SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT:

EASCOF EXPECTORANT (SALBUTAMOL SULPHATE, BROMHEXINE HYDROCHLORIDE, GUAIFENESIN, MENTHOL SYRUP)

1.1 Strength of drug product:

Bromhexine Hydrochloride BP: 4 mg

Salbutamol Sulphate BP equivalent

to Salbutamol: : 2mg

Guaifenesin BP : 100 mg

Menthol BP : 1 mg

1.2 PHARMACEUTICAL FORM

Liquid Oral Syrup.

Orange yellow colour clear liquid having sweet taste and pleasant flavour.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:

Each 10 ml contains:

Bromhexine Hydrochloride BP: 4 mg

Salbutamol Sulphate BP equivalent

to Salbutamol: : 2mg

Guaifenesin BP : 100 mg

Menthol BP : 1 mg

Colour- Sunset Yellow FCF

In flavoured syrupy base

UNIT FORMULA:

S. No.	Ingredients	Specification	Quantity / 10ml (mg)	Quantity / Batch in Kg	Function
1	Salbutamol Sulphate (Equivalent to Salbutamol)	BP	2.4	1.440	Bronchodilator
2	Bromhexine Hydrochloride (Overages 5%)	BP	4.2	2.520	Mucolytic
3	Guaifenesin	BP	100	60.00	Expectorant
4	Menthol (Overages 10%)	BP	1.1	0.66	Soothing Agent
5	Methyl Paraben	BP	8.75	5.25	Preservative
6	Propyl Paraben	BP	2.2	1.32	Preservative
7	Sodium Benzoate	BP	10	6.00	Preservative
8	Sucrose	BP	7.0	4200.00	Sweetener
9	Citric acid (Monohydrate)	BP	6.0	3.60	pH
10	Colour Sunset Yellow FCF	IH	0.25 mg	150.00 gm	Colorant
11	Sodium Chloride	BP	50.0	30.00	pH
12	Propylene glycol	BP	650	390.00	Viscosity builder
13	Flavour Strawberry ID 26236	IH	0.065 ml	39.00 L	Flavoring Agent
14	Saccharin Sodium	BP	5.00	3.00	Sweetener
15	Purified water	BP	Q.S.	Q.S.	Vehicle

3. PHARMACEUTICAL FORM

Syrup for Oral use

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Eascof Expectorant 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 (10ml)

Children: 6-12 yrs – 10ml thrice

Children: (under 6 yrs) -5-10 ml thrice daily

4.3 Method of administration: Oral

4.4 Contraindications:

Hypersensitivity to the components of the formulation.

4.5 Special Warnings and Precautions for use:

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

4.6 Paediatric population

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

4.7 Interaction with other medicinal products and other forms of interaction

Sympathomimetic agents: Concomitant use of Eascof Expectorant 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

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

4.8 Fertility, Pregnancy & Lactation:

Pregnancy

This combination is not recommended for use in pregnancy.

Lactation

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

Paediatric Use

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

4.9 Effects on ability to drive and use machines

When used as recommended and when there are no side effects, Eascof is not known to have any effect on the ability to drive or operate machinery.

4.10 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.

4.11 OVERDOSAGE

The most common signs and symptoms of overdose are transient beta agonist pharmacologically mediated events, including tachycardia, tremor, hyperactivity and metabolic effects including hypokalaemia.

Treatment

The preferred antidote for overdose is a cardioselective beta-blocking agent, which should be used with caution in patients with a history of bronchospasm. Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

5 PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Expectorant

ATC Code - Guaifenesin - R05CA03
Salbutamol - R03CC02
Bromhexine - R05CB02

Salbutamol is a beta-adrenergic stimulant which has a highly selective action on the β_2 - receptors in bronchial muscle resulting in bronchodilation, and in therapeutic doses, little or no action on the $\beta_1$cardiac 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 non-productive coughs.

Menthol is having soothing action

5.2 Pharmacokinetic properties

As a beta-adrenergic stimulant for relief of bronchospasm such as occurs with asthma, bronchitis, emphysema. It has a highly selective action on the receptors in bronchial muscle and in therapeutic dosage, little or no action on the cardiac receptors.

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 a less viscous mucus, which is easier to expectorate.

Guaifenesin is thought to act as an expectorant by increasing the volume and reducing the viscosity of secretions in the trachea and bronchi. It may aid in the flow of respiratory tract secretions, allowing ciliary movement to carry the loosened secretions upward toward the pharynx.

Salbutamol is readily absorbed from the gastro-intestinal tract and is subject to first pass metabolism in the liver. Peak plasma concentrations occur within one to four hours after oral administration. After multiple oral doses of salbutamol 4mg four times a day, steady-state plasma concentrations are obtained after 3 days. About half is excreted in the urine as an inactive sulphate conjugate following oral administration. The bioavailability of orally administered salbutamol is about 50%.

Bromhexine hydrochloride is rapidly absorbed from the gastrointestinal tract and 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 and is highly bound to plasma proteins.

The plasma half-life of Guaifenesin is approximately 1 hour. Guiafenesin is rapidly hydrolyzed (60% within seven hours) and then excreted in the urine, with beta-(2-methoxyphenoxy)-lactic acid as its major urinary metabolite. No unchanged drug was detected in the urine following administration.

5.3 Preclinical safety data

In common with other potent selective β2-agonists, salbutamol has been shown to be teratogenic in mice when given subcutaneously. In a reproductive study, 9.3% of foetuses were found to have cleft palate at 2.5mg/kg dose, 4 times the maximum human oral dose. In rats, treatment at the levels of 0.5, 2.32, 10.75 and 50mg/kg/day orally throughout pregnancy resulted in no significant foetal abnormalities. The only toxic effect was an increase in neonatal mortality at the highest dose level as the result of lack of maternal care. Reproductive studies in the rabbit at doses of 50mg/kg/day orally (i.e. much higher than the normal human dose) have shown foetuses with treatment related changes; these included open eyelids (ablepharia), secondary palate clefts (palatoschisis), changes in ossification of the frontal bones of the cranium (cranioschisis) and limb flexure.

In an oral fertility and general reproductive performance study in rats at doses of 2 and 50 mg/kg/day, with the exception of a reduction in number of weanlings surviving to day 21 post-partum at 50 mg/kg/day, there were no adverse effects on fertility, embryofoetal development, litter size, birth weight or growth rate.

Bromhexine has a low acute toxicity index. Guaiphenesin: Animal studies to assess the long-term carcinogenic and mutagenic potential or the effect on fertility in animals or humans have not been performed.

6. Pharmaceutical particulars

6.1 List of excipients:

S. No.	Ingredients	Specification
1	Methyl Paraben	BP
2	Propyl Paraben	BP
3	Sodium Benzoate	BP
4	Sucrose	BP
5	Citric acid (Monohydrsate)	BP
6	Colour Sunset Yellow FCF	IH
7	Sodium Chloride	BP
8	Propylene glycol	BP
9	Flavour Strawberry ID 26236	IH
10	Saccharin Sodium	BP
11	Purified water	BP

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Storage: Store below 30^0 C.

Protect from Light. Keep out of reach of Children

6.5 Nature and contents of container

100 ml/bottle

Primary Container: 100 ml in Orange coloured Pet Bottle sealed with 25 mm EPE WAD Cap
Secondary container: 10 ml Orange transparent Measuring cups & Sticker Label as per text matter. Such one bottle in a printed outer carton along with Pack insert.

6.6 Special Precaution for disposal.

Not required

7. Marketing Authorization Holder and Manufacturing site address

Cachet Pharmaceuticals Pvt. Ltd

415, Shah Nahar Industrial Estate,

Dr. E. Moses Road, Worli, Mumbai-400 018,

Maharashtra, India.

Manufacturer's Name and Address:

Cachet Pharmaceuticals PVT. LTD.

Village Thana, Baddi, Dist. Solan,

Himachal Pradesh – 173 205.

8. MARKETING AUTHORISATION NUMBER: Rwanda FDA-HMP-MA-0680

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

10/12/2023

10. DATE OF REVISION OF THE TEXT

04.01.2024