1. NAME OF THE MEDICINAL PRODUCT
Sinufed Cold Drops

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 1ml contains:-
Paracetamol 100mg
Chlorpheniramine Maleate 1mg
Pseudoephedrine hydrochloride 9.38mg

3. PHARMACEUTICAL FORM
Drops for oral administration.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
For the symptomatic relief of pains, fever and allergic conditions associated with common cold including headache, sore throat pain, nasal congestion and allergic rhinitis (runny and itchy nose) in babies and infants.

4.2 Posology and method of administration
Posology
Administer only on the advice of a physician.

0 – 3 months: 0.04 ml (as indicated on the dropper) every 4 to 6 hours.
4 – 11 months: 1ml (as indicated on the dropper) every 4 to 6 hours.

Do not exceed 4 doses in 24 hours.
If symptoms persist after two days, discontinue use and consult your doctor.

Method of administration
For oral administration only.

4.3 Contraindications
Sinufed Cold Drops is contraindicated in patients with known hypersensitivity to Pseudoephedrine, Chlorpheniramine and Paracetamol and also in persons under treatment with monoamine oxidase inhibitors. It is also contraindicated in patients on sedatives since it potentiates the drowsiness state.
It is also contraindicated in patients with diabetes, liver or kidney disease and in acute attack of asthma.

4.4 Special warnings and precautions for use
Sinufed Cold Drops already contains Paracetamol. Do not give with any Paracetamol containing products, decongestants and appetite stimulants. Do not administer to premature infants. The medication may cause drowsiness. Medical advice should be sought before administering to patients with cardiovascular, renal or hepatic impairments, patients on anticoagulant therapy and epileptic patients. Sinufed Cold Drops should not be taken concurrently with metoclopramide, colestyramine, probenecid or domperidone.

4.5 Interaction with other medicinal products and other forms of interaction
Paracetamol:
Anticholinergic agents or opoid analgesics delay the gastrointestinal absorption of paracetamol by decreasing gastric emptying. Repeated doses of paracetamol increase the anticoagulant response to coumarins.
Paracetamol increases chloramphenicol concentrations and toxicity may be increased by the concomitant use of enzyme-inducing agents such as alcohol or anti-epileptic drugs. Paracetamol increases the blood concentrations of unhydrolysed aspirin.
The absorption of Paracetamol may be accelerated by drugs such as Metoclopramide. Excretion may be affected and plasma concentrations altered when given with Probenecid. Colestyramine reduces the absorption of Paracetamol if given within 1hour of Paracetamol.

Chlorpheniramine Maleate:
Chlorpheniramine may enhance the sedating effects of CNS depressants including alcohol, barbiturates,

hypnotics, opoid analgesics, anxiolytic sedatives and psychotics. It is incompatible with calcium chloride, kanamycin sulphate, noradrenaline tartrate and meglumine adiopone.
It has additive antimuscarinic action with other antimuscarinic drugs like atropine, tricyclic antidepressants, and MAOIs.
It has been suggested that sedating antihistamins could mask the warning signs of damage caused by ototoxic drugs such as aminoglycoside antibiotics.
Chlorpheniramine may suppress cutaneous histamine response to allergen extracts. Its therapy should be stopped several days before skin testing.

Pseudoephedrine Hydrochloride:
The absorption rate of pseudoephedrine hydrochloride is increased by the concomittant administration of Aluminium hydroxide mixture.
Pseudoephedrine may cause a hypertensive crisis in patients receiving MAOI (including a RMA).

4.6 Pregnancy and lactation
Pregnancy
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.

Although pseudoephedrine has been in widespread use for many years without apparent ill consequence, there is no specific data on its use during pregnancy. Caution should therefore be exercised by balancing the potential benefit of treatment to the mother against any possible hazards to the developing foetus. Systemic administration of pseudoephedrine, up to 50 times the human daily dosage in rats and up to 35 times the human daily dosage in rabbits, did not produce teratogenic effects.

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

Pseudoephedrine is excreted in breast-milk in small amounts but the effect of this on breast-fed infants is not known. It has been estimated that approximately 0.5 to 0.7% of a single dose of pseudoephedrine ingested by a mother will be excreted in the breast-milk over 24 hours.

4.7 Effects on ability to drive and use machines
Sinufed Cold Drops may cause drowsiness. Patients should not drive or operate machinery until they have determined their own response.

4.8 Undesirable effects
Side effects are mild and usually well tolerated. These include drowsiness, headache, gastrointestinal disturbances like nausea and vomiting, constipation or diarrhoea and hypersensitivity reactions like rashes. Their incidence might be reduced by giving the drug with meals. If the product is taken within the recommended dose, side effects do not usually present.

4.9 Overdose
Symptoms
Overdosage tor oxicity of Pseudoephedrine is manifested as in-coordination, weakness, palpitation, irritability, hypertension convulsions, difficulty in urination which may lead to ureteric or biliary spasm. Respiratory depression and circulatory collapse or failure has been reported.

Toxic effects of Paracetamol include severe liver damage, haematological problems such as agranulocytosis, haemolytic anaemia, pancytopenia and thrombocytopenia. Acute tubular necrosis has also been observed.

Overdosage associated with chlorpheniramine include antimuscarinic, extrapyramidal and CNS effects. When CNS stimulation predominates, symptoms of toxicity include; hallucinations, excitement, ataxia, incoordination, athetosis, and convulsions. Fixed, dilated pupils with a flushed face, together with sinus tachycardia, urinary retention, dry mouth and fever. Terminally there is deepening coma with cardio-respiratory collapse and death usually within 2 to 18 hours. Large doses may produce an irritant effect on the gastric mucosa causing nausea, vomiting and diarrhoea.

Management
Necessary measures should be taken to maintain and support respiration and control convulsions. Gastric lavage should be performed up to 3 hours after ingestion if indicated. Catheterisation of the bladder may be necessary. If desired, the elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol
Paracetamol a Para – aminophenol derivative has antipyretic and analgesic properties but has no anti-inflammatory properties. Paracetamol acts by its selective depressant action on pain perception apparatus of the thalamus and hypothalamus in the CNS. Paracetamol reduces fever by a direct effect on the heat regulating centres of the CNS, increasing dissipation of body heat by increasing peripheral blood flow and perspiration.

Chlorpheniramine Maleate
Chlorpheniramine is an akylamine derivative with the actions and uses of the antihistamines. It has significant sedative properties. It also has anti-muscarinic properties.
Chlorpheniramine diminishes or abolishes the main actions of histamine in the body by competitive, reversible blockade of histamine receptor sites on the tissues. It does not inactivate or prevent the release or synthesis of histamine. Chlorpheniramine is often used in combination preparations for the treatment of coughs and colds. The mechanism of its antitussive action may involve reduction in cholinergic nerve transmission or may simply result from its sedative effects.

Pseudoephedrine Hydrochloride
Pseudoephedrine is a direct- and indirect-acting sympathomimetic. It is a stereoisomer of ephedrine and has a similar action but has been stated to have less pressor activity and fewer central nervous system effects. Pseudoephedrine and its salts are given orally for the symptomatic relief of nasal congestion. It is commonly combined with other ingredients in preparations intended for the relief of cough and cold symptoms. Pseudoephedrine has alpha - and beta - adrenergic activity and has pronounced stimulating effects on the central nervous system. It reduces intestinal tone and motility, causes bronchodilatation, relaxes the bladder wall. It has a stimulant action on the respiratory centre.
Pseudoephedrine produces its decongestant effect within 30 minutes, persisting for at least 4 hours.

5.2 Pharmacokinetic properties

Paracetamol
Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentration occurring about 30 minutes to 2 hours after ingestion. It is distributed into most body tissues and metabolised In the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged Paracetamol. The elimination half lives varies from 1 to 4 hours. Plasma protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.
A minor hydroxylated metabolite (N – acetyl – P – benzoquinoneimine) which is usually produced in very small amounts by mixed-function oxidases in the liver, and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol over-dosage and cause liver damage.

Chlorpheniramine Maleate
Chlorpheniramine is absorbed slowly from the GIT, peak plasma concentration occurring about 2.5 to 6 hours after administration. Chlorpheniramine appears to undergo considerable first-pass metabolism. About 70% of chlorpheniramine in the circulation is bound to plasma proteins.
There is wide inter-individual variation in the pharmacokinetics of chlorpheniramine; values ranging from 2 to 43 hours have been reported for the half-life. Chlorpheniramine is widely distributed in the body and enters the CNS.
Chlorpheniramine is extensively metabolised. Metabolites include desmethyl- and didesmethyl-chlorpheniramine. Unchanged drug and metabolites are excreted primarily in the urine; excretion is dependent on urinary PH and flow rate. Only trace amounts have been found in the faeces.
More rapid and extensive absorption, faster clearance and a shorter half-life have been reported in children.

Pseudoephedrine Hydrochloride
Pseudoephedrine is readily absorbed from the gastro-intestinal tract. It is resistant to metabolism by monoamine oxidase and is largely excreted unchanged in the urine together with small amounts of its hepatic metabolite. It has a half-life of about 5 to 8 hours, elimination is enhanced and half-life accordingly shorter in acid urine. It has been shown to accumulate to toxic concentrations in children with renal tubular acidosis.

5.3 Preclinical safety data
Systematic administration of pseudoephedrine in rats, up to 7 times the human daily dosage in females and 35 times the human daily dosage in males, did not impair fertility nor alter foetal morphological development and survival.
Systemic administration of pseudoephedrine, up to 50 times the human daily dosage in rats and up to 35 times the human daily dosage in rabbits, did not produce teratogenic effects.

6. Pharmaceutical particulars
6.1 List of excipients
Propylene Glycol
Sodium Benzoate
Acesulfamine Potassium
Raspberry Flavour
Glycerol

6.2 Incompatibilities
None known

6.3 Shelf life
3 Years

6.4 Special precautions for storage
Store below 30°C. Protect from light.

6.5 Nature and contents of container
15ml bottle with calibrated dropper.

6.6 Special precautions for disposal and other handling
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT/MANUFACTURER
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