Not to be sold by retail without the prescription of a Registered Medical Practitioner

Prescribing Information

1. Generic Name

Phenylephrine Hydrochloride and Chlorpheniramine Maleate Drops IP
(Brand Name: KOLQ ® - AF Oral Drops)

2. Qualitative and Quantitative Composition

Each ml (approx. 20 drops) contains:
Phenylephrine Hydrochloride IP ……..…..... 5 mg.
Chlorpheniramine Maleate IP …….. 2 mg.
Flavoured syrupy base ……...…….…..…… q.s.

3. Dosage Form and Strength

Dosage Form: Oral liquid.
Dosage Strength: Phenylephrine hydrochloride 5 mg with chlorpheniramine maleate 2 mg per ml.

4. Clinical Particulars

4.1 Therapeutic Indication

KOLQ-AF Oral Drops are indicated for the symptomatic treatment of common cold and allergic rhinitis in children.

4.2 Posology and Method of Administration

For oral administration in pediatric patients. Shake well before use.

- **Children Between 4 to 6 years:** 0.5 ml to be administered every 4 to 6 hours daily
- **Children > 6 to 12 years**: 1 ml to be administered every 4 to 6 hours daily

Or, as prescribed by the physician.

KOLQ-AF Drops should not be used in children below 4 years of age.

4.3 Contraindications

KOLQ-AF Oral Drops are contraindicated in the following:

- Known hypersensitivity to phenylephrine hydrochloride or to chlorpheniramine maleate or to any component of the formulation.
- In patients who have been treated with monoamine oxidase (MAO) inhibitors within the last 14 days.
- In patients who are currently receiving other sympathomimetic drugs.
- Cardiovascular disorders.
- In patients with peripheral vascular insufficiency.

- In patients with hyperthyroidism.
- In patients with glaucoma.
- In patients with prostate problems (including hypertrophy).
- Pheochromocytoma.

4.4 Special Warnings and Precautions for Use

Phenylephrine Hydrochloride

Sympathomimetic amines should be used with caution in patients with hypertension, diabetes mellitus, heart disease (angina), peripheral vascular disease, increased intraocular pressure, hyperthyroidism, or prostatic hypertrophy.

Phenylephrine should not be used with other sympathomimetics (such as decongestants, appetite suppressants, and amphetamine-like psychostimulants).

Sympathomimetics may act as cerebral stimulants giving rise to insomnia, nervousness, hyperpyrexia, tremor, and epileptiform convulsions.

Chlorpheniramine Maleate

Chlorpheniramine maleate may cause drowsiness and may have additive central nervous system (CNS) effects with alcohol or other CNS depressants (e.g., hypnotics, sedatives, tranquilizers).

Antihistamines should be used with caution in patients with peptic ulcer, pyloroduodenal obstruction, and urinary bladder obstruction due to symptomatic prostatic hypertrophy and narrowing of the bladder neck.

Chlorpheniramine maleate, in common with other drugs having anticholinergic effects, should be used with caution in the following conditions: Epilepsy; raised intra-ocular pressure including glaucoma; severe hypertension or cardiovascular disease; bronchitis, bronchiectasis or asthma; hepatic impairment. Children and the elderly are more likely to experience the neurological anticholinergic effects and paradoxical excitation (e.g., increased energy, restlessness, nervousness).

Chlorpheniramine maleate should not be used with other antihistamine-containing products.

4.5 Drug Interactions

Phenylephrine Hydrochloride

MAO Inhibitors: Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and MAO inhibitors, thus concomitant use is contraindicated.

Sympathomimetic Amines: Concomitant use of phenylephrine with other sympathomimetic amines can increase the risk of cardiovascular side effects.

Beta-Blockers and Other Antihypertensives (Including Debrisoquine, Guanethidine, Reserpine, and Methyldopa): Phenylephrine may reduce the efficacy of beta-blocking drugs and antihypertensive drugs. The risk of hypertension and other cardiovascular side effects may be increased.

Tricyclic Antidepressants (Amitriptyline): Concomitant use of phenylephrine with amitriptyline may increase the risk of cardiovascular side effects.
Ergot Alkaloids (Ergotamine and Methylsergide): Concomitant use of phenylephrine with these drugs increases risk of ergotism.
Digoxin and Cardiac Glycosides: Co-administration of phenylephrine with these drugs increases risk of irregular heartbeat or heart attack.

Chlorpheniramine Maleate
Alcohol, Hypnotics, Anxiolytics, Sedatives, Opioid Analgesics, and Neuroleptics: Concurrent use of chlorpheniramine maleate with any of these drugs may enhance the sedative effect.
Phenytoin: Chlorpheniramine maleate inhibits phenytoin metabolism and can lead to phenytoin toxicity.
MAO Inhibitors and Tricyclic Antidepressants: The antimuscarinic effects of chlorpheniramine maleate are enhanced by other antimuscarinic drugs and both antimuscarinic and sedative effects are enhanced by MAO inhibitors (concurrent therapy is contraindicated) and tricyclic antidepressants.

4.6 Use in Special Populations
Pregnant Women
The safety of this formulation during pregnancy has not been established. There is a possible association of fetal abnormalities with first trimester exposure to phenylephrine. In addition, there is a potential for increased uterine contractility and vasoconstriction, with the possibility of fetal hypoxia. Phenylephrine may also reduce placental perfusion and thus, should not be used in patients with a history of pre-eclampsia. Use of chlorpheniramine maleate during the third trimester of pregnancy may result in reactions in the newborn or premature neonates, thus, its use is not recommended. KOLQ-AF Oral Drops should be avoided during pregnancy.

Lactating Women
Phenylephrine is excreted in breast milk, but not in a clinically significant amount. Chlorpheniramine maleate may inhibit lactation and may be secreted in breast milk. Because of higher risk of intolerance of antihistamines in small infants (newborns and premature), KOLQ-AF Oral Drops should not be administered to a nursing mother. Accordingly, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Patients
KOLQ-AF Oral Drops should not be used in children below 4 years of age. For use in children above 4 years, please refer ‘Posology and Method of Administration’ section.

Geriatric Patients

Elderly patients with normal renal and hepatic function should be given the same dose as recommended for adults. The risk of toxic reactions with this formulation may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

4.7 Effect on Ability to Drive and Use Machines

Phenylephrine has no adverse effects on the patient's ability to drive and use machines. The anticholinergic properties of chlorpheniramine may cause drowsiness, dizziness, blurred vision, and psychomotor impairment, which can seriously hamper the patients' ability to drive and use machinery. Patients should be advised not to drive or operate machinery if affected by dizziness.

4.8 Undesirable Effects

Phenylephrine Hydrochloride

Phenylephrine may elevate blood pressure with headache, vomiting and rarely palpitations, tachycardia or reflex bradycardia, tingling and coolness of the skin. There have been rare reports of allergic reactions.

Chlorpheniramine Maleate

Central Nervous System (CNS): Sedation (varying from slight drowsiness to deep sleep), headaches, inability to concentrate, lassitude, dizziness, twitching, muscular weakness and inco-ordination, tinnitus, depression, irritability and nightmares may occur infrequently. Paradoxical excitation in children and confusional psychosis in the elderly can occur. The effects of alcohol may be increased.

Gastrointestinal: Nausea, vomiting, diarrhea, abdominal pain, dyspepsia, anorexia.

Anticholinergic: Urinary retention, dryness of mouth, blurred vision.

Cardiovascular: Tachycardia, arrhythmias, hypotension, tightness in chest.

Hepatic: Jaundice.

Hematological: Haemolytic anaemia; other blood dyscrasias.

Allergic Reactions: Urticaria, exfoliative dermatitis, photosensitivity reactions.

4.9 Overdose

Phenylephrine Hydrochloride

Symptoms: Overdose symptoms may include hypertension and possibly reflex bradycardia. In severe cases confusion, hallucinations, seizures, and arrhythmias may occur.

Treatment: Treatment measures include early gastric lavage and symptomatic and supportive measures. The hypertensive effects may be treated with an α-receptor blocking agent (such as phentolamine mesylate, 6 to 10 mg) given intravenously, and the bradycardia treated with atropine, preferably only after the pressure has been controlled.

Chlorpheniramine Maleate

Symptoms: The estimated lethal dose of chlorpheniramine maleate is 25 to 50 mg/kg body weight. Overdose with chlorpheniramine maleate is associated with antimuscarinic, extrapyramidal, gastrointestinal, and CNS effects. In children, CNS stimulation predominates over CNS depression, causing ataxia, excitement, tremors, psychosis, hallucinations, and convulsions. Hyperpyrexia may also occur. Other symptoms of overdose in children include dilated pupils, dry mouth, facial flushing. In adults, CNS depression is more common with drowsiness, coma and convulsions, progressing to respiratory failure or possibly cardiovascular collapse including arrhythmias.

Treatment: In severe overdose the stomach should be emptied. If overdose is by the oral route, treatment with activated charcoal should be considered (treatment is most effective if given within an hour of ingestion). Convulsions may be controlled with intravenous diazepam or phenytoin, although it has been suggested that CNS depressants should be avoided. Other treatment is supportive and symptomatic and may include artificial respiration, external cooling for hyperpyrexia, and intravenous fluids. Vasopressors such as noradrenaline or phenylephrine may be used to counteract hypotension. Forced diuresis, peritoneal dialysis or haemodialysis appear to be of limited benefit. Haemoperfusion may be used in severe cases.

5. Pharmacological Properties

5.1 Mechanism of Action

Phenylephrine Hydrochloride - Sympathomimetic Nasal Decongestant.

Phenylephrine is a nasal decongestant with a potent postsynaptic α-receptor agonist activity. Dilated blood vessels can cause nasal blocks or stuffy nose. Phenylephrine shrinks blood vessels in the nasal passages and thus, reduces nasal congestion. A direct action at the receptors accounts for the greater part of its effects, whereas only a small part of effect is due to its ability to release norepinephrine.

Sympathomimetic amines, such as phenylephrine, act on α-adrenergic receptors of the respiratory tract to produce vasoconstriction effect. This result in temporarily reduction of swelling associated with inflammation of the mucous membranes lining the nasal and sinus passages. This allows the free drainage of the sinusoidal fluid from the sinuses. In addition to reducing mucosal lining swelling, phenylephrine also suppresses the production of mucous, therefore preventing a buildup of fluid within the nasal cavities.

Chlorpheniramine Maleate – Antihistamine.

Chlorpheniramine maleate is H_1 receptor antagonist (antihistamine effect). Chlorpheniramine maleate diminishes or abolishes the actions of histamine in the body by competitive (reversible) blockade of histamine H_1 receptor sites on tissues. Chlorpheniramine maleate prevents released histamine from dilating capillaries and causing edema of the respiratory mucosa.

5.2 Pharmacodynamic Properties

Phenylephrine Hydrochloride

Phenylephrine is an orally active sympathomimetic amine and exerts a decongestant action on the nasal mucosa.

Chlorpheniramine Maleate

Chlorpheniramine maleate produces antihistamine effect by blocking H_1 receptor. Chlorpheniramine maleate also possesses anticholinergic activity.

5.3 Pharmacokinetic Properties

Phenylephrine Hydrochloride

Absorption: After oral administration, phenylephrine is rapidly absorbed from the intestine and undergoes first-pass metabolism by MAO in the gut and liver. As a consequence, systemic bioavailability of oral route is only about 40%. Following oral administration, peak plasma concentration is achieved in 1 to 2 hours.

Distribution: Distribution in the brain appears to be minimal.

Metabolism and Excretion: Following absorption, the drug is extensively metabolised in the liver as the sulphate conjugate. Both phenylephrine and its metabolites are excreted in the urine. The mean plasma half-life is in the range 2 to 3 hours.

Chlorpheniramine Maleate

Absorption: Chlorpheniramine maleate is almost completely absorbed after oral administration with peak plasma concentrations occurring at about 2.5 to 6 hours. Bioavailability is low with values of 25 to 50% have been reported.

Distribution: Chlorpheniramine is widely distributed in the body, and enters the CNS. About 70% of chlorpheniramine in the circulation is protein-bound.

Metabolism and Excretion: Chlorpheniramine maleate undergoes some first pass metabolism (10%) and enterohepatic recycling. Chlorpheniramine maleate is extensively metabolised, principally to inactive desmethylated metabolites which are excreted primarily in the urine (50%), together with about 35% unchanged drug. Only trace amounts are excreted in the faeces. The mean elimination half-life has been reported to be about 30 hours, with mean values ranging from 2 to 43 hours.

6. Nonclinical Properties

6.1 Animal Toxicology

Phenylephrine Hydrochloride

Toxicity: LD50 values for phenylephrine have been determined in several species by various routes of administration. In Wistar rats, the LD50 value by intraperitoneal injection was 17 mg/kg and by subcutaneous injection was 33 mg/kg. The LD50 values in male Swiss mice were 89 mg/kg

(intraperitoneal) and 22 mg/kg (subcutaneous). New Zealand rabbits had LD50 values of 0.5 mg/kg (intravenous), 7.2 mg/kg (intramuscular), and 22 mg/kg (subcutaneous).
Mutagenicity: Phenylephrine hydrochloride was not mutagenic in four tester strains of *Salmonella typhimurium* (TA100, TA1535, TA1537, and TA98) in the presence or absence of Aroclor 1254-induced male Sprague-Dawley rat or male Syrian hamster liver S9.
Carcinogenicity: In the mouse study, the mean daily dose (males and females) in the low dose animals was 133 mg/kg and in the high dose animals 270 mg/kg. The study demonstrated no evidence of carcinogenicity in rats and mice under the testing conditions employed.

Chlorpheniramine Maleate

Toxicity: LD50 values reported for chlorpheniramine maleate by oral route in rats, mice, and guinea pigs were 118, 121, and 186 mg/kg respectively.
Chlorpheniramine maleate was administered by gavage to groups of 12 female Sprague-Dawley rats for 29 days at doses of 0, 2, 5, 10, or 25 mg/kg body weight and in feed (average daily dose, 1 mg/kg) for three successive generations to male and female Sprague-Dawley rats. No clinical, hematologic, or pathologic alterations were apparent in either study.
No compound-related effects were reported after chlorpheniramine maleate was administered by gavage to groups of 8 male and 8 female rats 5 days per week for 6 weeks at doses of 5 or 10 mg/kg per day. Similar experiments in which two rhesus monkeys were administered 20 mg/kg per day 5 days per week for 7 weeks resulted in no apparent adverse effects.
Mutagenicity: Chlorpheniramine maleate was not mutagenic to *Salmonella typhimurium* strains TA98, TA100, TA1535, or TA1537 in the presence or absence of S9 metabolic activation systems prepared from the livers of Aroclor 1254-treated male Sprague-Dawley rats or male Syrian hamsters.
Carcinogenicity: A 2-year oncogenicity study of chlorpheniramine maleate was conducted in which groups of 50 male and 50 female CD albino rats were fed diets containing SCH 190 (Chlor-trimeton') for 103 weeks. The doses (approximately 2, 10, or 20 mg/kg per day) were formulated based on group mean values for body weight and feed consumption. There were no reported increases in the incidences of neoplastic lesions attributed to dosing with chlorpheniramine maleate.

7. Description

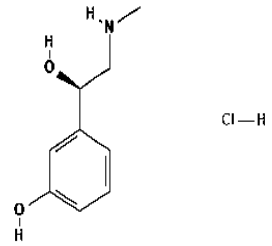
KOLQ-AF Oral Drops is clear colorless liquid with orange flavour.

Each ml of KOLQ-AF Drops contains 5 mg of phenylephrine hydrochloride and 2 mg of chlorpheniramine maleate for oral administration.

Phenylephrine Hydrochloride

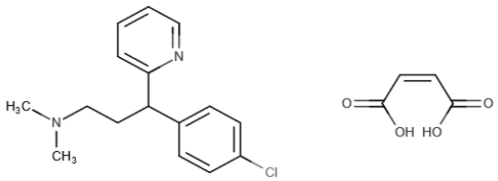
Phenylephrine hydrochloride is an odorless white microcrystalline powder with a bitter taste.
Molecular Weight: 203.66 g/mol.

Molecular Formula: C9H14ClNO2.
Chemical Name: 3-[(1R)-1-hydroxy-2-(methylamino) ethyl]phenol; hydrochloride.
Structural Formula:



Chlorpheniramine Maleate

Chlorpheniramine maleate appears as odorless white crystalline solid or white powder with a bitter taste.
Molecular Weight: 390.9 g/mol.
Molecular Formula: C20H23ClN2O4.
Chemical Name: (2Z)-but-2-enedioic acid; [3-(4-chlorophenyl)-3-(pyridin-2-yl)propyl] dimethylamine
Structural Formula:



Inactive ingredients (excipients) of KOLQ-AF Oral Drops contains Glycerine, Sodium Benzoate, Sucrose, Saccharin Sodium, Sodium Citrate, Citric Acid Monohydrate, Sodium Meta Bisulphite, Ess. Orange Oil Fanta, Propylene Glycol, and Hyflosuper Cell.

8. Pharmaceutical Particulars

8.1 Incompatibilities

None known.

8.2 Shelf-life

18 months.

8.3 Packaging Information

15 ml bottle with dropper.

8.4 Storage and Handling Instructions

Store protected from light and moisture, at a temperature not exceeding 30°C.
Keep out of reach of children

9. Patient Counseling Information

Administration Instructions

- Instruct caregivers to use medication exactly as prescribed by the doctor. Don't exceed the recommended dose or duration of treatment. Shake well before each use.
- Instruct caregivers not to use this product in children below 6 months of age.
- Instruct patients not to use this product during pregnancy and lactation.
- Instruct caregivers not to share this medication for other child even though symptoms are similar. Also, don't use medication prescribed for other children.
- Instruct caregivers not to use this medicine with other cough and cold relief products (prescription or over-the- counter - OTC) without consulting a doctor.

10. Details of Manufacturer

M/s. Akums Drugs and Pharmaceuticals Ltd.,
22, Sector – 6A, I.I.E., SIDCUL, Haridwar – 249 403, Uttarakhand, India.

11. Details of Permission or License Number with Date

DCG(I) NOC Date: 10th April 2017.
Manufacturing License No. 123/UA/2007. Date of Product Permission – 05th December 2016.

12. Date of Revision

December 2023.

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