihypertensive effects may be reduced when these medications are used concurrently with salbutamol; the patient should be carefully monitored to confirm that the desired effect is being obtained)

Beta - adrenergic blocking agents
(concurrent use with salbutamol may result in mutual inhibition of therapeutic effects; of beta - blocking may antagonize the beta- 2 adrenergic bronchodilation effect of salbutamol; use of a cardioselective beta- adrenergic blocker, such as atenolol or metoprolol, at low doses, may prevent antagonism of the bronchodilating effect)

CNS stimulation producing medications, other
(concurrent use with salbutamol may result in additive CNS stimulation to excessive levels, which may cause unwanted effects such as nervousness, irritability, insomnia, or possibly convulsions or cardiac arrhythmias; close observation is recommended)

Digital is glycosides
(concurrent use with salbutamol may increase the risk of cardiac arrhythmias; caution and close electrocardiographic monitoring are very important if concurrent use is necessary).

Epinephrine or Sympathomimetic aerosol bronchodilators, other
(concurrent use with salbutamol however, salbutamol inhalation aerosol has been used to relieve acute bronchospasm in patients receiving chronic oral sympathomimetic therapy).

Levodopa
(concurrent use with salbutamol may increase the possibility of cardiac arrhythmias; dosage reduction of the sympathomimetic is recommended).

Monoamine oxidase (MAO) inhibitors, including furazolidone, pargyline and procarbazine or Tricyclic antidepressants
(concurrent use may potentiate the action of salbutamol on the vascular system).

Nitrates
(Concurrent use with salbutamol may reduce the antianginal effects of nitrates)

Sympathomimetics oral, other
(in addition to possibly increasing CNS stimulation, concurrent use may increase the cardiovascular effects of either the other oral sympathomimeties or salbutamol, possibly resulting in toxicity)

Thyroid hormones
(concurrent use may increase the effects of either these medications or salbutamol; thyroid hormones enhance risk of coronary insufficiency when sympathomimetic agents are administered to patients with coronary artery disease; dosage adjustment is recommended, although problem is reduced in euthyroid patients)

Xanthines
(in addition to possibly increasing CNS stimulation, concurrent use with salbutamol may result in other additive toxic effects)

RECOMMENDED DOSAGE, DOSAGE SCHEDULE AND ROUTE OF ADMINISTRATION:
Route of administration: Oral.
Usual adult dose: Bronchospasm in obstructive pulmonary disease (treatment) - the equivalent of salbutamol: 2 to 6 mg three or four times a day initially, the dosage being increased as needed and tolerated up to a maximum of 8 mg four times a day.
Note: Geriatric patients and patients sensitive to beta- adrenergic stimulants – oral, the equivalent of salbutamol: 2 mg, three or four times a day initially, the dosage being increased as needed and tolerated up to a maximum of 8 mg, three or four times a day.
Usual pediatric dose: Bronchospasm in obstructive pulmonary disease (treatment)-
Children up to 2 years of age; Dosage has not been established.
Children 2 to 6 years of age: Oral, the equivalent of salbutamol - 100 mcg (0.1 mg) per kg of body weight three times a day initially; the dosage being increased as needed and tolerated up to 200 mcg (0.2 mg) per kg of body weight, not to exceed 4 mg three times a day.
Children 6 to 14 years of age: the equivalent of salbutamol 2 mg three or four times a day initially, the dosage being increased as needed and tolerated up to a maximum of 24 mg per day in divided doses.
Children 14 years of age and over: same as adult dose.

SYMPTOMS AND TREATMENT FOR OVERDOSE AND ANTIDOTE(S):
A cardioselective beta-adrenergic blocker such as metoprolol may be used, if necessary, it should be used with caution since as asthmatic attack could be induced by beta-blocker. Dialysis is most appropriate treatment for overdosage of salbutamol.

PACKING / PACK SIZES:
Plastic bottles of 60 ml and 100 ml.

STORAGE CONDITIONS, USER INSTRUCTIONS AND PHARMACEUTICAL PRECAUTIONS:
Store in well-closed containers below 30°C. Protect from light and freezing.
User Instructions:
It is very important that you use this medicine only as directed. Do not use more of it and do not use more than your doctor instructed. Check with your doctor immediately if you experience the following side effects: Chest pain, severe dizziness, severe or continuing headache, continuing nausea or vomiting, unusual fast or pounding heartbeat

SHELF LIFE: 3 years

MANUFACTURER AND PRODUCT REGISTRATION HOLDER:

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