1. Name of the Medicinal Product

1.1 Name of the Medicinal Product

KOLD TIME SUSPENSION

(Paracetamol, Phenylephrine Hydrochloride & Cetirizine Oral Suspension)

1.2. Strength

Paracetamol BP	125 mg
Phenylephrine Hydrochloride BP	5 mg
Cetirizine Hydrochloride BP	2 mg

1.3. Pharmaceutical Dosage Form

Oral Liquid Dosage Form (Suspension)

Qualitative And Quantitative Composition

Qualitative Declaration

The **KOLD TIME SUSPENSION** contains Paracetamol BP, Phenylephrine Hydrochloride BP, and Cetirizine Hydrochloride BP

Quantitative Declaration

Each 5ml contains:

Paracetamol BP	125 mg
Phenylephrine Hydrochloride BP	5 mg
Cetirizine Hydrochloride BP	2 mg
In a flavoured syrupy base	q.s.

Approved colour used

3. Pharmaceutical Form

Oral Liquid Dosage Form (Suspension)

4. Clinical Particulars

4.1 Therapeutic Indications

Kold Time Suspension is indicated for the treatment of nasal and bronchial congestion, sore or scratchy throat, sneezing, hoarseness, cough, fever, headache, bodyache, cold & flu.

4.2 Posology and Method of Administration

It is important to **shake the bottle** for at least 10 seconds before use.

Children aged 3 months – 6 years

Child's Age	How Much	How often (in 24 hours)
3 months up to 6 months	2.5 ml	4 times
6 months up to 2 years	5 ml	4 times
2 years up to 4 years	7.5 ml	4 times
4 years up to 6 years	10 ml	4 times
Don't give more than 4 times in any 24 hours Leave at least 4 hours between doses.		

Babies over 2 months in age

For the relief of fever after vaccination at 2, 3 and 4 months

2.5 ml. This dose may be given up to 4 times a day at the time of vaccination. Don't give more than 4 doses in any 24 hour period. Leave at least 4 hours between doses. If your baby still needs this medicine 2 days after receiving the vaccine talk to your doctor or pharmacist

Method of administration

Oral administration after a meal

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in formulation.

4.4 Special Warning and Precautions for Use

Caution in patients with severely impaired liver or kidney function.

The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

Methyl hydroxybenzoate (E218) may cause allergic reactions (possibly delayed).

Carmoisine (E122) may cause allergic reactions.

Very rare cases of serious skin reactions have been reported.

The label should contain the following statements:

Contains paracetamol.

Do not give this medicine with any other paracetamol-containing product.

For oral use only.

Do not take more medicine than the label tells you to. If you do not get better talk to your doctor.

Always use the syringe supplied with the pack.

Do not give to babies less than 2 months of age.

Do not give more than 4 doses in any 24 hour period.

Leave at least 4 hours between doses.

Do not give this medicine to your child for more than 3 days without speaking to your doctor or pharmacist.

If your child is currently taking any other medicines talk to your doctor or pharmacist before giving this medicine.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

Patients who have taken barbiturates, tricyclic antidepressants and alcohol may show diminished ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.

Alcohol can increase the hepatotoxicity of paracetamol overdosage and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol.

4.6 Pregnancy and Lactation

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of their doctor regarding its use.

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

Cetirizine is excreted in human milk at concentrations representing 25% to 90% those measured in plasma, depending on sampling time after administration.

Caution should be exercised when prescribing to breast feeding women because cetirizine passes into breast milk

4.7 Effects on Ability to Drive and Use Machines

Objective measurements of driving ability, sleep latency and assembly line performance have not demonstrated any clinically relevant effects at the recommended dose of 10 mg

4.8 Undesirable Effects

Adverse effects of paracetamol are rare but hypersensitivity including skin rash may occur.

Very rare cases of serious skin reactions have been reported.

Clinical studies have shown that cetirizine at the recommended dosage has minor undesirable effects on the CNS, including somnolence, fatigue, dizziness and headache. In some cases, paradoxical CNS stimulation has been reported.

Although cetirizine is a selective antagonist of peripheral H1-receptors and is relatively free of anticholinergic activity, isolated cases of micturition difficulty, eye accommodation disorders and dry mouth have been reported.

Instances of abnormal hepatic function with elevated hepatic enzymes accompanied by elevated bilirubin have been reported. Mostly this resolves upon discontinuation of the treatment with cetirizine dihydrochloride.

4.9 Overdose

a) Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.

b) Regularly consumes ethanol in excess of recommended amounts.

c) Is likely to be glutathione deplete e.g eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms observed after an overdose of cetirizine are mainly associated with CNS effects or with effects that could suggest an anticholinergic effect.

Adverse events reported after an intake of at least 5 times the recommended daily dose are: confusion, diarrhoea, dizziness, fatigue, headache, malaise, mydriasis, pruritus, restlessness, sedation, somnolence, stupor, tachycardia, tremor, and urinary retention

Phenylephrine overdosage is likely to result in effects similar to those listed under adverse reactions.

Additional symptoms may include hypertension and possibly reflux bradycardia. In severe cases confusion, hallucinations, seizures and arrhythmias may occur. However the amount required to produce serious phenylephrine toxicity would be greater than required to cause paracetamol-related toxicity.

Treatment

Treatment should be as clinically appropriate. Severe hypertension may need to be treated with an alpha blocking drug such as phentolamine.

5.0 Pharmacological Properties

5.1 Pharmacodynamic Properties

ATC code

Paracetamol	N02BE01
Phenylephrine HCl	R01AB01
Cetirizine HCl	R06AE07

Non-steroidal anti-inflammatory drugs (NSAIDs).

Mechanism of action:

Paracetamol is a peripherally acting analgesic with antipyretic activity.

Cetirizine, a human metabolite of hydroxyzine, is a potent and selective antagonist of peripheral H1-receptors. In vitro receptor binding studies have shown no measurable affinity for other than H1-receptors. Ex vivo experiments in mice have shown that systemically administered cetirizine does not significantly occupy the cerebral H1-receptors

Phenylephrine Hydrochloride is a sympathomimetic decongestant

5.2 Pharmacokinetic Properties

Absorption

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion.

The steady - state peak plasma concentrations is approximately 300 ng/ml and is achieved within 1.0 ± 0.5 h. No accumulation is observed for cetirizine following daily doses of 10 mg for 10 days. The distribution of pharmacokinetic parameters such as peak plasma concentration (Cmax) and area under curve (AUC), is unimodal in human volunteers.

Phenylephrine hydrochloride is irregularly absorbed from the gastrointestinal tract and undergoes first-pass metabolism by monoamine oxidase in the gut and liver; orally administered phenylephrine has reduced bioavailability. It is excreted in the urine almost entirely as the sulphate conjugate.

Metabolism

Paracetamol is metabolised in the liver

Cetirizine does not undergo extensive first pass metabolism.

Elimination

Excreted in the urine mainly as the glucuronide and sulphate conjugates, with about 10% as glutathione conjugates. Less than 5% is excreted as unchanged paracetamol. Plasma protein binding is negligible at usual therapeutic concentrations, although this is dose dependent. The plasma elimination half life varies from about one to four hours.

About two third of the dose are excreted unchanged in urine. The terminal half-life is approximately 10 hours.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6.0 Pharmaceutical Particulars

6.1 List of excipients

Paracetamol	BP
Cetirizine Hydrochloride	BP
Phenylephrine Hydrochloride	BP
Sodium Chloride	BP
Flavor Melon	IH
Aspartame	BP
Hydrophobic Colloidal Anhydrous Silica	BP
Xanthan Gum	BP
Poysorbate-80	BP
Citric Acid Monohydrate	BP
Sodium Citrate	BP
Bronopol	BP
Croscarmellose sodium	BP
Colour Sunset yellow Supra	IH
Sodium Methyl Hydroxybenzoate	BP
Sodium Propyl Hydroxybenzoate	BP
Saccharin Sodium	BP
DiSodium Edetate	BP
Sucrose	BP
Microcrystalline cellulose	BP
Purified Water	BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

<36 Months>

6.4 Special Precautions for Storage

Store in a cool place. Protect from heat & light.

Keep out of reach of children.

6.5 Nature and Contents of Container

100 ml oral suspension filled in amber coloured PET bottle and such one bottle packed in unit carton along with Patient Information leaflet.

6.6 Special Precautions for Disposal and Other Handling

No special requirements.

7.0 Registrant/Sole Agent

EMBASSY PHARMACEUTICAL & CHEMICAL LTD.

41, Ademola Street, South West Ikoyi,

Lagos, Nigeria.Tel.: 01-2900791

8. Manufacturer

LABORATE PHARMACEUTICALS INDIA LIMITED

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HO: E-11, Industrial Area, Panipat – 132103.

laborate@laborate.com

9. Date of Revision of Text

To be given after approval of product

10. Dosimetry (If applicable)

Not applicable

11. Instructions for Preparation of Radiopharmaceuticals (If applicable)

Not applicable