

For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

PIRITON EXPECTORANT

1. GENERIC NAME

Chlorpheniramine Maleate, Ammonium Chloride and Sodium Citrate Expectorant

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml (one teaspoonful) contains:

Chlorpheniramine Maleate IP 2.5 mg

Ammonium Chloride IP 125 mg

Sodium Citrate IP 55 mg

Colour: Sunset Yellow FCF in a flavoured syrup base containing Menthol IP.

3. DOSAGE FORM AND STRENGTH

Syrup.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

For symptomatic treatment of cough.

4.2 Posology and Method of Administration

Do not use continuously for more than one week; re-evaluate if use beyond one week is required.

Do not exceed the stated dose or frequency of dosing.

Adults and children over 12 years

8 ml every 6 hour.

Children 6-12 years of age

4 ml every 6 hour.

Children below 6 years of age

Not recommended.

Special Populations

Elderly

8 ml every 6 hour.

Maximum daily dose 24 ml in any 24 hours.

Renal Impairment

Exercise caution in patient with mild to moderate renal impairment (see 4.3 *Contraindications*).

Hepatic Impairment

Exercise caution in patients with mild to moderate hepatic impairment (see 4.3 *Contraindications*).

4.3 Contraindications

Patients with a history of hypersensitivity to chlorpheniramine maleate, antihistamines or to any of the product ingredients.

Patients who have been treated with monoamine oxidase inhibitors (MAOIs) within the previous fourteen days, as the anticholinergic properties of chlorpheniramine are intensified by MAOIs.

In patients with severe hepatic disease (e.g., cirrhosis or hepatitis) because drug retention and subsequent ammonium toxicity or hepatic coma can occur in these patients.

In patients with severe renal impairment (renal failure).

Should not be used in patients with metabolic acidosis or respiratory acidosis because these disease states can be worsened.

In patients when severe metabolic alkalosis due to vomiting of hydrochloric acid is accompanied by a significant loss of sodium (hyponatremia, and excretion of sodium bicarbonate in the urine).

Should not be used in patients with preexisting hyperchloremia.

4.4 Special Warnings and Precautions for Use

Chlorpheniramine, in common with other drugs having anticholinergic effects, should be used with caution in epilepsy, severe hypertension and cardiovascular disease, raised intra-ocular pressure including glaucoma; prostatic hypertrophy; bronchitis, bronchiectasis and bronchial asthma.

The anticholinergic properties of chlorpheniramine may cause drowsiness, dizziness, blurred vision and psychomotor impairment in some patients which may seriously affect ability to drive and use machinery.

Chlorpheniramine may increase the effects of alcohol and therefore concurrent use of *PIRITON EXPECTORANT* should be avoided.

Concurrent use with drugs which cause sedation such as anxiolytics and hypnotics may cause an increase in sedative effects, therefore exercise caution before prescribing *PIRITON EXPECTORANT* concurrently with these medicines.

Children and the elderly are more likely to experience neurological anticholinergic effects and paradoxical excitation (e.g. increased energy, restlessness, nervousness). Avoid use in elderly patients with confusion.

PIRITON EXPECTORANT should not be used with other anti-histamine containing products, including antihistamine containing cough and cold preparations.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

PIRITON EXPECTORANT contains sucrose. This should be taken into account in patients with diabetes mellitus.

Should be used cautiously in patients with cardiac insufficiency or pulmonary edema because of the risk of developing severe acidosis.

Keep out of sight and reach of children.

4.5 Drug Interactions

Concurrent use of chlorpheniramine and hypnotics or anxiolytics may potentiate drowsiness. Concurrent use of alcohol may have a similar effect. (see 4.4 *Special Warnings and Special Precautions for Use*).

Chlorpheniramine inhibits phenytoin metabolism and can lead to phenytoin toxicity.

The anticholinergic effects of chlorpheniramine are intensified by MAOIs (see 4.3 *Contraindications*).

4.6 Use in Special Population

Pregnancy and Lactation

Pregnancy

There are no adequate data from the use of chlorpheniramine maleate in pregnant women. The potential risk for humans is unknown.

There is no good evidence of an association between first trimester exposure to ammonium chloride and foetal abnormalities.

Should not be used during pregnancy unless the benefit to the mother outweighs the potential risk to the foetus.

Lactation

Chlorpheniramine maleate may inhibit lactation and may be secreted in breast milk.

The safety of use of ammonium chloride during lactation has not been established.

Should not be used during lactation unless the benefit to the mother outweighs the potential risk to the new born.

Renal Impairment

Exercise caution in patient with mild to moderate renal impairment (see 4.3 *Contraindications*).

Hepatic Impairment

Exercise caution in patients with mild to moderate hepatic impairment (see 4.3 *Contraindications*).

4.7 Effects on Ability to Drive and Use Machines

The anticholinergic properties of chlorpheniramine may cause drowsiness, dizziness, blurred vision and psychomotor impairment in some patients which may seriously affect ability to drive and use machinery (see 4.4 *Special Warnings and Precautions for Use*).

4.8 Undesirable Effects

The following convention has been utilised for the classification of the frequency of adverse reactions: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1000$) and very rare ($< 1/10,000$), not known (cannot be estimated from available data).

Adverse reactions identified during post-marketing use with chlorphenamine are listed below. As these reactions are reported voluntarily from a population of uncertain size, the frequency of some reactions is unknown but likely to be rare or very rare.

System organ class	Adverse Reaction	Frequency
<i>Nervous system disorders*</i>	Sedation, somnolence	Very common
	Disturbance in attention, abnormal coordination, dizziness, headache	Common
<i>Eye disorders</i>	Blurred vision	Common
<i>Gastrointestinal disorders</i>	Nausea, dry mouth	Common
	Vomiting, abdominal pain, diarrhoea, dyspepsia	Unknown
<i>General disorders and administration site conditions</i>	Fatigue	Common
	Chest tightness	Unknown

<i>Immune system disorders</i>	Anaphylactic reactions, angioedema, allergic reactions	Unknown
<i>Metabolism and nutritional disorders</i>	Anorexia	Unknown
<i>Musculoskeletal and connective tissue disorders</i>	Muscle twitching, muscle weakness	Unknown
<i>Psychiatric disorders*</i>	Confusion, excitation, irritability, nightmares, paradoxical excitation (e.g. increased energy, restlessness, nervousness)	Unknown
<i>Renal and urinary disorders:</i>	Urinary retention	Unknown
<i>Skin and subcutaneous disorders</i>	Exfoliative dermatitis, rash, urticaria, photosensitivity	Unknown
<i>Respiratory, thoracic and mediastinal disorders</i>	Thickening of bronchial secretions	Unknown
<i>Vascular disorders</i>	Hypotension	Unknown

*Children and elderly are more susceptible to neurological anticholinergic effects and paradoxical excitation due to chlorpheniramine maleate.

4.9 Overdose

Symptoms and Signs

Chlorpheniramine maleate: Overdose is likely to result in effects similar to those listed under adverse reactions. Additional symptoms may include, toxic psychosis, convulsions, apnoea, dystonic reactions and cardiovascular collapse including arrhythmias.

Ammonium chloride: Large doses may cause nausea, vomiting, thirst, headache, hyperventilation and progressive drowsiness and lead to profound acidosis and hypokalaemia.

Treatment

Management should be as clinically indicated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action and Pharmacodynamic Effects

Chlorpheniramine maleate is an antihistamine inverse agonist of H₁-receptor. Chlorpheniramine also has anticholinergic activity.

Pharmacodynamic Properties

Chlorpheniramine maleate

Pharmacotherapeutic group: Antihistamines for systemic use; ATC code: R06AB024. Antihistamines act to decrease antigen presentation, mediator release and diminish expression of pro-inflammatory cytokines, cell adhesion molecules and chemotactic factors. The actions of chlorpheniramine include inhibition of histamine on smooth muscle, capillary permeability and hence reduction of oedema and wheal in hypersensitivity reactions such as allergy.

Duration of action of 3 to 6 hours has been reported with significant intersubject variation in reported duration of action.

Ammonium chloride

Ammonium chloride has an irritant effect on mucous membranes and is considered to have expectorant properties.

Sodium Citrate

Sodium citrate is considered to increase bronchial secretion by salt action.

5.2 Pharmacokinetic Properties

Chlorpheniramine maleate

Absorption

The peak plasma concentrations occur from about 2.5 to 6 hours after administration. The bioavailability is low: values of 25 to 50% have been reported.

Distribution

Approximately 70% of chlorpheniramine in the circulation is bound to plasma proteins. It is distributed in the body, including the CNS. Extensive uptake by lungs, kidneys, liver, and brain have been shown. Volume of distribution of 7.0 L/kg has been reported after oral dosing.

Metabolism

Chlorpheniramine undergoes considerable first-pass metabolism. Chlorpheniramine is extensively metabolized via demethylation in the liver, forming desmethyl- and didesmethylchlorpheniramine.

Elimination

The half-life varies from 2 to 43 hours. Unchanged drug and metabolites are excreted mainly in urine. Considerable intersubject variation (two- to fivefold differences in urinary metabolite excretion) in chlorpheniramine metabolism is found.

Ammonium Chloride

Ammonium salts are effectively absorbed from the gastrointestinal tract. The ammonium ion is converted into urea in the liver; the anion thus liberated into the bloodstream and extracellular fluid causes a metabolic acidosis and decreases the pH of the urine, this is followed by a transient diuresis.

6. NONCLINICAL PROPERTIES

Preclinical safety data on chlorpheniramine maleate have not revealed findings which are of relevance to the recommended dosage and use of the product.

No relevant data available for the other ingredients.

7. DESCRIPTION

Each 5 ml (one teaspoonful) contains:

Chlorpheniramine Maleate IP 2.5 mg

Ammonium Chloride IP 125 mg

Sodium Citrate IP 55 mg

Colour: Sunset Yellow FCF in a flavoured syrup base containing Menthol IP.

8. PHARMACEUTICAL PARTICULARS

List of Excipients

Sucrose, Sodium Benzoate, Sodium Saccharin, Citric Acid Monohydrate, Propylene Glycol, Menthol, Vanillin, Colour Sunset Yellow FCF, Flavour Ginger Beer RS -77777.

8.1 Incompatibilities

There are no relevant data available.

8.2 Shelf Life

The expiry date is indicated on the label and packaging.

8.3 Packaging Information

Amber glass bottle.

8.4 Storage and Handling Information

Store in a well-closed container at a temperature not exceeding 30°C protected from direct sunlight.

Keep out of reach of children.

It is dangerous to take this preparation except under medical supervision.

There are no other special requirements for use and handling of this product.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients and/or their patients' parents about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contra-indications of *PIRITON EXPECTORANT*. Patients and/or patients' parents may also be informed about posology, method of administration and storage/handling information as applicable.

10. DETAILS OF MANUFACTURER

The Manufacturing Site details are mentioned on the label and packaging.

For further information please contact:

GlaxoSmithKline Pharmaceuticals Limited.

Registered Office

Dr. Annie Besant Road, Worli,
Mumbai 400 030, India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Manufacturing License number is indicated on the label and packaging.

12. DATE OF REVISION

26-May-2020

Trade marks are owned by or licensed to the GSK group of companies

Version: *PIREX/PI/IN/2020/01*

Adapted from:

- *Chlorpheniramine Maleate GDS (Cx) version 03 dated 19 February 2019.*
- *Bronchial Cough Mixture SPC updated on eMC 29 Jun 2010, date of revision of the text April 2010.*
- *Numark Chesty Cough Expectorant SPC on MHRA site dated 30 December 2019.*
- *Clinical Pharmacology (Ammonium Chloride Monograph) accessed on 26-April-2019 from:*

<https://www.clinicalkey.com/pharmacology/monograph/print?cpnum=28&type=0&printSections=monindi&printSections=mondesc&printSections=monadmi&printSections=monadve&printSections=moncontr&printSections=monmech&printSections=monphar&printSections=monpreg&printSections=moninte&printSections=monmp>

7