

Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Eascof-ls

2. Qualitative and quantitative composition

Generic Name: Levosalbutamol Sulphate, Ambroxol Hydrochloride and Guaiphenesin Syrup.

For a full list of excipients, see section 6.1

Table 1: composition of Eascof-LS

Sr. No.	Name of Product	Specification	Label Claim (mg)	Quantity /5ml (in mg)	Function
1.	*Levosalbutamol	IHS	1	1.205	Active ingredient
2.	Ambroxol Hydrochloride	BP	30	30	Active ingredient
3.	Guaiphenesin	BP	50	50	Active ingredient
4	Neotame	USP	--	4	Flavour Enhancer
5	Sucralose	BP	--	5	Artificial Sweetener
6	Sodium Citrate	BP	--	0.1	Buffering Agent
7	EDTA Sodium	BP	--	0.5	Stabilizing Agent
8	Glycerin	BP	--	500	Thickening agent
9	Sorbitol Solution 70% (Non-Crystallising)	BP	--	1500	Thickening agent
10	Methyl Paraben	BP	--	9	Preservative
11	Propyl Paraben	BP	--	1	Preservative
12	Propylene Glycol	BP	--	500	Solubilizing Agent
13	Colour Ponceau 4 R	IH	--	0.075	Colourant
14	Flavour Strawberry 14207 (OROR)	IH	--	0.015	Flavourant
15	Flavour Ecocool MP (C81D00001) Ideal	IH	--	0.0025	Flavourant
16	Flavour Raspberry IF - 1389 (Sensient)	IH	--	0.0075	Flavourant
17	Purified Water	BP	--	q.s. to 5 ml	Vehicle

3. Pharmaceutical form

Syrup for Oral Use

4. Clinical particulars

4.1 Therapeutic indications

In management of cough associated with
Bronchial Asthma

Bronchitis

Chronic obstructive pulmonary disease (COPD)

Respiratory tract Infection (RTI)

4.2 Posology and method of administration

Adults and adolescents above 11 years: Syrup: 5-10 ml three times daily

Children 6 to 11 years: Syrup: 5 ml three times daily.

4.3 Contraindications

Hypersensitivity to any of the components of the formulation mentioned in section 6.1. It should not be used in patients with pre-existing ischaemic heart disease or those patients with significant risk factors for ischaemic heart disease.

4.4 Special warnings and precautions for use

Levosalbutamol

Potentially serious hypokalemia may result from β_2 -agonist therapy. Particular caution is advised in acute severe asthma as this effect may be potentiated by hypoxia and by concomitant treatment with xanthine derivatives, steroids and diuretics. Serum potassium levels should be monitored in such situations. Levosalbutamol should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias or hypertension.

Ambroxol

Should be cautiously used in patients with increased sputum secretion and disorders of secretion discharge (such as the rare malignant cilia syndrome) due to a risk of airway obstruction because of impaired bronchi motor function and a large quantity of bronchial secretions. In case of renal and/or liver disease the dose is reduced or the interval between the drug intakes is extended. In case of severe renal insufficiency ambroxol metabolite accumulation is expected. Should be used cautiously in patients with peptic ulcer disease history as mucolytic products may weaken gastric mucosal barrier. There are very rare reports of severe skin reactions (e.g. Stevens-Johnson syndrome and Lyell's syndrome) occurrence during of Ambroxol administration. In case of changes of skin

and mucous membranes, Ambroxol administration should be immediately discontinued and the appropriate treatment should be carried out.

Guaiphenesin: Guaiphenesin should be not used for persistent or chronic cough, such as occurs with asthma, or where cough is accompanied by excessive secretions, unless directed by a physician. A persistent cough may be a sign of a serious condition. If cough persists for more than 7 days, tends to recur, or is accompanied by a fever, rash, or persistent headache, a physician should be consulted. Caution should be exercised in the presence of severe renal or severe hepatic impairment. The concomitant use of cough suppressants is not recommended. Patients with rare hereditary problems of fructose intolerance should not take this medicine. Not more than 4 doses should be given in any 24 hours. Avoid with any other cough and cold medicine. Consult a pharmacist or other healthcare professional before use in children under 6 years.

4.5 Interaction with other medicinal products and other forms of interaction

Levosalbutamol:

Other short-acting sympathomimetic bronchodilators or epinephrine should be used with caution with levosalbutamol. If additional adrenergic drugs are to be administered by any route, they should be used with caution to avoid deleterious cardiovascular effects. **Beta-blockers:** Beta-adrenergic receptor blocking agents not only block the pulmonary effect of beta agonists such as levosalbutamol but may also produce severe bronchospasm in asthmatic patients.

Diuretics:

Diuretics (such as loop or thiazide diuretics) can be acutely worsened by beta-agonists. Hence, caution is advised in the coadministration of beta agonists with non-potassium sparing diuretics.

Monoamine Oxidase Inhibitors or Tricyclic Antidepressants:

Levosalbutamol should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, or within 2 weeks of discontinuation of such agents, because the action of levosalbutamol on the vascular system may be potentiated.

Ambroxol:

Ambroxol is not recommended for co-administration with expectorants (e.g, codeine), Cough reflex depression may occur due to excessive accumulation of sputum and threatening obstruction of respiratory tract. Clinically significant adverse interactions with other drugs have not been observed. The drug can be used simultaneously with antibiotics such as

amoxicillin, cefuroxime, erythromycin and doxycycline, antibiotics penetration into lung tissues and their efficacy increase..

Guaiphenesin: If urine is collected within 24 hours of a dose of Guaiphenesin, its metabolite may cause a colour interference with laboratory determinations of urinary 5-hydroxyindoleacetic acid (5HIAA) and vanillylmandelic acid (VMA). Others:

Ambroxol hydrochloride and Guaiphenesin Expectorant should be used with caution in patients with diabetes mellitus, serious cardiovascular disorders, hypertension, hyperthyroidism and peptic ulcers.

4.6 Pregnancy and Lactation

Pregnancy

Levosalbutamol

Caution should be exercised when oral levosalbutamol is administered to a pregnant woman.

Ambroxol and Guaiphenesin:

There are no adequate and well-controlled studies of this combination in pregnant women.

Lactation

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

Guaiphenesin

is excreted in breast milk in small amounts. There is insufficient information on the effects of guaifenesin in new-borns/infants. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from therapy, taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman

Ambroxol

penetrates into breast milk. It is not allowed to use during breastfeeding.

4.7 Effects on ability to drive and use machines

The most frequent side effects are palpitation, fine tremors of the skeletal muscle (particularly the hand) and muscle cramps may occur due to levosalbutamol this may affects ability to drive and use of machines.

4.8 Undesirable effects

Levosalbutamol

The most frequent side effects are palpitation, fine tremors of the skeletal muscle (particularly the hand) and muscle cramps may occur. The other likely side effects are gastrointestinal disturbances such as nausea, vomiting, burning substernal or epigastric pain and diarrhoea. In some

cases, nervousness, headache, dizziness, fatigue and sleeplessness may occur.

Ambroxol:

Under individual hypersensitivity to Ambroxol allergic reactions such as skin rash, nettle-rash, and angioneurotic oedema are possible. Under the prolonged administration in large doses pain in epigastric area, nausea, vomiting can appear.

Guaiphenesin:

Side effects resulting from guaifenesin administration are very rare. Guaiphenesin has occasionally been reported to cause gastro-intestinal discomfort, nausea and vomiting, particularly in very high doses. Also, hypersensitivity reactions may occur

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poison board, Pharmacovigilance Electronic Reporting System (PvERS) <https://pv.pharmacyboardkenya.org>.

4.9 Overdose

Levosalmbutamol:

The expected symptoms with overdosage are tachycardia, nervousness, headache, tremor, nausea, dizziness, fatigue and sleeplessness.

Hypokalaemia also may occur. Treatment consists of discontinuation of oral levosalmbutamol together with appropriate symptomatic therapy. In the event of serious poisoning, the stomach should be emptied and, if necessary, a beta- blocker administered with caution in patients with a history of bronchospasm.

Ambroxol:

Acute potential health effects include skin irritation, eye irritation, respiratory tract irritation, gastrointestinal tract irritation with decreased motility or constipation, ulceration or bleeding from the stomach or duodenum, peritonitis. It may even affect behavior/central nervous system (tremor, convulsions, ataxia, and somnolence), respiration (dyspnea, respiratory stimulation), liver, blood (changes in white blood cell count), and urinary system. No data available on chronic potential health effects.

Guaiphenesin

The effects of acute toxicity from guaifenesin may include gastrointestinal discomfort, nausea and drowsiness. The drug is, however, rapidly

metabolised and excreted in the urine. Patients should be kept under observation and treated symptomatically.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Levosalbutamol

Levosalbutamol is a single isomer beta₂-agonist that differs from racemic salbutamol by elimination of (S)-salbutamol. Levosalbutamol is an effective bronchodilator whose primary mechanism of action is unimpeded by (S)-salbutamol. Therefore, when compared with racemic salbutamol, clinically comparable bronchodilation can be achieved with doses that substantially lessen beta-mediated side effects. Activation of beta₂-adrenergic receptors on airway smooth muscle leads to the activation of adenylyl cyclase and to an increase in the intracellular concentration of cyclic-3', 5'-adenosine monophosphate (cyclic AMP). The increase in cyclic AMP is associated with the activation of protein kinase A, which in turn, inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in muscle relaxation.

Ambroxol

Ambroxol (group of benzilamides) belongs to secretolytic and secretomotoric medicinal products. It possesses expressed expectorant effect.

Mechanism of action of the medicinal product is stipulated by stimulation of serous cells of tonsils of bronchial tubes' mucous membrane, increasing of mucous secretion content and changing of correlation of serous and mucous components of phlegm, breached under pathological processes in lungs. Under this hydrolyzing ferments activate and releasing of liposomes from Clark's cells strengthens, that causes decreasing of viscosity of phlegm. Ambroxol increases content of surfactant in lungs, which is dealt with strengthening of synthesis of the last and secretion in alveolar pneumocytes, and also with breach of its disintegration. The medicinal product increases mucociliary transport of phlegm. It suppresses coughing insignificantly. Ambroxol well penetrates through the placenta barrier, improving synthesis of surfactants during uterine life of foetus

Guaiphenesin:

Guaiphenesin is thought to exert its pharmacological action by stimulating receptors in the gastric mucosa. This increases the output from secretory glands of the gastrointestinal system and reflexly increases the flow of fluids from glands lining the respiratory tract. The result is an increase in volume and decrease in viscosity of bronchial secretions. Other actions may include stimulating vagal nerve endings in bronchial secretory glands and stimulating certain centres in the brain, which in

turn enhance respiratory fluid flow. Guaiphenesin produces its expectorant action within 24 hours.

5.2 Pharmacokinetic properties

Levosalbutamol

Enantioselective Disposition of (R, S)-Salbutamol: Racemic salbutamol is metabolized by sulphotransferase 1A3 (SULT1A3) to an inactive metabolite in human tissues. However (R)-salbutamol is sulphated eightfold faster than (S)-salbutamol because of its higher binding affinity for the enzyme.

Table 2: differences in the absorption of salbutamol enantiomers

Drug	AUC	Cmax	Tmax
(R, S)-	(ng.mL ⁻¹ .min ⁻¹)	(ng.mL ⁻¹)	(min)
(R)- Salbutamol	812	3.49	106
(S)- Salbutamol 5	5,230	23.16	111

Pharmacokinetic parameters were based on assay of plasma from 12 healthy men after a single oral dose of (R, S)-salbutamol. Following oral administration of 10 mg (R, S)-salbutamol, the median peak plasma concentration of (R)- salbutamol of 3.49 ng/mL was significantly less than the value of

(S)- salbutamol of

23.16 ng/mL. A similar study reported the ratio of AUCs for (S)- and (R)-salbutamol plasma concentrations to be about 8:1 (suggesting stereoselective metabolism of (R)- salbutamol). These observations indicate very efficient removal of the therapeutically beneficial (R)-enantiomer during (R, S)-salbutamol therapy, exposing the body to higher concentrations of the (S)-enantiomer for prolonged periods. In view of the potential opposing effects of (S)-salbutamol, it seems logical to remove this enantiomer from the currently used racemate to obtain safer bronchodilator therapy. On administration of racemic salbutamol, patients receive (R)- and (S)- salbutamol in equal amounts but are exposed to much greater amounts of the (S)-isomer for a prolonged period. Levosalbutamol appears to be stereo chemically stable in vivo and does not appear to interconvert metabolically to (S)-salbutamol.

Ambroxol

Absorption

Ambroxol is rapidly absorbed (70-80%) after oral administration. The time to reach peak plasma concentration is approximately 2 hours.

Distribution

The distribution half-life of ambroxol is around 1.3 hours.

Metabolism

Metabolite is dibromoanthranilic acid (activity unspecified).

Excretion

Excretion is primarily via the kidneys. Renal clearance (rate) is approximately 53 ml/minute; approximately 5-6% of a dose is excreted unchanged in the urine. The elimination half life of ambroxol is biphasic, with an alpha half-life of 1.3 hours and a beta half-life of 8.8 hours.

Guaiphenesin

Absorption

Guaiphenesin is well absorbed from the gastro-intestinal tract following oral administration, although limited information regarding its pharmacokinetics is available.

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 $t_{1/2}$ 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.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and toxicity to reproduction

6. Pharmaceutical Particulars

6.1 List of Excipients

Neotame
Sucralose
Sodium Citrate
EDTA Sodium

Glycerin
Sorbitol Solution 70% (Non-Crystallising)
Methyl Paraben
Propyl Paraben
Propylene Glycol
Colour Ponceau 4 R
Flavour Strawberry 14207 (OROR)
Flavour Ecocool MP (C81D00001) Ideal Cures
Flavour Raspberry IF- 1389 (Sensient)
Purified Water

6.2 Incompatibilities

Not Applicable

6.3 Shelf-Life

24 Months

6.4 Special Precautions for storage

Store below 30°C. Protect from light. Keep out of reach of Children.

6.5 Nature and Content of container

100 ml Pink Transparent Round Pet Bottle in one carton along with its pack insert.

6.6 Special precautions for disposal and other handling

Not applicable

7. Marketing Authorization Holder

CACHET PHARMACEUTICALS PRIVATE LIMITED
Address: 415, Shah Nahar Ind. Estate,
Dr. E. Moses Road, Worli, Mumbai-400 018
Maharashtra, India

8. Marketing Authorization Number

CTD 9310

9. Date of first authorization/renewal of the authorization

27/07/2023

10. Date of revision of the text

17/05/2025