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

Phenylephrine Hydrochloride and Chlorpheniramine Maleate Drops IP
KOLQ®-AF Oral Drops

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

DOSAGE FORM
Oral liquid.

INDICATIONS
KOLQ-AF Oral Drops are indicated for the symptomatic treatment of common cold and allergic rhinitis in children above 6 months of age.

DOSE AND METHOD OF ADMINISTRATION
For oral administration in paediatric patients. Shake well before use.

- **Children Between 6 Months to <1 Year:** 0.4 ml to be administered up to 4 times daily.
- **Children Between 1 to 2 years**: 0.5 ml to be administered up to 4 times daily.

Or, as prescribed by the physician.

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.

Paediatric Patients
KOLQ-AF Oral Drops are recommended in infants and children above 6 months of age [please refer 'DOSE 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.

CONTRAINDICATIONS
KOLQ-AF Oral Drops are contraindicated in the following:

- Known hypersensitivity to phenylephrine 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.

WARNINGS AND PRECAUTIONS
Phenylephrine
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.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take chlorpheniramine-containing preparations.
Effects on Ability to Drive and Use Machines: The anticholinergic properties of chlorpheniramine maleate 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.

DRUG INTERACTIONS

Phenylephrine

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.

UNDESIRABLE EFFECTS

Phenylephrine

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.

OVERDOSE

Phenylephrine

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.

PHARMACODYNAMICS

Phenylephrine: Sympathomimetic Decongestant

Phenylephrine is an orally active sympathomimetic amine and exerts a decongestant action on the nasal mucosa. Phenylephrine is a nasal decongestant with a potent postsynaptic α-receptor agonist activity. Dilated blood vessels can cause nasal congestion 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. This result in temporary reduction of swelling associated with inflammation of the mucous membranes lining the nasal and sinus passages, and free drainage of fluid from the sinuses. In addition to reducing mucosal lining swelling, phenylephrine also suppresses the production of mucus, therefore preventing a buildup of fluid within the nasal cavities.

Chlorpheniramine Maleate: Antihistamine

Chlorpheniramine maleate is an antihistamine drug (H_1 receptor antagonist) that also possesses anticholinergic activity. Antihistamines diminish or abolish 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.

PHARMACOKINETICS

Phenylephrine

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% having 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.

INCOMPATIBILITIES
None known.

SHELF-LIFE
Expiry date as mentioned on the product pack.

PACKAGING INFORMATION
15 ml bottle with dropper.

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

Last updated: March 2020.