

Sinarest-[®]AF

DROPS

(Paediatric)

1. Generic name: Phenylephrine Hydrochloride, Chlorpheniramine Maleate.

2. Qualitative and Quantitative composition

Each ml contains:

Phenylephrine Hydrochloride IP..... 2.5 mg

Chlorpheniramine Maleate IP.....1 mg

3. Dosage form and strength

Dosage form: Available in oral drops form.

Strength: Oral drops containing Phenylephrine Hydrochloride 2.5 mg, Chlorpheniramine Maleate 1 mg

4. Clinical particulars

4.1 Therapeutic indication:

Sinarest-AF drops is indicated for treatment of allergic rhinitis and common cold.

4.2 Posology and method of administration

The usual recommended oral dose of Sinarest-AF Drops 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

4.3 Contraindication

The use of Sinarest-AF Drops is contraindicated in patients with:

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

4.4 Special warnings and precautions for use

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

4.5 Drug interactions

Phenylephrine: The co-administration of Monoamine Oxidase Inhibitors (MAOIs) or tricyclic antidepressants and an indirect or mixed-acting sympathomimetic may result in a hypertensive crisis and hence such concomitant use is best avoided. Additionally sympathomimetic may reduce the efficacy of beta-blocking and anti-hypertensive drugs.

Not recommended for patients currently receiving or within two weeks of stopping therapy with monoamine oxidase inhibitors.

Digoxin and cardiac glycosides: concomitant use of phenylephrine may increase the risk of irregular heartbeat or heart attack.

Chlorpheniramine: Concurrent use of Chlorpheniramine and hypnotics or anxiolytics may cause an increase in sedative effects; therefore, medical advice should be sought before taking Chlorpheniramine concurrently with these medicines. Chlorpheniramine inhibits phenytoin metabolism and can lead to phenytoin toxicity. The anti-cholinergic effects of Chlorpheniramine are intensified by MAOIs.

4.6 Use in special population

- Pediatric: Safe.
- 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 Chlorpheniramine 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-AF Drops is recommended to be taken during pregnancy only under doctor's recommendation as safety of use of Sinarest-AF Drops in pregnancy and lactation has not been established.

4.7 Effects on ability to drive and use machine

It is advisable not to drive or operate machinery when on treatment with Sinarest-AF Drops.

4.8 Undesirable effects

Sinarest-AF Drops is generally well tolerated and adverse events are rare.

Anaphylactic reaction, Thrombocytopenia, Palpitations, Tachycardia, Bradycardia, Tinnitus, Vertigo, Periorbital oedema, Vision blurred, Periorbital swelling, Eye swelling, Conjunctivitis, Nausea, Vomiting Diarrhoea, Dry mouth, Dyspepsia, Constipation, Abdominal pain, Hepatic function abnormal, Decreased appetite, Back pain, Myalgia, Dysuria, Urinary retention, Dyspnoea, Rash, Pruritus, Urticaria, Angioedema, Diabetes insipidus, Metabolic acidosis, Lactic acidosis, Headache, Dizziness.

4.9 Overdose

There is limited experience of overdose with Sinarest-AF Drops. Initiate general symptomatic and supportive measures in all cases of overdosages where necessary.

5 Pharmacological properties

5.1 Mechanism of action

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 Ig E 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 blocks the action of endogenous histamine, which subsequently leads to temporary relief of the negative symptoms brought on by histamine.

5.2 Pharmacodynamic properties

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

5.3 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.

Chlorpheniramine 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. 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 maleate is extensively metabolised. Metabolites include desmethylchlorpheniramine and didesmethylchlorpheniramine. 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.

6 Nonclinical properties

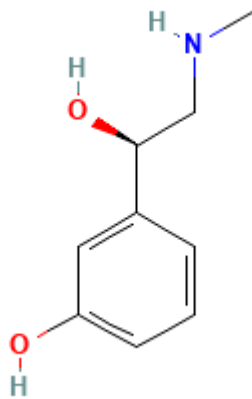
6.1 Animal Toxicology or Pharmacology

Not required.

7. Description

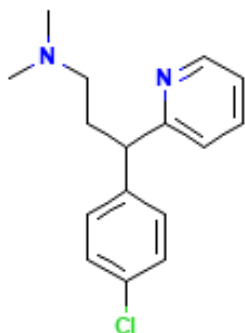
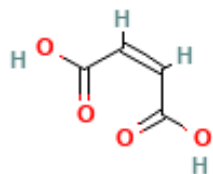
8. Pharmaceutical particulars

Phenylephrine is in a class of medications called nasal decongestants. Its chemical name is hydrogen 3-[(1*R*)-1-hydroxy-2-(methylamino)ethyl]phenol and its structural formula is:



Its empirical formula is $C_9H_{13}NO_2$, and its molecular weight is 167.20 g/mol.

Chlorpheniramine maleate is in a class of medications called antihistamines. Its chemical name is (Z)-but-2-enedioic acid;3-(4-chlorophenyl)-*N,N*-dimethyl-3-pyridin-2-ylpropan-1-amine and its structural formula is :



Its empirical formula is $C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$ or $C_{20}H_{23}ClN_2O_4$ and its molecular weight is 390.9 g/mol

8.1 Incompatibilities: There are no known incompatibilities.

8.2 Shelf-life: 24 months

8.3 Packaging Information: Sinarest-AF Drops are available in bottles of 15 ml.

8.4 Storage and handling instructions: Store below 30 °C in a dark place.

9. Patient Counselling Information

9.1 Adverse reactions: Refer part 4.8

9.2 Drug Interactions: Refer part 4.5

9.3 Dosage: Refer part 4.2

9.4 Storage: Refer part 8.4

9.5 Risk factors: Refer part 4.4

9.6 Self-monitoring information: NA

9.7 Information on when to contact a health care provider or seek emergency help:

Patient is advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications: Refer part 4.3

10. Details of manufacturer:

CENTAUR PHARMACEUTICALS PVT. LTD.

Plant I, Plot No. 3, 5B, 2C,

Tivim Industrial Estate, Karaswada,

Mapusa, Goa- 403 526.

Regd. Off.: Centaur House,

Santacruz (E), Mumbai - 400 055.

11. License number date: 175

12. Date of revision: November 2024.