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	Doc No. BML/EXC/011	Date rev 09/2020	Next rev date: 08/2025

Summary of Product Characteristics

For

Ex- coff Cough Syrup

(Diphenhydramine hydrochloride + Menthol)

1. NAME OF MEDICINAL PRODUCT

Ex-coff Cough syrup

2. QUALITATIVE AND QUANTITATIVE DESCRIPTION

Each 5ml of the syrup contains

Diphenhydramine hydrochloride	7mg
Sodium citrate	28.5mg
Menthol	0.55mg

3. PHARMACEUTICAL FORM

Reddish liquid oral preparation presented as sugar-based syrup and flavoured in 100ml amber PET bottle with dose measurement cap to facilitate easy dosing

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Excoff is an antitussive and expectorant cough mixture. It is indicated for the relief of cough, sneezing, nasal congestion, nasal discharge, itchy and watery red eyes, hay fever and cold.

4.2 Posology and method of administration

Posology

The safety and efficacy of all active pharmaceutical ingredients used in the formulation of Excoff cough syrup has been established in adults and paediatric populations when taken at the prescribed doses

Method of Administration

Age group	**Dose**
2-5yr	5ml three times daily
6-12yrs	5ml three times daily

Or as directed by the physician. Note: A maximum of four doses per day should not be exceeded.

4.3 Contraindications

Excoff is contraindicated in patients with known hypersensitivity to any ingredient of the product.

4.4 Special warnings and Precautions for Use

Driving and Operation of Machinery

Excoff should not be taken in this case as some of the active ingredients of Excoff can cause extreme sedation.

Alcohol

Avoid concomitant use of alcohol with this medication.

4.5 Drug Interactions

Anxiolytics

Concomitant use of Ex-coff with alcohol, tricyclic antidepressant, opioids, benzodiazepines, anticholinergic and muscle relaxants lead to exaggerated sedation due to the presence of diphenhydramine hydrochloride.

4.6 Pregnancy and Lactation

Pregnancy

There are no known defects with the use of any of the active ingredients of Ex-coff in pregnancy. Although, there have been insinuations that diphenhydramine causes birth defects when used in the first trimester, but the veracity of the claim is not substantial as the different studies undertaken to establish this claim do not all agree.

Lactation

Ex-coff would not be expected to cause any adverse effects in breastfed infants. Larger doses or more prolonged use may however cause effects in infants or decrease the milk supply. Mother may need to consider moderate dose after the last feeding of the day to minimize any effects of the drug.

4.7 Effects on ability to drive and use machine

Ex-coff can cause sedation and it should not be taken if there are plans to operate machine or drive.

4.8 Undesirable effects

There are no serious or deleterious effects with taking Ex-coff. The observed side effects with the ingredients of Ex-coff are such that do clear out as the dosage regimen is completed.

Diphenhydramine hydrochloride

Common side effects include dizziness, sedation, psychomotor impairment, cognitive impairment, dry mouth, blurred vision, constipation, urinary retention, and weight gain. Less commonly, diphenhydramine is associated with agitation and insomnia.

Sodium citrate

Common side effects of Sodium citrate include diarrhoea, nausea, muscle spasms, metabolic acidosis, vomiting, stomach pain and fluid retention

Usually well tolerated, but may cause mild GI disturbances. Rarely, hypersensitivity reactions.

Menthol

Prolonged use of very high doses can lead to symptoms of menthol poisoning, such as rash, wheezing, tightness in the chest, swelling of the mouth, face or throat

4.9 Overdose

Diphenhydramine hydrochloride

The toxicities associated with diphenhydramine are dose dependent. Common signs and symptoms of overdose include confusion, urinary retention, tachycardia, blurry vision, dry mouth, irritability and hallucinations. Diphenhydramine induced QRS widening and QTc prolongation can be seen on electrocardiogram. With ingestion greater than 1g, diphenhydramine may result in delirium, psychosis, seizures, coma, and death. There is an even greater risk of seizures, coma, and death when ingestions are greater than 1.5g of diphenhydramine. Fatal deaths have also been reported with oral doses greater than 20mg/kg.

Menthol

Menthol overdose is rare, except taken at extremely large doses. Orally, the lethal dose of Menthol has been estimated as 50-150mg/kg. Chronic exposure to menthol ingestion has

been reported to be associated with cutaneous, gastrointestinal and neurological manifestations. Renal dysfunction is common probably because of interstitial nephritis. An excessive amount of menthol is also reported to have caused agitation, dizziness, ataxia, hallucination, convulsion and coma.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Antitussive/expectorant

ATC code:

Mechanism of Action/Pharmacodynamics effects

Diphenhydramine hydrochloride

The histamine H1 receptor is located on respiratory smooth muscles. When the H1 receptor is stimulated in the tissues of the respiratory smooth muscles, it causes the stimulation of sensory nerves of airways producing coughing, smooth muscle contraction of bronchi and GIT, and eosinophilic chemotaxis promoting the allergic immune response. Diphenhydramine acts as an inverse agonist at the H1 receptor, thereby reversing the effects of histamine on capillaries, reducing allergic reaction symptoms, including coughing and mucus over secretion in the airways. It has also been demonstrated that diphenhydramine produces an antitussive effect by inhibiting the cough reflex sensitivity in patients with pathological cough.

Sodium citrate

Sodium citrate is a decongestant mucolytic agent which thins and loosens mucus (phlegm), making it easier to cough out.

Menthol

Menthol is a topical agent that acts as a counter-irritant by imparting a cooling effect and by initially stimulating nociceptors and then desensitizing them

5.2 Pharmacokinetics Properties

Diphenhydramine hydrochloride

Oral bioavailability of diphenhydramine is in the range of 40-60%, and peak plasma concentration occurs about 2 to 3 hours after administration. The primary route of metabolism is two successive demethylations of the amine. The resulting primary amine is further oxidized to the carboxylic acid.

The elimination half-life of diphenhydramine has not been fully elucidated but appears to range from between 2.4 to 9.3 hours in healthy adult.

Sodium citrate

Sodium citrate is a weak base. After absorption, it is metabolized to produce bicarbonate, and the generated bicarbonate is neutralized by the hydrogen ions in the blood.

Menthol

Menthol is rapidly absorbed from the small intestine and extracted in the urine predominantly (approximately 65%) as menthol glucuronide.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sucrose, Sodium benzoate, Sorbitol, Sodium carboxyl methyl cellulose, Sweet cherry flavour, Carmosine red

6.2 Incompatibilities

Ex-coff should not be mixed with any other medicinal products, as compatibilities study has not been carried out

6.3 Shelf life

3 years

6.4 Special Precautions for Storage

Ex-coff should be stored in a cool dry place at temperatures not more than 30^{o}C

6.5 Nature and Contents of Container

Plain Amber-coloured Polyethylene terephthalates (PET) bottle with ROPP cap placed inside a paperboard carton

6.6 Special Precautions for disposal

Container and/or any unused product should be disposed in accordance with the local requirement

7. MANUFACTURER

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