Salbutamol sulfate+ Carbocisteine

℞

Solmux® Broncho

2 mg / 500 mg Capsule • 2 mg / 500 mg per 5 mL Suspension

BRONCHODILATOR / MUCOLYTIC

Each capsule contains:
Salbutamol sulfate …….. 2 mg
Carbocisteine …….. 500 mg

Each 5 mL (1 teaspoonful) suspension contains:
Salbutamol sulfate …….. 2 mg
Carbocisteine …….. 500 mg

PRODUCT DESCRIPTION

Salbutamol sulfate 2 mg + Carbocisteine 500 mg (Solmux® Broncho) capsule: glossy, green-colored capsule.

Salbutamol sulfate 2 mg + Carbocisteine 500 mg (Solmux® Broncho) per 5 mL suspension: homogeneous suspension with the color, odor, and taste of orange.

CLINICAL PHARMACOLOGY

PHARMACODYNAMICS

Salbutamol
Salbutamol is a selective short-acting beta$_2$-agonist with a preferential effect on beta$_2$-receptors found in the respiratory tract. It stimulates adenyl cyclase, the enzyme which catalyzes the conversion of adenosine triphosphate (ATP) to cyclic-3',5'-adenosine monophosphate (cAMP). cAMP mediates cellular responses such as bronchial smooth muscle relaxation resulting in bronchodilation.

Carbocisteine
Carbocisteine, a derivative of acetylcysteine, is a mucoregulating agent. Its major action is thought to be on the metabolism of mucus-producing cells. The mucus produced under the influence of carbocisteine has an increased content of the less viscous sialomucin and a reduced content of the highly viscous fucomucin. Sialomucins influence the rheological properties of mucus and may also, through the inhibition of kinins, reduce or prevent bronchial inflammation.

Carbocisteine also reduces the number of exacerbations associated with chronic obstructive pulmonary disease (COPD) and inhibits the adherence of bacteria (*Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Escherichia* coli) and virus to human respiratory cells.

PHARMACOKINETICS

Salbutamol
Salbutamol is readily absorbed from the gastrointestinal tract after oral administration. Bronchodilation begins within 30 minutes after oral administration of salbutamol, peaks in 2 to 3 hours, and persists 4 to 6 hours. Plasma protein binding is around 10%.

Salbutamol undergoes first-pass metabolism in the liver, being converted to salbutamol 4'-O-sulfate. The plasma half-life of salbutamol has been estimated to range from 4 to 6 hours. Salbutamol is rapidly excreted, mainly in the urine, as metabolites and unchanged drug; a smaller proportion is excreted in the feces. Majority of a salbutamol dose given orally is excreted within 72 hours.

Carbocisteine
Carbocisteine is rapidly and well absorbed from the gastrointestinal tract. Peak serum concentration of 13.38 mg/L was achieved 1 to 2 hours after administration of 1.5 g carbocisteine. Plasma half-life was estimated to be 1.33 hours. Carbocisteine penetrates well into lung tissues and respiratory mucus, suggesting local action. Carbocisteine undergoes acetylation, decarboxylation and sulfoxidation. Most of the drug is excreted unchanged in the urine.

INDICATIONS

For the symptomatic treatment of productive cough associated with airway disorders, such as acute and chronic bronchitis, bronchial asthma and bronchiectasis

DOSAGE AND MODE OF ADMINISTRATION

Age Group	Oral dose of Salbutamol + Carbocisteine every 6 to 8 hours	
	Capsule	Suspension
Adults and Children over 12 years	1 capsule	5 mL (1 teaspoonful)
Children 6 to 12 years	-	2.5 mL (1/2 teaspoonful)
Or, as prescribed by a physician.		Shake well before using. Always keep container tightly closed.

CONTRAINDICATIONS

- Hypersensitivity to any ingredients in the product
- Certain maternal or fetal conditions may contraindicate tocolytic therapy (e.g., eclampsia or severe preeclampsia, intrauterine infection, intrauterine fetal death, antepartum hemorrhage, placenta previa, cord compression, or toxemia of pregnancy); salbutamol should not be used for threatened abortion
- Active stomach or intestinal ulcer

WARNINGS AND PRECAUTIONS

Seek medical advice if either the usual relief is diminished or the usual duration of action is reduced. Do not increase the dose or frequency of administration.

Paradoxical bronchospasm: Paradoxical bronchospasm, a potentially life- threatening event, has been observed with salbutamol. If it occurs, discontinue use of the product immediately.

Deterioration of asthma: Asthma may deteriorate acutely over a period of hours or chronically over several days or longer. Increased use of beta$_2$-agonists, especially daily use, is a sign of deterioration of asthma control and indicates the need to reassess treatment. Possible need for anti-inflammatory treatment (e.g., corticosteroids) should be considered.

Hypokalemia: Therapy with salbutamol and other beta$_2$-agonists may produce decrease in plasma potassium concentration possibly through intracellular shunting resulting in cardiovascular undesirable effects. Use with caution in acute severe asthma where concomitant therapy with steroid, xanthine derivatives, or diuretics, and by hypoxia may result in hypokalemia; potassium concentrations should be monitored in severe asthma.

Metabolic Effects: As with other beta$_2$-agonists, salbutamol can induce reversible metabolic changes (e.g., increased blood sugar levels). The diabetic patient may be unable to compensate for this; and thus, result in the development of ketoacidosis. Concomitant administration of corticosteroids can exaggerate this effect.

Coexisting Conditions: Use with caution in patients with the following conditions:

- Cardiovascular disorders including coronary insufficiency, cardiac arrhythmias, or hypertension: Salbutamol, like all other beta$_2$-agonists, can produce clinically significant cardiovascular effects such as changes in pulse rate or blood pressure.
- Convulsive disorders
- Hyperthyroidism
- Diabetes mellitus
- In patients who are unusually responsive to sympathomimetic amines
- Stomach or intestinal ulcer and gastrointestinal bleeding

INTERACTIONS WITH OTHER MEDICAMENTS

Sympathomimetic agents: Salbutamol should not be administered concomitantly with other sympathomimetic agents or epinephrine since serious adverse cardiovascular effects may occur.

Beta-adrenergic blocking agents (e.g., propranolol): Beta-adrenergic blocking agents may inhibit the effect of beta-agonists such as salbutamol. It may also produce severe bronchospasm in asthmatic patients.

Diuretics: Administration of nonpotassium-sparing diuretics (e.g., loop or thiazide diuretics) may result in electrocardiographic changes/and or hypokalemia and can be acutely worsened by administration of beta$_2$-agonists such as salbutamol, especially when the recommended dose of the beta$_2$-agonist is exceeded.

Digoxin: Following administration of single-dose intravenous or oral salbutamol to healthy individuals who had received digoxin for 10 days, a 16% to 22% decrease in serum digoxin concentration was observed. Although the clinical importance of these findings for patients who are receiving inhaled salbutamol and digoxin on a chronic basis is unclear, patients receiving such concomitant therapy should have their serum digoxin concentration carefully evaluated.

Monoamine oxidase inhibitors (MAOIs) or Tricyclic antidepressants (TCAs): Salbutamol should be used with caution in patients receiving MAOIs or TCAs, or within 2 weeks of discontinuation of such agents, because the effect of salbutamol on the vascular system may be potentiated. Alternative therapy should be considered in patients taking MAOIs or TCAs.

STATEMENT ON USAGE FOR HIGH RISK GROUPS

Salbutamol

Pregnancy: Pregnancy Category C. There have been reports of congenital anomalies (e.g., cleft palate and limb defects) in children of patients treated with salbutamol. Some of the mothers, however, were receiving various medications in the course of their pregnancies. Since there is no consistent pattern of congenital abnormality development, a relationship between the use of salbutamol and the development of congenital anomalies cannot be established. The safe use of carbocisteine during pregnancy has not been established. Therefore, this product should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery: Since beta$_2$-agonists may interfere with uterine contraction, salbutamol should be used in labor only if the potential benefit justifies the potential risk.

Lactation: Salbutamol may be secreted in breast milk. It is not known if carbocisteine is excreted in human milk. Therefore, do not administer to breastfeeding women unless, in the opinion of a physician, the potential benefit of the drug justifies the potential risk.

UNDESIRABLE EFFECTS

Salbutamol

Infections and infestations: Conjunctivitis
Immune system disorders: Erythema multiforme, hypersensitivity (anaphylaxis, angioedema, bronchospasm, collapse, hypotension, oropharyngeal edema, rash, urticaria), Stevens-Johnson syndrome
Metabolism and nutrition disorders: Hypokalemia, increased appetite
Psychiatric disorders: Drowsiness, hoarseness, hyperactivity, insomnia, nervousness
Nervous system disorders: Central nervous stimulation, dizziness, headache, restlessness, tremor, vertigo

Eye disorders: Mydriasis
Ear and labyrinth disorders: Tinnitus
Cardiac disorders: Angina, cardiac arrythmias (including atrial fibrillation, supraventricular tachycardia, and extrasystoles), chest discomfort, myocardial ischemia, palpitations, tachycardia
Vascular disorders: Epistaxis, flushing, hypotension, pallor, peripheral vasodilatation
Respiratory, thoracic and mediastinal disorders: Cough paradoxical bronchospasm
Gastrointestinal disorders: Dyspepsia, epigastric pain, nausea, stomach ache
Musculoskeletal and connective tissue disorders: Feeling of muscle tension, muscle cramps
Renal and urinary disorders: Difficulty in micturition
General disorders and administration site conditions: Increased sweating, irritability, weakness

Carbocisteine
Carbocisteine is generally safe.

Nausea, diarrhea, stomach discomfort, gastrointestinal bleeding and skin rashes are the most common undesirable effects.

Carbocisteine rarely causes dizziness, insomnia, headache, palpitations, mild lowering of blood glucose, dryness of mouth, abnormal heart rhythm (atrial fibrillation), and flatulence (gassiness).

OVERDOSE AND TREATMENT

Salbutamol

Overdosage with salbutamol produces symptoms that may be expected with beta$_2$-agonists such as tachycardia, central nervous system stimulation, tremor, hypokalemia, and hypoglycemia.

Nausea, vomiting and hyperglycemia have been reported, predominantly in children and when salbutamol overdose has been taken via the oral route.

Lactic acidosis has been reported in association with high therapeutic doses as well as overdoses of short-acting beta-agonist therapy.

Cardiac arrest and even death may occur following excessive use of salbutamol.

Discontinue salbutamol and institute appropriate symptomatic therapy in cases of salbutamol overdosage. Administration of a beta-adrenergic blocking agent may be appropriate, but use with caution in patients with a history of bronchospasm. There is no adequate evidence to support the use of dialysis in the treatment of salbutamol overdose.

Carbocisteine

Carbocisteine overdose is usually associated with stomach or intestinal discomfort. No active treatment is necessary.

STORAGE CONDITIONS

- (Capsule) Store at temperatures not exceeding 25^{O}C
- (Suspension) Store at temperatures not exceeding 30^{O}C
- Keep the product out of sight and reach of children

AVAILABILITY

Salbutamol sulfate + Carbocisteine (Solmux Broncho®) capsule in box of 100s (in flex foil)
Salbutamol sulfate + Carbocisteine (Solmux Broncho®) suspension in bottle of 60 mL

CAUTION

Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

Date of Revision: April 21, 2015

ADVERSE DRUG REACTION REPORTING STATEMENT

For suspected adverse drug reaction, seek medical attention immediately and report to the FDA at www.fda.gov.ph **AND** Unilab at (+632) 858-1000 or productsafety@unilab.com.ph. By reporting undesirable effects, you can help provide more information on the safety of this medicine.

Trusted Quality Healthcare

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Reg. IPOPHIL