1. NAME OF THE MEDICINAL PRODUCT

1.1 Brand Name	:	**XERIN**
1.2 Generic Name	:	Levocetirizine and Montelukast Tablets
1.3 Strength	:	5 / 10 mg
1.4 Pharmaceutical Form	:	Solid Dosage form -Tablets

2. QUALITY AND QUANTITATIVE COMPOSITION

Each Film Coated tablet contains:
Levocetirizine Hydrochloride.....5 mg
Montelukast Sodium
equivalent to Montelukast.....10 mg
Colour : Titanium Dioxide BP

3. PHARMACEUTICAL FORM VISUAL DESCRIPTION:

White to off white, round, biconvex, plain on both sides & film coated tablets.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS:

For Chronic Allergic conditions like seasonal allergic rhinitis , perennial allergic rhinitis, Rhinitis associated with Asthma.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Adults 1 tablet once daily

4.3 CONTRAINDICATIONS

Patients who are hypersensitive to any component of this product or to montelukast sodium, levocetirizine or cetirizine. Patients with completely impaired renal function (anuria).

Use in special populations

Pregnancy

The combination should be used in pregnancy only if clearly needed but should not be continued lactation. Since levocetirizine is excreted in breast-milk the combination is not recommended during breast-feeding.

Others

The combination should be used with caution in patients with impaired hepatic and renal function and patients having closed-angle glaucoma. Patients on concurrent administration of CNS depressants should also administer caution

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Montelukast

General

Montelukast is not indicated for use in the reversal of bronchospasm in acute asthma attacks, including status asthmaticus. Patients should be advised to have appropriate rescue medication available. Therapy with Montelukast can be continued during acute exacerbations of asthma . While the dose of inhaled corticosteroid may be reduced gradually under medical supervision, Montelukast should not be abruptly substituted for inhaled or oral corticosteroids. Montelukast should not be used as monotherapy for the treatment and management of exercise -induced bronchospasm . Patients who have exacerbations of asthma after exercise should continue to use their usual regimen of inhaled (beta)-agonists as prophylaxis and have available for rescue a short-acting inhaled (beta)- agonist . Patients with known aspirin sensitivity should continue avoidance of aspirin or non-steroidal anti-inflammatory agents while taking Montelukast **Eosinophilic Conditions**

In rare cases, patients on therapy with Montelukast may present with systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome, a condition, which is often treated with systemic corticosteroid therapy. These events usually, but not always, have been associated with the reduction of oral corticosteroid therapy.

Levocetirizine

Precaution is recommended with intake of alcohol.Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 INTERATION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTIONS

The individual drugs are not known to have any interactions so far. Hence, no interactions would be expected with the combination

4.6 PREGNANCY AND LACTATION

Pregnancy

The combination should be used in pregnancy only if clearly needed but should not be continued.

Lactation Since levocetirizine is excreted in breast-milk the combination is not recommended during breast-feeding.

4.7 Effects on ability to drive and use machines
Clopidogrel has no or negligible influence on the ability to drive and use machines.
4.8 Undesirable effects
Montelukast & Levocetirizine are generally well tolerated. Common side effects, which might be seen with the combination, are dyspepsia, abdominal pain, rash, dizziness, headache, fatigue, and somnolence. Sometimes, hypersensitivity, irritability, restlessness, insomnia, vomiting and diarrhoea may occur. In rare cases, patients may present with systemic eosinophilia, sometimes presenting with clinical features of consistent with Churg-Strauss Syndrome.

4.9 OVERDOSE

There is no data to prove the overdosage of this combination. However, overdosage has been reported with individual molecules.
MONTELUKAST
There have been reports of acute over-dosage in post-marketing experience and clinical studies with montelukast. These include reports in adults and children with a dose as high as 1000 mg. The clinical and laboratory findings observed were 6 consistent with the safety profile in adults and pediatric patients. There were no adverse experiences in the majority of over-dosage reports. The most frequently occurring adverse experiences were consistent with the safety profile of montelukast and included abdominal pain, somnolence, thirst, headache, vomiting and psychomotor hyperactivity. It is not known whether montelukast is removed by peritoneal dialysis or hemodialysis.

LEVOCETIRIZINE Symptoms of overdose may include drowsiness in adults and initially agitation and restlessness followed by drowsiness, in children. There is no known specific antidote to levocetrizine. Should overdose occur, symptomatic or supportive treatment is recommended. Levocetrizine is not effectively removed by dialysis and dialysis will be ineffective unless a dialyzable agent has been concomitantly ingested.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMICS PROPERTIES

5.2 Levocetirizine
Pharmacodynamic properties
Pharmacotherapeutic group:
antihistamine for systemic use, piperazine derivative, Levocetirizine, the (R) enantiomer of cetirizine, is a potent and selective antagonist of peripheral H 1 -receptors.Binding studies revealed that levocetirizine has high affinity for human H 1 -receptors. Levocetirizine has an affinity 2-fold higher than that of cetirizine. Levocetirizine dissociates from H 1 -receptors with a half-life of 115 Â± 38 min.

Pharmacodynamic studies in healthy volunteers demonstrate that, at half the dose, levocetirizine has comparable activity to cetirizine, both in the skin and in the nose.

Pharmacokinetic / pharmacodynamic relationship

5 mg levocetirizine provide a similar pattern of inhibition of histamine-induced wheal and flare than 10 mg cetirizine. As for cetirizine, the action on histamine-induced skin reactions was out of phase with the plasma concentrations. ECGs did not show relevant effects of levocetirizine on QT interval

MontelukastPharmacodynamics

Montelukast causes inhibition of airway cysteinyl leukotriene receptors as demonstrated by the ability to inhibit bronchoconstriction due to inhaled LTD 4 in asthmatics. Doses as low as 5 mg cause substantial blockage of LTD 4 -induced bronchoconstriction.

5.3 Pharmacokinetic properties

Levocetirizine

Pharmacokinetic properties

The pharmacokinetics of levocetirizine are linear with dose and time-independent with low inter-subject variability. The pharmacokinetic profile is the same when given as the single enantiomer or when given as cetirizine. No chiral inversion occurs during the process of absorption and elimination.

Absorption

Levocetirizine is rapidly and extensively absorbed following oral administration. Peak plasma concentrations are achieved 0.9 g h after dosing. Steady state is achieved after two days. Peak concentrations are typically 270 ng/ml and 308 ng/ml following a single and a repeated 5 mg o.d. dose, respectively. The extent of absorption is dose-independent and is not altered by food, but the peak concentration is reduced and delayed.

Distribution

No tissue distribution data are available in humans. Levocetirizine is 90% bound to plasma proteins. The distribution of levocetirizine is restrictive, as the volume of distribution is 0.4 l/kg.

Biotransformation

The extent of metabolism of levocetirizine in humans is less than 14% of the dose and therefore differences resulting from genetic polymorphism or concomitant intake of enzyme inhibitors are expected to be negligible. Metabolic pathways include aromatic oxidation, N- and O-dealkylation and taurine conjugation.Dealkylation pathways are primarily mediated by CYP 3A4 while aromatic oxidation involved multiple and/or unidentified CYP isoforms. Levocetirizine had no effect on the activities of CYP isoenzymes 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4 at concentrations well above peak concentrations achieved following a 5 mg oral dose.Due to its low metabolism and absence of metabolic inhibition potential, the interaction of levocetirizine with other substances, or vice-versa, is unlikely.The plasma half-life in adults is 7.9 + 1.9 hours. The mean apparent total body clearance is 0.63 ml/min kg. The major route of excretion of levocetirizine and metabolites is via urine, accounting for a mean of 85.4% of the dose. Excretion via faeces accounts for only 12.9% of the dose. Levocetirizine is excreted both by glomerular filtration and active tubular secretion.

Montelukast

Absorption

After administration of the 10-mg film-coated tablet to fasted adults, the mean peak montelukast plasma concentration (C max) is achieved in 3 to 4 hours (T max). The mean oral bioavailability is 64%. The oral bioavailability and C max are not influenced by a standard meal in the morning.

Distribution
Montelukast is more than 99% bound to plasma proteins. The steady-state volume of distribution of montelukast averages 8 to 11 liters.
Metabolism
Montelukast is extensively metabolized. In studies with therapeutic doses, plasma concentrations of metabolites of montelukast are undetectable at steady state in adults and pediatric patients.
Elimination
The plasma clearance of montelukast averages 45 mL/min in healthy adults. Following an oral dose of radiolabeled montelukast, 86% of the radioactivity was recovered in 5-day fecal collections and 0.2% was recovered in urine . Coupled with estimates of montelukast oral bioavailability , this indicates that montelukast and its metabolites are excreted almost exclusively via the bile.In several studies, the mean plasma half- life of montelukast ranged from 2.7 to 5.5 hours in healthy young adults. The pharmacokinetics of montelukast are nearly linear for oral doses up to 50 mg. During once daily dosing with 10-mg montelukast, there is little accumulation of the parent drug in plasma (~14%).

5.4 Preclinical safety data
---

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Maize Starch
Microcrystalline Cellulose
Sodium Starch Glycolate (Type A)
Sodium Lauryl Sulfate
Povidone (K-30)
Isopropyl Alcohol
Purified Talc
Colloidal Anhydrous Silica
Croscarmellose Sodium
Magnesium Stearate
Hypromellose (E-15)
Polyethylene Glycol (6000)
Titanium Dioxide
Colour Red Oxide of Iron
Dichloromethane

6.2 INCOMPATIBILITIES
No effect noted to date.

6.3 SHELF LIFE
36 Months

6.4 SPECIAL PRECAUTIONS FOR STORAGE
Store below 30°C. Protected from moisture & light.

6.5 NATURE AND CONTENTS OF CONTAINER

10 Alu-Alu blisters of 10 tablets each, packed in printed carton along with a pack insert.

6.6 SPECIAL PRECAUTION FOR DISPOSAL

There are no special instructions.

7. MARKETING AUTHORIZATION HOLDER

Name : UNOSOURCE PHARMA LTD
Address: UNIT : 503-504, 5TH FLOOR,
HUBTOWN SOLARIS, N.S. PHADKE MARG,
ANDHERI (EAST) MUMBAI – 400 069
Phone : +91-22-61056105
Fax : +91-22-61056106
E-mail : anurag@unosourcepharma.com

8. MARKETING AUTHORIZATION NUMBERS

Not Applicable.

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Not applicable

10. DATE OF REVISION OF THE TEXT

Not applicable

11. NAME AND ADDRESS OF THE MANUFACTURE

Name : AKUMS DRUGS & PHARMACEUTICALS LTD.
Address: Plot No. 19, 20 & 21, Sector-6A, IIE, SIDCUL,
Ranipur, Haridwar, Uttarakhand.
Phone : 91-01334-239401-404
Fax : 91-01334-239405
E-mail : works@akums.net