

Albutamol[®] Plus

Tablet

1. Generic Name

Salbutamol, Etofylline and Bromhexine

2. Qualitative and Quantitative composition

Salbutamol 1mg

Etofylline 50mg

Bromhexine 8 mg

3. Dosage form and strength

Oral tablet containing Salbutamol 1mg, Etofylline 50mg and Bromhexine 8mg

4. Clinical particulars

4.1 Therapeutic indication

Albutamol Plus Tablet is indicated for the relief of bronchospasm in adults and children 6 years of age and older with reversible obstructive airway disease due to asthma or chronic bronchitis.

4.2 Posology and method of administration

The usual recommended oral dose of Albutamol Plus Tablet is one tablet 3-4 times a day.

4.3 Contraindication

Albutamol Plus tablets is contraindicated in patients with hypersensitivity to any ingredient of the formulation.

4.4 Special warnings and precautions for use

While treating cough as a symptom, it is important to make every effort to determine and treat appropriately the underlying cause, such as a specific infection.

Caution should be observed while prescribing Albutamol Plus tablets to children with hypertension, cardiovascular disease, uncontrolled juvenile diabetes mellitus, hyperthyroidism, seizures or in patients who are unusually hypersensitive to sympathomimetic amines.

4.5 Drug interactions

- Hypokalemia with high doses of β_2 -agonists may result in increased susceptibility to digitalis induced cardiac arrhythmias.
- Hypokalemia may be enhanced by concomitant administration of aminophylline or other xanthines, corticosteroids or by diuretic therapy.
- Other sympathomimetic bronchodilators or epinephrine should not be used concomitantly with salbutamol, since their combined effect on the cardiovascular system may be deleterious to the patient.
- Salbutamol should be administered with caution in patients being treated with monoamine oxidase (MAO) inhibitors or tricyclic antidepressants, since the action of salbutamol on the vascular system may be potentiated.
- Concomitant use of propranolol, cimetidine, erythromycin, allopurinol, verapamil, diltiazem and quinolone group of antibacterials may increase Etofylline plasma levels. Plasma concentrations are reduced by rifampicin, phenobarbitone, phenytoin, carbamazepine, sulphinpyrazone and smoking.

4.6 Use in special population

- Pediatric: Safety and effectiveness of Albutamol Plus Tablet in children below 2 years of age have not been established.
- Geriatric: Safety and effectiveness of Albutamol Plus Tablet in geriatric patients have not been established.
- Liver impairment: Use with caution.
- Renal failure: Use with caution.
- Pregnancy and lactation: Category C: Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women

despite potential risks. Doctor consultation is recommended for breast feeding patients.

4.7 Effects on ability to drive and use machine

Patients should be cautioned against engaging in activities requiring complete mental alertness, and motor coordination such as operating machinery until their response to Albutamol Plus tablets is known.

4.8 Undesirable effects

- The frequency of these side effects appears to diminish with continued therapy.
- Other commonly reported reactions include:

Salbutamol: Anaemia, Eosinophilia, Thrombocytopenia, Palpitations, Tachycardia, Cardiac flutter, Arrhythmia, Myocardial infarction, Atrial fibrillation, Cardiac failure congestive, Vertigo, Tinnitus, Visual impairment, Cataract, Vision blurred, Nausea, Vomiting, Dry mouth, Diarrhoea, Abdominal pain, Stomatitis, Dysphagia, Dyspepsia, Abdominal discomfort, Hypokalaemia, Lactic acidosis, Diabetes mellitus, Decreased appetite, Hyperglycaemia, Muscle spasms, Back pain, Myalgia, Pain in extremity, Arthralgia, Tremor, Dizziness, Headache, Dysgeusia, Hypoaesthesia, Seizure, Anxiety, Insomnia, Nervousness, Agitation, Urinary retention, Dyspnoea, Asthma, Cough, Wheezing, Chronic obstructive pulmonary disease, Bronchospasm, Dysphonia, Throat irritation, Oropharyngeal pain, Productive cough, Rash, Urticaria, Pruritus, Hypertension, Flushing, Hypotension.

Etofylline: Nausea, Vomiting, Chest pain, Tremor, Restlessness, Dyspnoea, Pruritus, rash.

Bromhexine: Thrombocytopenia, Palpitations, Cardiac flutter, Vertigo, Periorbital oedema, Nausea, Vomiting, Dry mouth, Diarrhoea, Abdominal pain, Hepatic function abnormal, Decreased appetite, Muscle spasms, Back pain, Myalgia, Dizziness, Headache, Tremor, Insomnia, Dysuria, Dyspnoea, Rash, Urticaria, Pruritus, Phlebitis, Flushing

4.9 Overdose

There is limited experience of overdose with Albutamol Plus tablets. Initiate general symptomatic and supportive measures in all cases of overdosages where necessary.

5. Pharmacological properties

5.1 Mechanism of action

Salbutamol is a beta (2)-adrenergic agonist and thus it stimulates beta (2)-adrenergic receptors. Binding of albuterol to beta (2)-receptors in the lungs results in relaxation of bronchial smooth muscles. It is believed that salbutamol increases cAMP production by activating adenylate cyclase, and the actions of salbutamol are mediated by cAMP. Increased intracellular cyclic AMP increases the activity of cAMP-dependent protein kinase A, which inhibits the phosphorylation of myosin and lowers intracellular calcium concentrations. A lowered intracellular calcium concentration leads to a smooth muscle relaxation and bronchodilation. In addition to bronchodilation, salbutamol inhibits the release of Broncho constricting agents from mast cells, inhibits microvascular leakage, and enhances mucocilliary clearance.

Etofylline is the ethyl salt of Theophylline. It inhibit phosphodiesterase enzyme which degrades cyclic nucleotides intracellularly and it results the cyclic AMP accumulation in the cell. This causes bronchodilation.

Bromhexine is an oral mucolytic agent with a low level of associated toxicity. Bromhexine acts on the mucus at the formative stages in the glands, within the mucus-secreting cells. Bromhexine disrupts the structure of acid mucopolysaccharide fibres in mucoid sputum and produces less viscous mucus, which is easier to expectorate.

5.2 Pharmacodynamic properties

Salbutamol, a moderately selective beta (2)-receptor agonist similar in structure to terbutaline, is widely used as a bronchodilator to manage asthma and other chronic obstructive airway diseases. The R-isomer, levalbuterol, is responsible for bronchodilation while the S-isomer increases bronchial reactivity. The R-enantiomer is sold in its pure form

as Levalbuterol. The manufacturer of levalbuterol, Sepracor, has implied (although not directly claimed) that the presence of only the R-enantiomer produces fewer side-effects.

Etofylline release calcium from sarcoplasmic reticulum, especially in cardiac muscles and results increased cardiac muscle contraction. This drug also blocks adenosine receptors (adenosine acts as a local mediator in CNS & CVS and other organs- which contracts smooth muscles, especially in bronchi, blood vessels etc). This results in bronchodilation and vasodilatation.

5.3 Pharmacokinetic properties

Salbutamol is readily absorbed from the gastrointestinal tract. When given by inhalation, 10 to 20% of the dose reaches the lower airways. The remainder is retained in the delivery system or is swallowed and absorbed from the gut. Salbutamol is subject to first-pass metabolism in the liver and possibly in the gut wall but does not appear to be metabolised in the lung; the main metabolite is the inactive sulfate conjugate. Salbutamol is rapidly excreted, mainly in the urine, as metabolites and unchanged drug; a smaller proportion is excreted in the faeces. The plasma half-life of salbutamol has been estimated to range from 4 to 6 hours.

Etofylline is well absorbed after oral administration. Rapidly and well absorbed after intravenous administration. Widely distributed in the body and 40% bound to the plasma proteins. Metabolized in the liver to its metabolites by demethylation and oxidation. 1-methyluric acid is its metabolite excreted through urine.

Bromhexine hydrochloride is rapidly absorbed from the gastrointestinal tract; peak plasma concentrations occur after about 1 hour. Bromhexine undergoes extensive first-pass metabolism in the liver: its oral bioavailability is stated to be only about 20%. It is widely distributed to body tissues. About 85 to 90% of a dose is excreted in the urine mainly as metabolites. Ambroxol is a metabolite of Bromhexine. Bromhexine is highly bound to plasma proteins. It has a terminal elimination half-life of 13 to 40 hours. Bromhexine crosses the blood-brain barrier and small amounts cross the placenta.

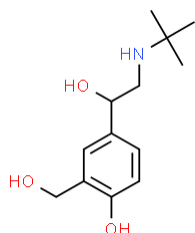
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Not required.

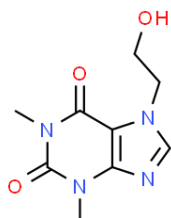
7. Description

Salbutamol belongs to a class of drugs known as bronchodilators. Its chemical name is bis(4-[2-(tert-butylamino)-1-hydroxyethyl]-2-(hydroxymethyl)phenol); sulfuric acid and its chemical structure is:



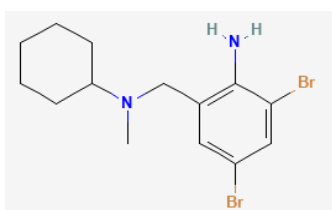
Its empirical formula is C₁₃H₂₁NO₃ and its molecular weight is 239.31 g/mol.

Etofylline belongs to a class of drugs known as xanthines. Its chemical name is 2-(1,3-dimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1H-purin-7-yl)ethyl pyridine-3-carboxylate and its chemical structure is:



Its empirical formula is C₉H₁₂N₄O₃ and its molecular weight is 224.22 g/mol.

Bromhexine hydrochloride is a secretolytic, with mucolytic activity. Its chemical name is 2,4-dibromo-6-[[cyclohexyl(methyl)amino]methyl]aniline and its chemical structure is:



Its empirical formula is C₁₄H₂₀Br₂N₂ and its molecular weight is 376.13 g/mol.

8. Pharmaceutical particulars

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life

24 months.

8.3 Packaging Information

Albutamol Plus tablets is available in pack of 10 tablets.

8.4 Storage and handling instructions

Store below 30°C in a dark place. Keep the bottle tightly closed.

9. Patient Counselling Information

9.1 Adverse Reactions

Refer part 4.8

9.2 Drug Interactions

Refer part 4.5

9.3 Dosage

Refer part 4.2

9.4 Storage

Refer part 8.4

9.5 Risk Factors

Refer part 4.4

9.6 Self-monitoring information

NA

9.7 Information on when to contact a health care provider or seek emergency help

Patient is advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3

10. Manufactured by

CENTAUR PHARMACEUTICALS PVT. LTD.

11. Details of permission or license number with date

158(7)/MFG/DFDA/2015/6407 dated. 23.03.2015 for domestic.

12. Date of revision:

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