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

PIRITON CS

1. GENERIC NAME

Chlorpheniramine Maleate with Dextromethorphan Hydrobromide Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml (one teaspoonful) contains:

Chlorpheniramine Maleate IP 4 mg
Dextromethorphan Hydrobromide IP 10 mg
in a flavoured syrup base containing Menthol IP
Colour: Carmoisine

List of Excipients

Sucrose, Sodium Benzoate, Sodium Chloride, Citric Acid Monohydrate, Sodium Citrate, Saccharin Sodium, Glycerin, Sorbitol Solution (70%), Propylene Glycol, Colour Carmoisine, Flavour Strawberry, Flavour Raspberry, Flavour peppermint, Menthol, Purified Water.

3. DOSAGE FORM AND STRENGTH

Syrup

For information on strength(s) refer *2. Qualitative and Quantitative Composition* above.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

PIRITON CS is indicated for the temporary relief of cough due to throat irritation, sneezing and running nose.

4.2 Posology and Method of Administration

Oral administration only.
Do not exceed the stated dose or frequency of dosing.
The minimum interval between the doses should be 4 hours.

Adults and Children aged 12 years and over

5 ml every 4 hours

Maximum daily dose 30 ml in any 24 hours.

Children (6-12 years)

2.5 ml every 4 hours

Maximum daily dose 15 ml in any 24 hours.

PIRITON CS should not be used in children aged less than 6 years.

Special Populations

Elderly

The elderly are more likely to experience neurological anticholinergic effects of chlorpheniramine maleate. Consideration should be given to using a lower daily dose.

2.5 ml every 4 hours.

Maximum daily dose is 15 ml in any 24 hours.

Hepatic or Renal Impairment

Information on the use of *PIRITON CS* in patients with impaired liver or renal function is limited. *PIRITON CS* should be used with caution in those patients, particularly in patients with severe impairments. Patients with severe renal or liver insufficiency should have their doses lowered or intervals between doses increased.

4.3 Contraindications

PIRITON CS is contraindicated in patients who are:

- hypersensitive to antihistamines or dextromethorphan or to any of the inactive ingredients in the formulation (see *List of Excipients, 4.8 Undesirable Effects*).
- taking monoamine oxidase inhibitors (MAOIs) or in patients who have taken MAOIs in the previous two weeks.

PIRITON CS is also contraindicated in the following cases:

- bronchial asthma
- chronic obstructive pulmonary disease
- pneumonia
- respiratory insufficiency
- respiratory depression
- breastfeeding

4.4 Special Warnings and Precautions for Use

PIRITON CS contains chlorphenamine, and hence should be used with caution in epilepsy; raised intra-ocular pressure including glaucoma; prostatic hypertrophy; severe hypertension or cardiovascular disease; hepatic impairment; renal impairment. Children and the elderly are more likely to experience the neurological anticholinergic effects and paradoxical excitation (e.g. increased energy, restlessness, nervousness). Avoid use in elderly patients with confusion.

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

Piriton CS should not be used with other antihistamine containing products, including antihistamine containing cough and cold medicines.

Concurrent use of *PIRITON CS* with drugs which cause sedation such as anxiolytics and hypnotics may cause an increase in sedative effects, therefore medical advice should be sought before taking chlorphenamine concurrently with these medicines.

Avoid drinking alcoholic beverages while using *PIRITON CS*. The effects of alcohol may be increased and therefore concurrent use should be avoided.

PIRITON CS should not be used for chronic persistent cough accompanying a disease state, or for cough associated with excessive secretions.

In cases of productive cough with considerable mucus production (e.g., patients with conditions such as bronchiectasis, cystic fibrosis) or in patients with neurological illness associated with a markedly reduced cough reflex (such as stroke, Parkinson's disease and dementia) antitussive treatment should be administered with particular caution and only after careful benefit-risk assessment (refer to *4.5 Drug Interactions*).

PIRITON CS contains dextromethorphan which should not be given to patients with or at risk of developing respiratory failure, e.g. asthma, chronic obstructive airways disease, and pneumonia. Caution is needed in patients with a history of asthma and it should not be given during an acute attack.

Dextromethorphan is metabolised by cytochrome P450 2D6 (CYP2D6). Serotonergic effects, including the development of a potentially life-threatening serotonin syndrome, have been reported for dextromethorphan with concomitant administration of serotonergic agents, such as selective serotonin re-uptake inhibitors (SSRIs), drugs which impair metabolism of serotonin (including monoamine oxidase inhibitors (MAOIs)) and CYP2D6 inhibitors that may exaggerate or prolong the effects of dextromethorphan (see *4.5 Drug Interactions*).

Serotonin syndrome may include mental-status changes (e.g. agitation, excitement, confusion), autonomic instability (e.g. diaphoresis, fever, tachycardia, tachypnea, mydriasis), neuromuscular abnormalities (e.g. tremor, clonus, myoclonus, hyperreflexia, and pyramidal rigidity), and/or gastrointestinal symptoms. Thus, Piriton CS should not be used with MAOIs (see *4.3 Contraindications*) and be used with caution in patients receiving other serotonergic drugs (see *4.5 Drug Interactions*)

If serotonin syndrome is suspected, treatment with should be discontinued.
The activity of this enzyme is genetically determined. About 10% of the general population are poor CYP2D6 metabolisers. Poor metabolisers and patients with concomitant use of CYP2D6 inhibitors may experience exaggerated and/or prolonged effects of dextromethorphan. Caution should therefore be exercised in patients who are slow metabolizers of CYP2D6 or use CYP2D6 inhibitors (refer to *4.5 Drug Interactions*).

Due to potential histamine release *PIRITON CS* should be avoided in patients with the rare disease of mastocytosis. Dextromethorphan can activate mast cells resulting in possible histamine release with associated clinical manifestations.

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

PIRITON CS contains sucrose. This should be taken into account in patients with diabetes mellitus.
Long term use increases the risk of dental caries and it is essential that adequate dental hygiene is maintained.

Keep out of the reach and sight of children.

4.5 Drug Interactions

Chlorpheniramine Maleate

Concurrent use of chlorpheniramine and hypnotics or anxiolytics may cause an increase in sedative effects. Concurrent use of alcohol may have a similar effect.

Chlorpheniramine inhibits phenytoin metabolism and can lead to phenytoin toxicity.

The anticholinergic effects of chlorpheniramine are intensified by MAOIs.

Dextromethorphan

Dextromethorphan possesses weak serotonergic properties. Thereby dextromethorphan may increase the risk of serotonin toxicity (serotonin syndrome) particularly if taken with other serotonergic agents, such as MAOIs, SSRIs and CYP2D6 inhibitors. Especially pre-treatment or concomitant treatment with drugs that impair metabolism of serotonin, such as antidepressants of the MAO inhibitor type, may result in the development of a serotonin syndrome.

Dextromethorphan should not be used in patients taking monoamine oxidase inhibitors (MAOIs) or who have taken MAOIs within the previous 14 days. The use of dextromethorphan with, or within two weeks of taking MAOIs, may increase the risk of serious side effects such as hypertensive crisis, hyperpyrexia and convulsions.

Dextromethorphan when used with SSRI's (such as fluoxetine) or tricyclic antidepressants (such as clomipramine and imipramine) may result in a "serotonin syndrome" with changes in mental status (e.g agitation, excitement, confusion), hypertension, restlessness, myoclonus, hyperreflexia, diaphoresis, shivering and tremor.

Dextromethorphan is metabolized by CYP2D6 and has an extensive first-pass metabolism. Concomitant use of potent CYP2D6 enzyme inhibitors can increase the dextromethorphan concentrations in the body to levels multifold higher than normal. This increases the patient's risk for toxic effects of dextromethorphan (agitation, confusion, tremor, insomnia, diarrhoea and respiratory depression) and development of serotonin syndrome. Potent CYP2D6 enzyme inhibitors include fluoxetine, paroxetine, quinidine and terbinafine. In concomitant use with quinidine, plasma concentrations of dextromethorphan have increased up to 20-fold, which has

increased the CNS adverse effects of the agent. Amiodarone, flecainide and propafenone, sertraline, bupropion, methadone, cinacalcet, haloperidol, perphenazine and thioridazine also have similar effects on the metabolism of dextromethorphan. If concomitant use of CYP2D6 inhibitors and dextromethorphan is necessary, the patient should be monitored and the dextromethorphan dose may need to be reduced. The above cited effects may occur if any of these medicines have been administered recently, even if they are no longer being taken.

Concomitant use of dextromethorphan and other CNS depressants (e.g. alcohol, narcotic analgesics and tranquillizers) may increase the CNS depressant effects of these drugs.
If dextromethorphan is used in combination with secretolytics in patients with pre-existing chest disease such as cystic fibrosis and bronchiectasis who are affected by mucus hypersecretion reduced cough reflex can lead to serious accumulation of mucus.

4.6 Use in Special Populations

Fertility

Based on available non-clinical experience and observations in humans there are no reported harmful effects of the use of dextromethorphan on reproduction or foetal development.

No data available for chlorpheniramine.

Pregnancy

The potential risk for humans is unknown. Use during the third trimester may result in reactions in the newborn or premature neonates.

PIRITON CS should not be used during pregnancy unless considered essential by a physician.

Lactation

Chlorpheniramine maleate may inhibit lactation and may be secreted in breast milk.
The extent of excretion in breast milk is not known; therefore, the use of *PIRITON CS* is contraindicated during lactation since a respiratory depressive effect on infants cannot be ruled out.

4.7 Effects on Ability to Drive and Use Machines

PIRITON CS may cause drowsiness, dizziness, blurred vision and psychomotor impairment, which can seriously hamper the patients' ability to drive and use machinery.

Even when used as recommended this medication may cause mild drowsiness and alter reaction times to the extent that the ability to drive or to operate machinery is impaired. The risk is increased when it is taken in combination with alcohol or with medications that can impair reaction times.
Refer to *4.4 Special Warnings and Precautions for Use* and *4.5 Drug Interactions*.

4.8 Undesirable Effects
In absence of availability of adverse event data on the fixed dose combination of dextromethorphan and chlorpheniramine, adverse event data of the individual ingredients is presented below.

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

Chlorpheniramine Maleate

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**
Nervous system disorders*	Sedation, somnolence	Very common
	Disturbance in attention, abnormal coordination, dizziness, headache	Common
Eye disorders	Blurred vision	Common
Gastrointestinal disorders	Nausea, dry mouth	Common
	Vomiting, abdominal pain, diarrhoea, dyspepsia	Unknown
General disorders and administration site conditions	Fatigue	Common
	Chest tightness	Unknown
Immune system disorders	Allergic reactions, angioedema, anaphylactic reactions	Unknown
Metabolism and nutritional disorders	Anorexia	Unknown
Blood and lymphatic system disorders	Haemolytic anaemia, blood dyscrasias	Unknown
Musculoskeletal and connective tissue disorders	Muscle twitching, muscle weakness	Unknown
Psychiatric disorders	Confusion*,	Common
	Excitation*, irritability*, nightmares*, depression	Unknown
Renal and urinary disorders:	Urinary retention	Unknown
Skin and subcutaneous disorders	Exfoliative dermatitis, rash, urticaria, photosensitivity	Unknown
Respiratory, thoracic and mediastinal disorders	Thickening of bronchial secretions	Unknown
Vascular disorders	Hypotension	Unknown
Hepatobiliary disorders	Hepatitis, including jaundice	Unknown
Ear and labyrinth disorders	Tinnitus	Unknown
Cardiac disorders	Palpitations, tachycardia, arrythmias	Unknown
General Disorders and administration site conditions	Fatigue	Common
	Chest tightness	Unknown

*Children and the elderly are more susceptible to neurological anticholinergic effects and paradoxical excitation (eg increased energy, restlessness, nervousness).

Dextromethorphan

System organ class	Adverse Reaction	Frequency
Psychiatric disorders	Confusion	Common
	Drug dependence	Very rare
	Hallucinations	Unknown
Nervous system disorders	Somnolence, dizziness	Very common
	Vertigo, slurred speech and nystagmus, dystonia especially in children	Unknown
Skin and subcutaneous tissue disorders	Skin reactions such as rash with pruritis	Unknown
Immune system disorders	Hypersensitivity, urticaria, fixed drug eruption, anaphylactic reaction, angioedema, bronchospasm	Unknown
Gastro-intestinal disorders	Gastrointestinal disorders (nausea, vomiting, constipation)	Common
General disorders and administration site conditions	Fatigue	Common

4.9 Overdose

Symptoms and Signs

The estimated lethal dose of chlorphenamine is 25 to 50mg/kg body weight. Symptoms and signs include sedation, paradoxical excitation of the CNS, toxic psychosis, convulsions, apnoea, anticholinergic effects, dystonic reactions and cardiovascular collapse including arrhythmias.

In case of overdose known side effects may occur with higher frequency or severity. Dextromethorphan overdose may be associated with nausea, vomiting, dizziness, fatigue, dystonia, agitation, confusion, somnolence, stupor, nystagmus, cardiotoxicity (tachycardia, abnormal ECG including QTc prolongation), ataxia, toxic psychosis with visual hallucinations, hyperexcitability.

In the event of massive overdose, the following symptoms may be observed: coma, respiratory depression, convulsions.
Restlessness and excitability may develop into agitation with increasing overdose. In addition, symptoms such as psychotic disorders like disorientation and delusions up to confusional or paranoid states, changes in blood pressure, impaired concentration and consciousness up to coma as a sign of severe intoxication, slurred speech, changes in mood such as dysphoria and euphoria, dysarthria, increased muscle tone, vision disturbance, convulsions, as well as respiratory depression, and light-headedness may occur.
Dextromethorphan may increase the risk of serotonin syndrome, and this risk is increased by overdose, particularly if taken with other serotonergic agents.
Cases of fatal outcomes have been reported with combination overdose with dextromethorphan and other drugs (combination poisoning).

Treatment

Management should be as clinically indicated or as recommended by the national poisons centres where available. Symptomatic and supportive measures should be provided with special attention to cardiac, respiratory, renal and hepatic functions and fluid and electrolyte balance. If overdosage is by the oral route, treatment with activated charcoal should be considered provided there are no contraindications for use and the overdose has been taken recently (treatment is most effective if given within an hour of ingestion). Treat hypotension and arrhythmias vigorously. CNS convulsions may be treated with i.v. diazepam. Haemoperfusion may be used in severe cases.

The mainstay of treatment is supportive and symptomatic care. If necessary close intensive care monitoring with symptom-related treatment should be initiated.
Activated charcoal can be administered to asymptomatic patients who have ingested overdoses of dextromethorphan within the preceding hour.
For patients who have ingested dextromethorphan and are sedated or comatose, Naloxone, in the usual doses for treatment of opioid overdose can be considered. Benzodiazepines for seizures and benzodiazepines and external cooling measures for hyperthermia from serotonin syndrome can be used.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action/Pharmacodynamic Properties

Chlorpheniramine Maleate

Chlorphenamine is a potent antihistamine (H1-antagonist).

Antihistamines diminish or abolish the actions of histamine in the body by competitive reversible blockade of histamine H1-receptor sites on tissues. Chlorphenamine also has anticholinergic activity.

Antihistamines act to prevent the release of histamine, prostaglandins and leukotrienes and have been shown to prevent the migration of inflammatory mediators. The actions of chlorphenamine include inhibition of histamine on smooth muscle, capillary permeability and hence reduction of oedema and wheal in hypersensitivity reactions such as allergy and anaphylaxis.

Dextromethorphan

Dextromethorphan is a non-opioid cough suppressant. It is the methylated dextrorotatory analogue of levorphanol, a codeine analogue. Dextromethorphan acts centrally on the cough centre in the medulla and nucleus tractus solaris to increase the cough threshold. It does not have classical analgesic, sedative or respiratory depressant effects at usual antitussive doses.
The onset of antitussive effect occurs within an hour and the duration of action is approximately 3 – 6 hours.

5.2 Pharmacokinetic Properties

Chlorpheniramine Maleate

Chlorphenamine is well absorbed from the gastro-intestinal tract, following oral administration. The effects develop within 30 minutes, are maximal within I to 2 hours and last 4 to 6 hours. The plasma half-life has been estimated to be 12 to 15 hours.
Chlorphenamine is metabolised to the monodesmethyl and didesmethyl derivatives. About 22% of an oral dose is excreted unchanged in the urine.

Dextromethorphan

Dextromethorphan is well absorbed from the gastrointestinal tract after oral administration.
It is metabolised in the liver, exhibiting polymorphic metabolism involving the cytochrome P450 isoenzyme (CYP 2D6).
It is excreted in the urine as unchanged dextromethorphan and demethylated metabolites, including dextrorphan, which has some cough suppressant activity. The plasma elimination half-life of dextromethorphan is 1.2 to 3.9 hours. However, the rate of metabolism varies between individuals according to phenotype (extensive v poor metabolisers), with half-life being as long as 45 hours in patients who are poor metabolisers.

6. NONCLINICAL PROPERTIES

6.1 Animal Toxicology and Pharmacology

No information available.

7. DESCRIPTION

Syrup

Each 5 ml (one teaspoonful) contains:

Chlorpheniramine Maleate IP	4 mg
Dextromethorphan Hydrobromide IP	10 mg

in a flavoured syrup base containing Menthol IP
Colour: Carmoisine

List of Excipients

Sucrose, Sodium Benzoate, Sodium Chloride, Citric Acid Monohydrate, Sodium Citrate, Saccharin Sodium, Glycerin, Sorbitol Solution (70%), Propylene Glycol, Colour Carmoisine, Flavour Strawberry, Flavour Raspberry, Flavour peppermint, Menthol, Purified Water.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

No incompatibilities have been identified

8.2 Shelf Life

The expiry date is indicated on the label and packaging.

8.3 Packaging Information

Bottle with a measure cup.

8.4 Storage and Handling Information

Store in a well closed container at temperature not exceeding 30ºC, protected from direct sunlight.

Keep out of reach of children.

For oral use only.

It is dangerous to take this preparation except under medical supervision

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or patients' caregiver as applicable) about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contra-indications of *PIRITON CS*. Patients (and/or patients' caregiver) 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

21-Oct-2025

Version No: PIRCS/PI/IN/2025/01.

Adapted from:

1. *Piriton Syrup SmPC (last updated on emc: 17 Apr 2023). Available from: https://www.medicines.org.uk/emc/product/3928)*
2. *Bisolvon Dry New Zealand Data Sheet (date of revision of text: 25 July 2025). Available from: https://www.medsafe.govt.nz/profs/datasheet/b/bisolvondryoralsolution.pdf*
3. *Clinical Pharmacology – Chlorpheniramine monograph. Available from: https://www.clinicalkey.com/pharmacology/monograph/119.*
4. *Clinical Pharmacology - Dextromethorphan Monograph. Available from: https://www.clinicalkey.com/pharmacology/monograph/179.*