SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF THE MEDICINAL PRODUCT

SALBUMOL PLUS SYRUP (Salbutamol Sulfate, Bromhexine Hydrochloride, Guaifenesin & Levomenthol Syrup)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml Contains

Salbutamol Sulfate eq to Salbutamol	2 mg
Bromhexine Hydrochloride	4 mg
Guaifenesin BP	100 mg
Levomenthol BP	1 mg

Colour: Ponceau 4R

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Syrup

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications:

SALBUMOL PLUS SYRUP is indicated for clinical relief of cough associated with bronchitis, bronchial asthma, emphysema and other bronchopulmonary disorders where bronchospasm, mucous plugging and problems of expectoration co-exist.

4.2 Posology and Method of Administration:

Adults:10- 20ml thrice daily (10 ml)
Children: 6-12 yrs. – 10 ml thrice
Children: (under 6 yrs.) -5-10 ml thrice daily

4.3 Contraindication:

Hypersensitivity to the components 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 specific infection. Caution should be observed while prescribing SALBUMOL PLUS SYRUP to patients with hypertension, cardiovascular disease (including arrhythmias, coronary insufficiency, uncontrolled diabetes mellitus & patients with hyperthyroidism, history of seizures or in patients who are unusually

responsive to sympathomimetic amines. Patients susceptible to hypokalemia should be monitored because transient early falls in serum potassium have been reported with beta agonists. Since, mucolytics, such as bromhexine may disrupt the gastric mucosal barriers, bromhexine should be used with care in patients with a history of peptic ulceration.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction:

Sympathomimetic agents: Concomitant use of SALBUMOL PLUS SYRUP with other oral sympathomimetic agents is not recommended.

Beta-receptor blocking agents and Salbutamol inhibit the effect of each other.

Monoamine oxidase inhibitors: Salbutamol should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants since the action of Salbutamol on the vascular system may be potentiated.

Others

SALBUMOL PLUS SYRUP should be used with caution in patients with diabetes mellitus, serious cardiovascular disorders, hypertension, hyperthyroidism and peptic ulcers.

4.6 Pregnancy and Lactation:

Pregnancy

This combination is not recommended for use in pregnancy.

Lactation

It is not known whether this combination is secreted in breast milk

Pediatric Use

Safety and effectiveness in children under the age of two years has not yet been adequately demonstrated.

4.7 Effects on Ability to Drive and Use Machines:

This product has no or negligible influence on the ability to drive or operate machinery.

4.8 Undesirable Effects:

These are generally mild and very rare. However, In isolated cases, fine finger tremors, palpitation gastrointestinal disturbances, fatigue, dry mouth and dysuria may be seen.

4.9 Overdose:

Symptoms and signs

The effects of acute toxicity may include gastro-intestinal discomfort, nausea and drowsiness. fatigue, dry mouth and dysuria.

Treatment

Treatment should be symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties:

Salbutamol is a beta-adrenergic stimulant which has a highly selective action on the β2 - receptors in bronchial muscle resulting in 2 bronchodilations, and in therapeutic doses, little or no action on the β1cardiac receptors.

Bromhexine is a derivative of the alkaloid vasicine and possesses mucokinetic (improvement in mucus transport) and mucolytic properties. It depolymerises mucopolysaccharides directly as well as liberating lysosomal enzymes. It promotes the removal of tenacious secretions in the respiratory tract and reduces mucus stasis (arresting the secretion of mucus).

Guaifenesin, by increasing respiratory tract fluid, reduces the viscosity of tenacious secretions and acts as an expectorant. Another possible mechanism by which it acts is by increasing the water bonding in the sputum, thereby decreasing its viscosity and leading to an increase in mucokinesis. is effective in both productive and nonproductive coughs.

Levomenthol is having soothing action.

5.2 Pharmacokinetic Properties:

Bromhexine:

Absorption

Oral, well absorbed. Rapidly absorbed from the gastrointestinal tract. Peak plasma concentrations occur after about 1 hour following oral administration.

Distribution

It is widely distributed to body tissues. Bromhexine is highly bound to plasma proteins. Bromhexine crosses the blood-brain barrier and small amounts cross the placenta.

Metabolism

Bromhexine undergoes extensive first-pass metabolism in the liver: Ambroxol is a metabolite of bromhexine.

Excretion

Bromhexine is excreted primarily in the urine as metabolites. Only small amounts appear as unchanged drug. About 85 to 90% of a dose is excreted in the urine mainly as metabolites.

Approximately 70% of an oral dose of bromhexine has been recovered in the urine within 24 hours.

Other excretion: faeces, 4%

Elimination Half-life: It has a terminal elimination half-life of 13 to 40 hours

Guaiphenesin:

Absorption:

Guaiphenesin is well absorbed from the gastro-intestinal tract following oral administration, although limited information regarding its pharmacokinetics is available. After the administration of 600 mg Guaiphenesin to healthy adult volunteers, the Cmax was approximately 1.4ug/ml, with tmax occurring approximately 15 minutes after drug administration.

Distribution:

No information is available on the distribution of Guaiphenesin in humans.

Metabolism and elimination:

Guaiphenesin appears to undergo both oxidation and demethylation. Following an oral dose of 600 mg guaifenesin to 3 healthy male volunteers, the t½ was approximately 1 hour and the drug was not detectable in the blood after approximately 8 hours.

Pharmacokinetics in Renal/Hepatic Impairment:

There have been no specific studies of Guaiphenesin in subjects with renal or hepatic impairment. Caution is therefore recommended when administering this product to subjects with severe renal or hepatic impairment.

Menthol

Absorption

Menthol is highly lipid soluble and, when taken orally, is rapidly absorbed from the small intestine.

Distribution

There is insufficient data on the distribution of menthol.

Metabolism

In humans, menthol is partially metabolized to menthol glucuronide by rapid conjugation. Animal studies in rats have demonstrated that menthol then undergoes extensive enterohepatic recirculation after being cleaved from the glucuronide conjugate and reabsorbed in the small intestine. The reabsorbed menthol is then subsequently metabolized

by oxidative processes in the liver. There is support for this model in humans as well because menthol has been shown to be oxidized by CYP2A6 in human liver microsomes.

A study in humans has demonstrated that approximately 50% of a menthol dose is excreted in the urine as menthol glucuronide. Other studies in rats have shown that menthol glucuronide is excreted in both the bile and the urine, but with the bile containing the majority of menthol glucuronide and with the urine also containing various oxidation products.

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%.

5.3 Preclinical Safety Data:

No further information other than that which is included in the summary of products characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients:

Sucrose
Sodium methyl Paraben
Sodium Propyl Paraben
Sodium Benzoate
Propylene Glycol
Citric Acid Monohydrate
Flavor Raspberry Liquid no. 1 IFF
Colour Ponceau 4R supra
Purified water

6.2 Incompatibilities:

Not applicable

6.3 Shelf Life:

36 Months

6.4 Special Precautions for Storage:

Store below 30^0C. Protect from Light.

Keep medicine out of reach of children.

6.5 Nature and Contents of Container:

Primary Packing: 50 ml, 100 ml & 120 ml of Amber colored Pet bottle

Secondary Packing: Such one bottle with measuring cup is to be packed in printed carton along with pack insert.

6.6 Special Precautions for Disposal and other Handling

Not Applicable

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORIZATION NUMBER

07405/07819/VAR/2022

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF AUTHORIZATION

FIRST AUTHORIZATION : 10/08/2016

10. DATE OF REVISION OF THE TEXT

11/07/2023

11. REFERENCES