1.3 PRODUCT INFORMATION

1.3.1 Summary of Product Characteristics (SmPC)

Enclosed

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1. Name of the medicinal product: ALKOLD PLUS (Chlorpheniramine Maleate & Phenylephrine HCl Capsule)

2. Qualitative and Quantitative composition:

Sr. No.	Ingredients	Specification	Quantity /Capsule (mg)	Std. Qty /Batch (kg)	% overages	Reason for inclusion
1.	Phenylephrine HCl	BP	2.5	0.25	--	Active
2.	Chlorpheniramine Maleate	BP	4.0	0.40	--	Active
Total weight of filled Pellets			**265 mg**	**26.50 kg**		
3.	Pink/Clear size "2" hard gelatin capsules	IH	1 Nos.	1,00,000 Nos.		Capsule Shell

Where,
BP: British Pharmacopoeia,
IH: In-house

3. Pharmaceutical Form: Capsules for Oral Administration.

4. Clinical Particulars:

4.1 Therapeutic indications

It is indicated for:

- Relief of nasal and sinus congestion.
- Relief of allergic symptoms of the nose or throat due to upper respiratory tract allergies.
- Relief of sinus pain and headache.
- Adjunct with antibacterials in sinusitis, tonsillitis and otitis media.

4.2 Posology and method of administration

Adults: 1 Capsule is s 3 OR 4 daily or as directed by the physician
Not for Children under 12 years

4.3 Contraindications

- Hypersensitivity to any of the ingredients of the formulation.
- Severe hypertension.

Patients sensitive to Paracetamol or to any of the excipients of the product.
Patients in whom aspirin or other NSAIDs, precipitate attacks of bronchospasm, acute rhinitis or urticaria or patients hypersensitive to these drugs.
Patients with active or suspected peptic ulcer or gastrointestinal bleeding or bleeding disorders.
Patients with severe heart failure, hypertension, hepatic or renal insufficiency.
Last trimester of pregnancy.

4.4 Special warnings and precautions for use

Phenylephrine HCL

Special caution should be exercised when phenylephrine is administered to patients suffering from cardiovascular diseases, hyperthyroidism or diabetes.

Care is also advised when simultaneously administering anaesthetics that sensitize the myocardium to sympathicomimetics (e.g. trichloroethylene, cyclopropane, halothane), when simultaneously administrating other sympathicomimetics, in case of asthma and increased risk of cerebral arteriosclerosis.

Chlorphenamine Maleate

Because of chlorphenamine maleate, caution should be taken in case of simultaneous administration of drugs with sedative effects, such as neuroleptics, anxiolytics and hypnotics.

Caution should be exercised with asthma, obstruction of the bladder neck, liver impairment, pyloroduodenal obstruction and peptic ulcer with stenosis.

4.5 Interaction with other medicinal products and other forms of interaction

Chlorpheniramine/ Alcohol/ CNS Depressants/ Tricyclic Antidepressants:
Concurrent use may potentiate the effects of either these medications or antihistamines.

Antihistamines/ Ototoxic Medications:
Symptoms of ototoxicity may be masked if antihistamines are used concurrently with ototoxic medications, particularly aminoglycoside antibiotics such as amikacin, dihydrostreptomycin, gentamicin, kanamycin, neomycin, streptomycin, tobramycin and viomycin.

Drug Interactions Involving Chlorpheniramine Maleate:

Antihistamines/Alcohol/CNS Depressants (including Tricyclic Antidepressants):
Antihistamines may have additive effects when used concurrently with alcohol or other CNS depressants, e.g. hypnotics, sedatives, tranquilizers, antianxiety agents, narcotic analgesics, anticonvulsants, general anesthetics, other antihistamines.

Antihistamines/ Monoamine Oxidase Inhibitors:
Concurrent administration of antihistamines and monoamine oxidase (MAO) inhibitors may prolong and intensify the anticholinergic (drying) effects of antihistamines. Therefore concurrent use of antihistamines with monoamine oxidase (MAO) inhibitor therapy or within 14 days of discontinuation of such therapy is contraindicated.

Antihistamines/ Ototoxic Medications:
Symptoms of ototoxicity may be masked if antihistamines are used concurrently with ototoxic medications, particularly aminoglycoside antibiotics such as amikacin, dihydrostreptomycin, gentamicin, kanamycin, neomycin, streptomycin, tobramycin, and viomycin.

Antihistamines/Anticholinergic Agents or Other Agents Possessing Anticholinergic Activity:
Concurrent use may lead to a potentiation of the anticholinergic effects. Therefore caution should be exercised and patients should be advised to promptly report occurrence of gastrointestinal problems, since paralytic ileus may occur upon concurrent therapy of antihistamines and anticholinergic agents.

Drug Interactions Involving Phenylephrine Hydrochloride:
Phenylephrine/ β-Blockers: β-Blockers increase the effects of sympathomimetics.
Phenylephrine/ α-Blockers: The vasopressor response to phenylephrine is decreased by prior administration of an adrenergic blocking agent.
Phenylephrine/Oxytocic Drugs: When a vasopressor, e.g. phenylephrine, is used in conjunction with oxytocic drugs, the pressor effect is potentiated.
Phenylephrine/Sympathomimetic Agents: Combination products containing phenylephrine and a bronchodilator sympathomimetic agent should not be used concomitantly with epinephrine or other sympathomimetic agents, because tachycardia or other serious arrhythmias may occur.
Phenylephrine/ General Anesthetics: Rarely, administration of phenylephrine to patients who have received cyclopropane or halogenated hydrocarbon general anesthetics that increase cardiac irritability and seem to sensitize the myocardium to phenylephrine may result in arrhythmias. Vasopressors should therefore be used only with extreme caution or not at all with these general anesthetics.
Phenylephrine/ Monoamine Oxidase (MAO) Inhibitors: The cardiac and pressor effects of phenylephrine are potentiated by administration of monoamine oxidase (MAO) inhibitors because metabolism of phenylephrine is reduced. Oral administration of phenylephrine to patients receiving a MAO inhibitor should be avoided (see Contraindications).
Phenylephrine/Tricyclic Antidepressants: Tricyclic antidepressants may potentiate the vasopressor effects of phenylephrine.
Phenylephrine/Atropine: Atropine sulfate may block the reflex tachycardia caused by phenylephrine and enhances the pressor response to phenylephrine.
Phenylephrine/Injectable Ergot Alkaloid: An excessive rise in blood pressure may occur if phenylephrine is administered to patients receiving a parenteral injection of an ergot alkaloid such as ergonovine maleate.
Phenylephrine/Digitalis: The possibility that digitalis can sensitize the myocardium to the effects of sympathomimetic drugs should be considered. Phenylephrine/ Furosemide or Other Diuretics: Administration of furosemide or other diuretics may decrease arterial responsiveness to vasopressors such as phenylephrine.

4.6 Fertility, pregnancy and lactation

Chlorpheniramine maleate:

Pregnancy: There are no adequate data from the use of chlorphenamine in pregnant women. The potential risk for humans is unknown, Use during the third trimester may result in reactions in the newborn or premature neonates. Not to be used during pregnancy unless considered essential by a physician.

Lactation: Chlorpheniramine maleate and other antihistamines may inhibit lactation and may be secreted in breast milk. Not to be used during lactation unless considered essential by a physician.

Phenylephrine hydrochloride:

The safety of this medicine during pregnancy and lactaction has not been established but in view of a possible association of foetal abnormalities with first trimester exposure to phenylephrine, the use of the product during pregnancy should be avoided. In addition, because phenylephrine may reduce placental perfusion, the product should not be used in patients with a history of pre-eclampsia. In view of the lack of data on the use of phenylephrine during lactation, this medicine should not be used during breast feeding.

4.7 Effects on the ability to drive and use machines

It is advisable not to drive or operate machinery when on treatment with capsule.

4.8 Undesirable effects:

Chlorpheniramine maleate:

Constipation; diarrhea; dizziness; drowsiness; dry mouth, nose, or throat; excitability; headache; loss of appetite; nausea; nervousness or anxiety; trouble sleeping; upset stomach; vomiting; weakness.

General disorders and administration site conditions:

Common: fatigue

Unknown: chest tightness

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

Phenylephrine hydrochloride:

High blood pressure with headache and vomiting, probably only in overdose. Rarely palpitations. Also, rare reports of allergic reactions and occasionally urinary retention in males.

4.9 Overdose

Chlorpheniramine maleate:

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.

Treatment

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.

Phenylephrine hydrochloride: Phenylephrine overdose is likely to result in: nervousness, headache, dizziness, insomnia, increased blood pressure, nausea, vomiting, mydriasis, acute angle closure glaucoma, tachycardia, palpitations, and allergic reactions. Treatment should be as clinically appropriate. Severe hypertension may need to be treated with alpha blocking medicinal products such as phentolamine

5. Pharmacological Particulars:

5.1 Pharmacodynamic properties

Chlorphenamine maleate: Antihistamines for Systemic Use
ATC Code: R06AB04

Phenylephrine Hydrochloride: Nasal Decongestants for Systemic Use
ATC Code: R01BA53

Pharmacodynamics

Chlorpheniramine maleate:
Pharmacodynamics:
Antihistamines diminish or abolish the actions of histamine in the body by competative reversible blockade of histamine H_1-receptor sites on tissues. Chlorphenamine also has anticholinergic activity.
Antihistamines act to prevent the release of histamine, prostaglandins and leukotrines and have been shown to prevent the migration of inflammatory mediators. The actions of chlorphenmine include inhibition of histamine on smooth muscle, cappillary permeability and hence reduction of oedma and wheal in hypersneitivity reactions such as allergy and anaphylaxis.

Phenylephrine Hydrochloride:
Pharmacodynamics:
Phenylephrine is a post-synaptic α-receptor agonist, with low cardioselective β-receptor affinity. It is has a recognised decongestant activity, by vasoconstriction to reduce oedema of the nasal mucosa .No additional pharmacodynamic studies have been presented

5.2 Pharmacokinetic properties

Chlorpheniramine maleate:
Pharmacokinetics:
Chlorphenamine is well absorbed from the gastro-intestinal tract, following oral administration. The effects develop within 30 minutes, are maximal within 1 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.

Phenylephrine Hydrochloride:
Pharmacokinetics:
Phenylephrine has low bioavailability (~38%) from the gastrointestinal tract owing tovariable absorption and first-pass metabolism. There is significant biotransformationin the intestinal wall. However, phenylephrine is active as a decongestant by the oralroute, the drug distributes through the systemic circulation to the vascular bed of the nasal mucosa.

5.3 Pre-clinical Safety:
None known**.**

6. Pharmaceutical Particulars:
List of Excipients:
Not applicable

6.2 Incompatibilities: Nil

6.3 Shelf Life: 36 months.

6.4 Special Precautions for storage:
Store below 30°C.Protect from light and moisture.

6.5 Nature and contents of container:
10 x 10 Capsule in Alu **-** PVC Blister packed in a printed carton along with pack insert.

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

7. Marketing Authorization Holder:
UGOLAB PRODUCTION NIG.LTD.
31-A, BURMA ROAD, SABON-GARI,
KANO STATE, KANO, NIGERIA

8. Marketing Authorization Number: ---
B4-2113

9. Date of first Authorization /renewal of the authorization: ---

10. Date of revision of text: -----