Sinarest® CCF
Capsules

1. Composition

Dextromethorphan Hydrobromide	10mg
Phenylephrine	10mg
Chlorpheniramine Maleate	2mg

2. Dosage form and strength

Sinarest CCF new Capsules are available in blister pack of 10 capsules.

3. Clinical particulars

3.1 Therapeutic indication

Sinarest New CCF Capsule is indicated for dry cough associated with cold.

3.2 Posology and method of administration

The usual recommended oral dose for adult is 1 capsule thrice a day.

3.3 Contraindication

The use of Sinarest New CCF Capsule is contraindicated in patients with:

- Hypersensitivity to any of the ingredients of the formulation.
- Severe hypertension.
- Monoamine oxidase (MAO) inhibitors prescription.

3.4 Special warnings and precautions for use

- In case a hypersensitivity reaction occurs which is rare, Sinarest new CCF Capsule should be discontinued.
- Sinarest new CCF Capsule should be used with caution in patients with renal or hepatic dysfunction, diabetes mellitus, hyperthyroidism, cardiovascular problems, epilepsy and closed angle glaucoma.

3.5 Drug interactions

Clinically significant drug interactions may occur on concomitant administration of Sinarest New CCF Capsule with monoamine oxidase inhibitors, tricyclic antidepressants, beta-adrenergic agents, methyldopa, reserpine and veratrum alkaloids, Quinidine, linezolid and fluoxetine

3.6 Use in special population

- Paediatric: Sinarest New CCF Capsule should be used with caution in children and generally avoided in those less than 2 years of age.
- Geriatric: Elderly population may be at greater risk for the side-effects.
- Liver impairment: Use with caution.
- Renal failure: Use with caution.
- Pregnancy and lactation: US Food and Drug Administration (FDA) has specified Chlorphenamine maleate as a pregnancy category B drug which indicates that animal and human studies have failed to demonstrate a risk to the foetus in any trimester. Sinarest CCF capsule is recommended to be taken during pregnancy only under doctor's recommendation.

3.7 Effects on ability to drive and use machine

It is advisable not to drive or operate machinery when on treatment with Sinarest new CCF Capsule.

3.8 Undesirable effects

- Sinarest new CCF Capsule is generally well tolerated and adverse events are rare.
- Hypersensitive individuals may display ephedrine-like reactions such as tachycardia, palpitations, headache, dizziness and nausea.
- Use of sympathomimetics has been associated with fear, anxiety, restlessness, tremor, weakness, dysuria, insomnia, hallucinations and convulsions.
- Chlorpheniramine in Sinarest new CCF Capsule may cause sedation.

3.9 Overdose

There is limited experience of overdose with Sinarest CCF new Capsules. Initiate general symptomatic and supportive measures in all cases of overdosages where necessary.

4. Pharmacological properties

4.1 Mechanism of action

Dextromethorphan suppresses the cough reflex by a direct action on the cough center in the medulla of the brain. Thus suppresses non-productive cough associated with cold.

Phenylephrine decreases nasal congestion by acting on α_1-adrenergic receptors in the arterioles of the nasal mucosa to produce constriction; this leads to decreased edema and increased drainage of the sinus cavities.

In allergic reactions an allergen interacts with and cross-links surface IgE antibodies on mast cells and basophils. Once the mast cell-antibody-antigen complex is formed, a complex

series of events occurs that eventually leads to cell-degranulation and the release of histamine (and other chemical mediators) from the mast cell or basophil. Once released, histamine can react with local or widespread tissues through histamine receptors. Histamine, acting on H_1-receptors, produces pruritis, vasodilatation, hypotension, flushing, headache, tachycardia, and bronchoconstriction. Histamine also increases vascular permeability and potentiates pain. Chlorpheniramine maleate binds to the histamine H1 receptor. This block the action of endogenous histamine, which subsequently leads to temporary relief of the negative symptoms brought on by histamine.

4.2 Pharmacodynamic properties

Dextromethorphan shows high affinity binding to several regions of the brain, including the medullary cough center. This compound is an NMDA receptor antagonist and acts as a non-competitive channel blocker. It is one of the widely used antitussives, and is also used to study the involvement of glutamate receptors in neurotoxicity.

Phenylephrine is a powerful vasoconstrictor. It is used as a nasal decongestant and cardiotonic agent. Phenylephrine is a postsynaptic α_1-receptor agonist with little effect on β-receptors of the heart. Parenteral administration of phenylephrine causes a rise in systolic and diastolic pressures, a slight decrease in cardiac output, and a considerable increase in peripheral resistance; most vascular beds are constricted, and renal, splanchnic, cutaneous, and limb blood flows are reduced while coronary blood flow is increased. Phenylephrine also causes pulmonary vessel constriction and subsequent increase in pulmonary arterial pressure. Vasoconstriction in the mucosa of the respiratory tract leads to decreased edema and increased drainage of sinus cavities.

Chlorpheniramine maleate is a histamine H1 antagonist of the alkylamine class. It competes with histamine for the normal H_1-receptor sites on effector cells of the gastrointestinal tract, blood vessels and respiratory tract. It provides effective, temporary relief of sneezing, watery and itchy eyes, and runny nose due to hay fever and other upper respiratory allergies.

4.3 Pharmacokinetic properties

Dextromethorphan is rapidly absorbed from the gastrointestinal tract. It is metabolised in the liver and excreted in the urine as unchanged dextromethorphan and demethylated metabolites including dextrorphan, which has some cough suppressant activity.

Phenylephrine has low oral bioavailability owing to irregular absorption and first-pass metabolism by monoamine oxidase in the gut and liver. When injected subcutaneously or intramuscularly it takes 10 to 15 minutes to act; subcutaneous and intramuscular injections are effective for up to about 1 hour and up to about 2 hours, respectively. Intravenous injections are effective for about 20 minutes. Systemic absorption follows topical application.

Chlorphenamine maleate is absorbed relatively slowly from the gastrointestinal tract, peak plasma concentrations occurring about 2.5 to 6 hours after oral doses. Bioavailability is low, values of 25 to 50% having been reported. Chlorphenamine appears to undergo considerable first-pass metabolism. About 70% of chlorphenamine in the circulation is bound to plasma proteins. There is wide inter individual variation in the pharmacokinetics of chlorphenamine; values ranging from 2 to 43 hours have been reported for the half-life. Chlorphenamine is widely distributed in the body, and enters the CNS. Chlorphenamine maleate is extensively metabolised. Metabolites include desmethyl- and didesmethylchlorphenamine. 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. Duration of action of 4 to 6 hours has been reported; this is shorter than may be predicted from pharmacokinetic parameters. More rapid and extensive absorption, faster clearance, and a shorter half-life have been reported in children.

5. Nonclinical properties

5.1 Animal Toxicology or Pharmacology

Not required.

6. Description

Already mentioned and covered in the above points.

7. Pharmaceutical particulars

7.1 Incompatibilities

There are no known incompatibilities.

7.2 Shelf-life

24 months.

7.3 Storage and handling instructions

Store below 30 ^{o}C in a dark and dry place.