

Sinarest[®] AF

Syrup/Drops

Each 5 ml of Sinarest AF syrup contains

Phenylephrine	5 mg
Chlorpheniramine maleate	1mg
Sodium Citrate	60mg
Menthol	1ml

Each ml of Sinarest AF drops contain

Phenylephrine	2.5 mg
Chlorpheniramine maleate	1mg

Pharmacokinetic properties:

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.

Sodium citrate is metabolised after absorption to bicarbonate. Bicarbonate ions are excreted in the urine, which is rendered alkaline, and there is an accompanying diuresis.

Mechanism of Action



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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 H_1 receptor. This block the action of endogenous histamine, which subsequently leads to temporary relief of the negative symptoms brought on by histamine.

The Sodium citrate in Sinarest AF syrup/drops liquefies mucus and helps expectoration.

Menthol has a cooling and soothing effect.

Other pharmacodynamic properties:

Phenylephrine is a powerful vasoconstrictor. It is used as a nasal decongestant and cardiogenic 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 H_1 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.

Citrate prevents activation of the clotting cascade by chelating calcium ions. Citrate neutralizes acid in the stomach and urine, raising the pH .

Indication:

Sinarest AF syrup/drops 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.

Contraindication:



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The use of Sinarest AF syrup/drops is contraindicated in patients with:

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

Drug Interaction:

Clinically significant drug interactions may occur on concomitant administration of Sinarest AF syrup/drops with monoamine oxidase inhibitors, tricyclic antidepressants, beta-adrenergic agents, and methyldopa, reserpine and veratrum alkaloids.

Adverse effects:

Sinarest AF syrup/drops 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 AF syrup/drops may cause sedation.

Warnings and Precautions:

- In case a hypersensitivity reaction occurs which is rare, Sinarest AF syrup/drops should be discontinued.
- Sinarest AF syrup/drops should be used with caution in patients with renal or hepatic dysfunction, diabetes mellitus, hyperthyroidism, cardiovascular problems, epilepsy and closed angle glaucoma.
- It is advisable not to drive or operate machinery when on treatment with Sinarest AF syrup/drops.

Use in special population:

1. **Pediatric:** Sinarest AF syrup/drops should be used with caution in children less than 2 years of age.
2. **Geriatric:** Elderly population may be at greater risk for the side-effects.
3. **Liver impairment:** Use with caution.
4. **Renal failure:** Use with caution.
5. **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 fetus in any trimester. Sinarest is recommended to be taken during pregnancy only under doctor's recommendation.

Dosage:

The usual recommended dose of SINAREST AF Syrup in children is

Under 6 years =2.5 - 5 ml thrice a day.



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Above 6 years= 5 - 10 ml thrice a day.

The usual recommended dose of SINAREST AF Drops in infants is

1-6 months =0.2 ml thrice or four times a day

7-12 months= 0.2-0.4 ml thrice or four times a day

1-2 years =0.4-0.8 ml thrice or four times a day

Presentation:

SINAREST AF Syrup is available in 100 ml bottle

SINAREST AF Drops is available in a bottle of 15 ml with calibrated dropper

Storage and handling:

Store below 30 °C in a dark and dry place.



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