1. Generic Name

Levocetirizine, Ambroxol HCl

2. Qualitative and Quantitative composition

Levocetirizine	5mg
Ambroxol HCl	60mg

3. Dosage form and strength

Oral tablets containing Levocetirizine 5mg and Ambroxol HCl 60mg.

4. Clinical particulars

4.1 Therapeutic indication

Sinarest Levo new Tablet is used in treatment of:

- Sinusitis
- Allergic rhinitis
- Acute Suppurative Otitis Media (ASOM)

4.2 Posology and method of administration

Recommended oral dose of Sinarest Levo new Tablet for adult is one tablet once or twice a day.

4.3 Contraindication

Sinarest Levo new Tablet is contraindicated in patients with:

- Known hypersensitivity for any ingredient of Sinarest Levo new tablet

- End stage renal disease
- Renal impairment
- Stomach or duodenal ulcers, ciliary dyskinesia, and bronchial conditions.

4.4 Special warnings and precautions for use

None.

4.5 Drug interactions

Levocetirizine: In vitro data indicate that levocetirizine is unlikely to produce pharmacokinetic interactions through inhibition or induction of liver drug-metabolizing enzymes. No in vivo drug-drug interaction studies have been performed with levocetirizine. Drug interaction studies have been performed with racemic cetirizine.

Antipyrine, Azithromycin, Cimetidine, Erythromycin, Ketoconazole, Theophylline, and Pseudoephedrine: Pharmacokinetic interaction studies performed with racemic cetirizine demonstrated that cetirizine did not interact with antipyrine, pseudoephedrine, erythromycin, azithromycin, ketoconazole, and cimetidine. There was a small decrease (~16%) in the clearance of cetirizine caused by a 400 mg dose of theophylline. It is possible that higher theophylline doses could have a greater effect.

Ritonavir: Ritonavir increased the plasma AUC of cetirizine by about 42% accompanied by an increase in half-life (53%) and a decrease in clearance (29%) of cetirizine. The disposition of ritonavir was not altered by concomitant cetirizine administration.

Ambroxol HCl may increase the concentrations of antibiotics (e.g. cefuroxime, doxycycline, erythromycin, amoxicillin) in the lung tissue.

4.6 Use in special population

- Pediatric: As directed by doctor.
- Geriatric: No adaptation of the dose is necessary in elderly patients, provided their renal function is normal.
- Liver impairment: Patients who only have impaired liver function should take the usual prescribed dose.

- Renal failure: Patients who have severe impairment of kidney function must not take Sinarest levo new tablet.
- Pregnancy and lactation: Not recommended.

4.7 Effects on ability to drive and use machine

Use caution when driving or operating machinery until you know how Sinarest Levo new tablets affects you.

4.8 Undesirable effects

Levocetirizine: Anaemia, Thrombocytopenia, Palpitations, Vertigo, Eye pruritus, Dry mouth, Diarrhoea, Nausea, Dyspepsia, Constipation, Vomiting, Abdominal pain ,Abdominal discomfort , Decreased appetite, Myalgia, Insomnia, Dyspnoea, Rhinorrhoea, Sneezing, Cough, Pruritus, Rash, Urticaria, Hypotension.

Ambroxol: Palpitations, Cardiac flutter, Tachycardia, Vertigo , Eyelid oedema, Dry mouth , Diarrhoea, Nausea, Dyspepsia, Constipation, Vomiting, Abdominal pain ,Abdominal discomfort, Pain in extremity, Dysphoria, Insomnia, Dyspnoea, Cough, Tachypnoea, Dry throat, Suffocation feeling, Rash, Pruritus, Urticaria, Hyperhidrosis, Erythema, Rash maculo-papular, Rash erythematous, Angioedema, Stevens-Johnson syndrome, Rash pruritic, Rash popular.

4.9 Overdose

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

5. Pharmacological properties

5.1 Mechanism of action

Levocetirizine is an inverse agonist that decreases activity at histamine H1 receptors. This in turn prevents the release of other allergy chemicals and increased blood supply to the area, and provides relief from the typical symptoms associated with seasonal and perennial allergic rhinitis. It does not prevent the actual release of histamine from mast cells.

Ambroxol is a mucolytic agent. Excessive Nitric oxide (NO) is associated with inflammatory and some other disturbances of airways function. NO enhances the activation of soluble guanylate cyclase and cGMP accumulation. Ambroxol has been shown to inhibit the NO-dependent activation of soluble guanylate cyclase. It is also possible that the inhibition of NO-dependent activation of soluble guanylate cyclase can suppress the excessive mucus secretion; therefore it lowers the phlegm viscosity and improves the mucocilliary transport of bronchial secretions.

5.2 Pharmacodynamic properties

Levocetirizine is a second generation histamine H1 antagonist used to treat various allergic symptoms. It has a long duration of action as it is generally taken once daily, and a wide therapeutic window as animal studies show the maximal nonlethal dose is over 100x a normal dose. Patients are cautioned to avoid tasks that require complete alertness, avoid alertness, and use caution in patients with factors predisposing urinary retention.

Ambroxol hydrochloride is a well-known and widely used secretolytic and secret motoric agent used for inflammatory diseases of the respiratory tract. Hence its pharmacodynamic model is generally well known, and there are no clinically relevant pharmacodynamic issues known at this point.

5.3 Pharmacokinetic properties

Levocetirizine is rapidly and extensively absorbed following oral administration. In adults, peak plasma concentrations are achieved 0.9 hour after administration of the oral tablet. Levocetirizine is poorly metabolized and undergo renal excretion.

The bioavailability of orally administered Ambroxol HCl is high. Ambroxol HCl is highly protein-bound (80% to 90%) and is distributed widely and readily throughout the body. Ambroxol HCl is primarily cleared by metabolism and the resulting metabolites are eliminated renally. Unchanged Ambroxol HCl was present in urine at less than 5% of the administered dose. Ambroxol HCl is predominantly metabolised by hepatic biotransformation via UGTs and to a lesser extent by CYP450. Ambroxol HCl is metabolised by multiple pathways in humans, but only one metabolite (DBAA) was determined to be major.

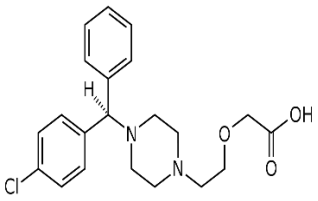
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

NA.

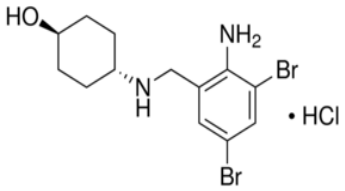
7. Description

Levocetirizine is in a class of medications called antihistamines. Its chemical name is 2-(2-{4-[(R)-(4-chlorophenyl)(phenyl)methyl]piperazin-1-yl}ethoxy)aceticaciddihydrochloride and its structural formula is:



Its empirical formula is $C_{21}H_{25}ClN_2O_3$, and its molecular weight is 388.8878 g/mol.

Ambroxol belongs to a group of medications called mucolytics. Its chemical name is (1r,4r)-4-{[(2-amino-3,5-dibromophenyl)methyl]amino}cyclohexan-1-ol hydrochloride and its structural formula is:



Its empirical formula is $C_{13}H_{19}Br_2ClN_2O$, and its molecular weight is 378.1028 g/mol.

8. Pharmaceutical particulars

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life

24 months.

8.3 Packaging Information

Sinarest Levo new tablet is available in strip of 10 tablets.

8.4 Storage and handling instructions

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

Pure and Cure Healthcare Pvt. Ltd

11. Details of permission or license number with date

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12. Date of revision: January 2022.