SUMMARY PRODUCT CHARACTERISTIC (SPC)

EXPECTORANT

Syrup

1.1 Trade name - Expectorant syrup

1.2 International non-property name – Guaifenesin, Chlorpheniramine maleate, Phenylpropanolamine hydrochloride

2. Qualitative and quantitative composition

This product contains 100mg guaifenesin, 2mg chlorpheniramine maleate, 5mg phenylpropanolamine hydrochloride in each 5ml.
For a full list of excipients, see section 6.1.

3. Pharmaceutical form

A clear, reddish colored, cherry flavored syrup.

4. Clinical Particulars

4.1 Therapeutic indications

The clinical uses of Expectorant are treatment of cough, nasal congestion and cold symptoms.

4.2 Posology and administration

Adults and adolescents of 12 years and above:
The propose therapeutic dose in adults and adolescents is 5 ml of syrup every 6-8 hours. Do not take more than 4 doses a day.
Pediatric population between 6-12 years:
The usual therapeutic dose in pediatric between 6-12 years old is 2.5-5 ml every 6-8 hours.
Do not take more than 4 doses a day.
Method of Administration:
For oral use.

4.3 Contraindications

Hypersensitivity to active substances or to any of the excipients listed in section 6.1.
Unless your doctor approves, do not use these products if you have:

- Heart and circulatory diseases, high blood pressure, insufficient blood flow in the coronary arteries as well as other insufficient blood flow including disorders of the cerebral blood flow with a tendency to dizziness.
- Bronchial asthma, chronic obstructive pulmonary disease (chronic bronchitis, emphysema), pneumonia, respiratory depression, respiratory failure.
- Severe liver dysfunction (Child-Pugh > 9), severe kidney dysfunction, pheochromocytoma.
- Prostate adenoma with residual urine or other bladder emptying disorders
- Patients with stroke,
- Use of MAOIs
- Thyroid disease,
- Diabetes,
- Intolerance with some sugar and fructose,

- Increased intraocular pressure (glaucoma),
- Epilepsy (children and high-risk groups such as patients with liver disease or epilepsy),
- Pregnancy and lactation,
- Children under 6 years of age.

4.4 Special warnings and precautions for use

If you become dizzy or nervous, or have trouble sleeping, stop taking these products and check with your doctor.
You should also check with your doctor immediately if you have a severe sore throat that lasts for more than 2 days, or if your sore throat is accompanied or followed by fever, headache, rash, nausea, or vomiting.
These products may cause drowsiness. Be especially cautious when driving, and when operating machinery. Check with your doctor before using these products if you consume 3 or more alcoholic drinks a day.
This formulation can also cause excitability, especially in children.
Because of its antimuscarinic actions chlorpheniramine should be used with care in conditions such as angle-closure glaucoma, urinary retention, prostatic hyperplasia, or pyloroduodenal obstruction.
Occasional reports of convulsions in patients taking chlorpheniramine also calls for caution in patients with epilepsy.
The dosage reduction may be necessary in renal impairment.
Chlorpheniramine should not be given to neonates owing to its increased susceptibility to antimuscarinic effects. Elderly patients are also more susceptible to many of the adverse effects of chlorpheniramine and, in particular, its inappropriate use for postural giddiness should be avoided.
Phenylpropanolamine should be given with care to patients with hyperthyroidism, diabetes mellitus, renal impairment, or angle-closure glaucoma. In patients with prostatic enlargement, Phenylpropanolamine may increase difficulty with micturition.
Irritability and distributed sleep have been reported in breast-fed infants.
Ponceau 4R (Cocheneal red A) (E124) - may cause allergic reactions.
Ethanol - This medicinal product contains 11.6 vol% ethanol(alcohol), i.e. up to 458,3 mg per dose (5ml), equivalent to 11.6 ml beer, 4.83 ml wine per dose.
Harmful for those suffering from alcoholism. To be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients wih liver disease, or epilepsy.
Sorbitol E420 - Sorbitol is a source of fructose. If your doctor has told you that you (or your child) have an intolerance to some sugars or if you have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your doctor before you (or your child) take or receive this medicine.
Sucrose –If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

Do not use these products within 2 weeks of taking a drug classified as an MAO inhibitor.
If you are taking a tranquilizer, or a sleep aid, do not take this medication without your doctor's approval; the combination could cause extreme drowsiness. For the same reason, avoid alcohol while taking these products.
Chlorpheniramine may enhance the sedative effects of CNS depressants including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives, and antipsychotics.
Chlorpheniramine has an additive antimuscarinic action with other antimuscarinic drugs, such as atropine and some antidepressants (both tricyclics and MAOI).
Chlorpheniramine may suppress the cutaneous histamine response to allergen extracts and should be stopped several days before skin testing.
Chlorpheniramine might have delayed the hepatic metabolism of phenytoin thereby increasing the plasma concentrations.

Phenylpropanolamine may cause a hypertensive crisis in patients receiving and MAOI (including an RIMA). Phenylpropanolamine should be avoided or used with care in patients undergoing anaesthesia with cyclopropane, halothane, or other volatile anaesthetics. An increased risk of arrhythmias may occur if given to patients receiving cardiac glycosides, quinidine, or trycyclic antidepressants, and there is an increased risk of vasoconstrictor or pressor effects in patients receiving ergot alkaloids or oxytocin.

4.6 Fertility, Pregnancy and Lactation

Pregnancy

There are no adequate and well-controlled studies in pregnant women for guaifenesin, chlorpheniramine maleate and phenylpropanolamine HCL.

Lactacy

Guaifenesin is excreted in breast milk in small amounts. There is insufficient information on the effects of guaifenesin, chlorpheniramine maleate and phenylpropanolamine HCL in newborns/infants.

Fertility

There is insufficient information available to determine whether of guaifenesin, chlorpheniramine maleate and phenylpropanolamine HCL has the potential to impair fertility.

4.7 Effects on ability to drive and use machines

These products may cause drowsiness. Be especially cautious when driving, and when operating machinery.

4.8 Undesirable effects

Guaifenesin

Gastrointestinal discomfort, nausea, and vomiting have occasionally been reported with guaifenesin, particularly in very large doses.

Abuse: urinary calculi have been reported in patients consuming large quantities of over-the counter preparations containing guaifenesin.

Porphyria: guaifenesin is considered to be unsafe in patients with porphyria because it has been shown to be porphyrogenic in animals.

Breast-feeding: it is known whether Guaifenesin is distributed into breast milk. However, problems in humans have not been documented.

Chlorfeniramine maleate

The most common side-effect of the sedating antihistamines in CNS depression, with effects varying from slight drowsiness to deep sleep, and including lassitude, dizziness, and in coordination (although paradoxical stimulation may occasionally occur, especially at high doses in children or the elderly). These sedative effects, when they occur, may diminish after a few days of treatment.

Other side effects include headache, psychomotor impairment, and antimuscarinic effects, such as dry mouth, thickened respiratory-tract secretions, blurred vision, urinary difficulty or retention, constipation, and increased gastric reflux.

Occasional gastrointestinal side-effects include nausea, vomiting, diarrhea, or epigastric pain.

Palpitations and arrhythmias have been reported.

Blood disorders, including agranulocytosis, leucopenia, haemolytic anaemia, and thrombocytopenia, although rare, have been reported.

Other adverse effects include convulsions, sweating, myalgia, paraesthesias, extrapyramidal effects, tremor, sleep disturbances, depression, confusion, tinnitus, hypotension, and hair loss.

Exfoliative dermatitis may develop.

Phenylpropanolamine

The commonest adverse effects of Phenylpropanolamine are tachycardia, anxiety, restlessness, and insomnia. Tremor, dry mouth, impaired circulation to the extremities, hypertension, and cardiac arrhythmias may also occur.

Paranoid psychosis, delusions, and hallucinations may also follow Phenylpropanolamine overdosage.
Tolerance to the therapeutic effects of Phenylpropanolamine has been reported with prolonged administration.

Children

Guaifenezine is recommended in children up to 12 years of age with persistent or chronic cough, such as occurs with asthma, or if the cough is accompanied by excessive phlegm (mucus). The condition of these children may need a physician's evaluation before Guaifenesin is administered.
Guaifenesin should not be given to children younger than 2 years of age unless recommended by physician.

Reporting of 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 Arpimed "LLC" by going to www.arpimed.com and fill out the appropriate form ″Report an adverse reaction or inefficiency of drug″. Hotline number: (+374 55) 05 79 86. And by using Scientific Centre of Drug and Medical Technology Expertise after academician E. Gabrielyan ″CJSC″, going to the site: www.pharm.am in ″Report about adverse effect of medicine″ section and fill out the ″Report of adverse reaction or manufacturing problem of medicinal product″. Hotline numbers: +37410200505; +37496220505.

4.9 Overdose

Guaifenesin

Symptoms and signs

The symptoms and signs of overdose may include abdominal pain, nausea and drowsiness.When taken in excess, guaifenesin may cause renal calculi.

Management

Treatment should be symptomatic and supportive.

Chlorpheniramine Maleate

Symptoms and signs

Overdose with sedating antihistamines is associated with antimuscarinic, extrapyramidal, and CNS effects. When CNS stimulation predominates over CNS depression, which is more likely inchildren or the elderly, it causes ataxia, excitement, tremors, psychoses, hallucinations, and convulsions; hyperpyrexia may also occur. Deepening coma and cardiorespiratory collapse may follow. In adults, CNS depression is more common with drowsiness, coma, and convulsions, progressing to respiratory failure and cardiovascular collapse.

Management

Treatment should be symptomatic and supportive.

Phenylpropanolamine HCL

Symptoms and signs

Fast heart rate (tachycardia), irregular heart beat (arrhythmia), high blood pressure,excitation, seizures, enlargement of the pupils, cases of heart attack, stroke, intracranial bleeding/cerebral hemorrhage (bleeding from a ruptured blood vessel in the brain), death, paranoid psychosis, delusions, and hallucinations may also follow Phenylpropanolamine overdose.

Management

Treatment should be symptomatic and supportive.

5.Pharmacological properties

5.1 Pharmacodynamic properties

Guaifenesin is reported to increase the volume and reduce the viscosity of tenacious sputum and is used as an expectorant for productive cough. Guaifenesin is thought to act as an expectorant by increasing the volume and reducing the viscosity of secretions in the trachea and bronchi. Thus, it may increase the efficiency of the cough reflex and facilitate removal of the secretions, however evidence for this is limited and conflicting.

Chlorpheniramine maleate, an alkylamine derivative, is a sedating antihistamine that causes a moderate degree of sedation; it also has antimuscarinic activity. Chlorpheniramine maleate diminishes or abolishes the major actions of histamine in the body by competitive, reversible blockade of histamine H_1-receptor sites on tissues; it does not inactivate histamine or prevent its synthesis, nor, in most cases, its release. Histamine H_1 receptors are responsible for vasodilation, increased capillary permeability, flare and itch reactions in the skin, and to some extent for contraction of smooth muscle in the bronchi and gastrointestinal tract.
Chlorpheniramine is a racemic mixture; the dextrorotatory isomer, dexchlorpheniramine, has approximately twice the activity of Chlorpheniramine by weight.
Phenylpropanolamine HCL is largely indirect-acting sympathomimetic with an action similar to that of ephedrine but less active as a CNS stimulant.

5.2 Pharmacocinetic properties

Guaifenesin is absorbed from the gastrointestinal tract. It is metabolized and then excreted in the urine, as inactive metabolites.
Chlorpheniramine maleate is absorbed relatively slowly from the gastrointestinal tract, peak plasma concentrations occurring about 2.5 to 6 hours after administration by mouth. Bioavailability is low, values of 25 to 50% having been reported. Chlorpheniramine appears to undergo considerable first-pass metabolism. About 70% of Chlorpheniramine in the circulation is bound to plasma proteins. There is wide inter-individual variation in the pharmacokinetics of Chlorpheniramine; values ranging from 2 to 43 hours have been reported for the half-life. Chlorpheniramine is widely distributed in the body, including passage into the CNS.
Chlorpheniramine maleate is extensively metabolized. Metabolites include desmethyl- and didesmethylchlorpheniramine. Unchanged drug and metabolites are excreted primarily in the urine; excretion is dependent on urinary pH and flow rate: Only trace amounts have been found in the feces.
A duration of action of 4 to 6 hours has been reported; this is shorter than may be predicted from pharmacokinetic parameters.
More rapid and extensive absorption, faster clearance, and a shorter half-life have been reported in children.
Phenylpropanolamine HCL is readily and completely absorbed from the gastrointestinal tract, peak plasma concentrations being achieved about 1 to 2 hours after oral administration. It undergoes some metabolism in the liver, to an active hydroxylated metabolite, but up to 80 to 90% of a dose is excreted unchanged in the urine within 24 hours. The half-life has been reported to be about 3 to 5 hours.

5.3 Preclinical safety data

There is insufficient information available to determine whether of guaifenesin, chlorpheniramine maleate and phenylpropanolamine has carcinogenic, mutagenic, teratogenic potential and to impair fertility potential.
Environmental risk assesment
There is insufficient information available to determine whether combination of guaifenesin, chlorpheniramine maleate and phenylpropanolamine has environmental risk assesment.

6. Pharmaceutical particulars

6.1 List of excipients

Sucrose
Sorbitol 70% solution
Sodium citrate
Citric acid
Methylparaben
Propylparaben
Aroma Cherry

Color Ponceau 4R (Cocheneal red A) (E124)
Ethanol 96% solution
Purified water

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years. Shelf life after opening the bottle is 6 months. Do not use after the expiration date.

6.4 Special precautions for storage
Store in dry place at a temperature not higher than 15^0C, out of the reach of children. Protect from light.

6.5 Nature and contents of the primary packaging
15 ml syrup is filled into amber glass bottle with calibrated dropper. The 1 bottle packed and inserted with the leaflet into cardboard box.
60 ml syrup is filled into amber glass bottle. The 1 bottle packed and inserted with the leaflet into cardboard box.
100 ml syrup is filled into amber glass bottle. The 1 bottle packed and inserted with the leaflet into cardboard box.

6.6 Special precautions for disposal and other handling
No special requirements.

7. Manufacturer
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9. Date of first authorisation/renewal of the authorization
27.04.2001

8. Date of revision of the text