

SINAREST-LEVO TABLETS

COMPOSITION

Each tablet of **Sinarest Levo** contains:

Levocetirizine	2.5 mg
Phenylephrine	10 mg

PHARMACOLOGY

Levocetirizine

Levocetirizine is an orally active and selective H1-receptor antagonist. It is the R-enantiomer of cetirizine, a racemic compound with antihistaminic properties.

Mechanism of Action

In vitro studies have revealed that levocetirizine has an affinity for the human H1-receptor, that is 2-fold higher than that of cetirizine. Levocetirizine dissociates from H1-receptors with a half-life of 115±38 minutes. Pharmacodynamic studies in healthy volunteers demonstrate that, at half the dose, levocetirizine has comparable activity to cetirizine.

Pharmacokinetics

Levocetirizine exhibits linear pharmacokinetics over the therapeutic dose range.

Absorption: Levocetirizine is rapidly and extensively absorbed following oral administration. In adults, peak plasma concentrations are achieved 0.9 hour after dosing. Food has no effect on the extent of exposure (AUC) of the levocetirizine tablet, therefore Sinarest-Levo can be administered with or without food.

Distribution: The mean plasma protein binding of levocetirizine is about 92% and the apparent volume of distribution is approximately 0.4 L/kg.

Metabolism: The extent of metabolism of levocetirizine is less than 14% of the administered dose.

Elimination: The plasma half-life in adult healthy subjects is about 8 hours. The major route of excretion of levocetirizine and its metabolites is via urine, accounting for a mean of 85% of the dose. Excretion via feces accounts for only 12.9%.

Pediatric Patients: Data from a pediatric pharmacokinetic study show that C_{max} and AUC values are about 2-fold greater than that reported in healthy adult subjects. The total body clearance was 30% greater, and the elimination half-life 24% shorter than in adults.

Phenylephrine

Mechanism of Action

Phenylephrine is sympathomimetic vasoconstrictor that has been used as a nasal decongestant for many years. It is a relatively selective alpha-adrenoceptor agonist. The majority of the sympathomimetic action is due to direct stimulation of the adrenoceptors and relatively little is due to an indirect effect via release of noradrenaline. Its pressor action is weaker than that of noradrenaline but of longer duration. At therapeutic doses, it does not cause significant stimulation of the central nervous system.

Pharmacokinetics

Absorption: Phenylephrine is readily and completely absorbed from the gastrointestinal tract after oral administration. Peak plasma concentrations are achieved in 1 - 2 hours and the mean plasma half-life is in the range of 2 - 3 hours.

Distribution: The volume of distribution is large (200 to 500 litres). Penetration of the brain and excretion in breast milk appear to be minimal. Phenylephrine does not cross the placenta. The extent of protein binding is unknown.

Metabolism: Phenylephrine is extensively metabolised in the gut wall and liver. The

principal routes of metabolism are sulphation, glucuronidation and oxidative deamination.

Excretion is via the kidneys.

Sympathomimetic decongestants like Phenylephrine, reduce the nasal congestion caused by increased nasal blood flow associated with colds and influenza. This effect forms the therapeutic basis for their use in these conditions.

Sinarest-Levo is an antihistamine-nasal decongestant combination used to treat the nasal congestion, sneezing, and runny nose caused by colds and nasal allergy. Antihistamines work by preventing the effects of histamine, which causes itching, sneezing, runny nose, and watery eyes. Decongestants, such as phenylephrine, produce vasoconstriction. The combination of **Sinarest-Levo** helps in clearing nasal congestion, reducing nasal discharge and improving nasal airflow.

INDICATIONS

For prompt, temporary relief of sneezing, itchy, watery eyes, itchy nose or throat, and runny nose caused:

- ✓ Seasonal allergic rhinitis
- ✓ Perennial allergic rhinitis

DOSAGE

Adults & children ≥12 years: 1 tablet twice daily

Children 6-11 years: ½ tablet twice daily

Renal Impairment:

Adjust the dose in patients 12 years of age and older with decreased renal function

CONTRAINDICATIONS

Sinarest Levo is not recommended for:

- ◆ Patients with a known hypersensitivity to levocetirizine, phenylephrine or any of the ingredients of **Sinarest-Levo**
- ◆ Patients with end-stage renal impairment of less than 10 mL/min creatinine clearance or patients undergoing hemodialysis
- ◆ Children 6 to 11 years of age with renal impairment

PRECAUTIONS

- ◆ Because Levocetirizine is substantially excreted by the kidneys, dose adjustment is needed in moderate to severe renal insufficiency.
- ◆ In elderly patients, the dosage should be based on renal function.
- ◆ Concurrent administration of CNS depressants may have additive effect leading to sedation/somnolence.
- ◆ Levocetirizine is a non-sedating antihistamine. In clinical trials the occurrence of somnolence, fatigue, and asthenia has been reported in some patients under therapy with Levocetirizine. Patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness, and motor coordination such as operating machinery or driving a motor vehicle while taking **Sinarest-Levo**.
- ◆ Patients with urinary retention, bladder-neck obstruction, or prostatic hypertrophy have the potential for exacerbation of urinary retention.
- ◆ Angle-closure glaucoma patients have the potential for increased intraocular pressure/precipitation of acute attack.

Pregnancy

There are, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, **Sinarest-Levo** should be used during pregnancy only if clearly needed.

Lactation

As Levocetirizine is excreted in breast milk, **Sinarest-Levo** is not recommended during breastfeeding.

Pediatrics

Do not exceed the recommended dose of 2.5 mg/day in children 6 to 11 years of age. The systemic exposure with the 5 mg dose is approximately twice that of adults.

The safety and effectiveness of **Sinarest-Levo** in pediatric patients under 6 years of age have not been established.

DRUG INTERACTIONS**Levocetirizine**

In vitro data indicate that levocetirizine is unlikely to produce pharmacokinetic interactions through inhibition or induction of liver drug metabolizing enzymes.

Phenylephrine

The coadministration of Monoamine Oxidase Inhibitors (MAOIs) or tricyclic antidepressants and an indirect or mixed-acting sympathomimetic may result in a hypertensive crisis. Although direct-acting sympathomimetics appear to interact minimally, if at all such concomitant use is best avoided with phenylephrine-containing products.

Additionally sympathomimetics may reduce the efficacy of beta-blocking and anti-hypertensive drugs.

ADVERSE EFFECTS

Sinarest Levo is well tolerated. Side effects are mild and often transient.

Levocetirizine: The most common adverse reactions reported in clinical trials were: somnolence, nasopharyngitis, fatigue, dry mouth, and pharyngitis in subjects 12 years of age and older, and pyrexia, somnolence, cough, and epistaxis in children 6 to 12 years of age.

Phenylephrine: As a class, sympathomimetic amines may also cause headaches, vomiting, diarrhea, insomnia, restlessness and palpitations. However, there have been few reports of these with normal doses of Phenylephrine.

PRESENTATION

Sinarest-Levo is available in blister pack of 10 tablets