Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

MONTIKAST-LA

2. Qualitative and quantitative composition

Each uncoated tablet contains montelukast sodium BP equivalent to montelukast 10 mg and levocetirizine hydrochloride 5 mg.
Excipients with known effect: each uncoated tablet contains 121.95 mg of lactose (as spray-dried lactose) and 0.346 mg of Ponceau 4R (E124).
For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Tablet, Solid Dosage form

4. Clinical particulars

4.1 Therapeutic indications

For treatment of allergic rhinitis and chronic asthma (Adults) : Consider administration of 10 mg once a day in the evening. For Prophylaxis of exercise-induced asthma (Adults):
Proplylactic treatment of asthma.

Chronic treatment of asthma associated with
allergy. Seasonal and perennial rhinitis.
Consider administration of 10 mg of Montelukast + Levocetirizine,
at least two hours before exercise.

4.2 Posology and method of administration

Posology

For treatment of allergic rhinitis and chronic asthma (Adults) : Consider administration of 10 mg once a day in the evening.
Consider administration of 10 mg of Montelukast + Levocetirizine, at least two hours before exercise.

Method of administration

For oral use.

4.3 Contraindications

Montelukast + Levocetirizine is contraindicated in patients with known hypersensitivity to montelukast sodium, levocetirizine or cetirizine or to any other component of this product. Montelukast + Levocetirizine is also contraindicated in patients with severe renal impairment at less than 10ml/min creatinine clearance. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medication

4.4 Special warnings and precautions for use

Montelukast – eosinophilic conditions

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

Levocetirizine

Patients should avoid engaging in hazardous occupation requiring complete mental alertness such as driving or operating machinery when taking levocetirizine. Precaution is recommended with intake of alcohol and in those who are on CNS depressants.

4.5 Interaction with other medicinal products and other forms of interaction

Phenobarbital: Used for treatment of epilepsy Pheytoin: Used for treatment of epilepsy

Rifampicin: Used for treatment of Tuberculosis and some other interactions. THEOPHYLLINE, PREDISOLONE, ORAL CONTRACEPTIVES, TERFENADINE, DIGOXIN, WARAFIN, THYROID HORMONES & SEDATIVE HYPNOTICS.]

4.6 Pregnancy and Lactation

Pregnancy category

B

Montelukast + Levocetirizine may not cause harm to an unborn foetus. Before Montelukast treatment, the patient should discuss with the physician, if they are planning for a pregnancy.

It is unclear whether the drug could pass through the breast milk to a breast feeding baby. Consult your physician before taking Montelukast + Levocetirizine, if you are nursing mother.

4.7 Effects on ability to drive and use machines

Not Known

4.8 Undesirable effects

Thirst was the only adverse experience commonly reported as medicinal-product related in children aged 2 to 5 years. Cough was reported as occurring frequently (>1/10) in trials, regardless of causality.

In older children (6 to 14 years), headache was the most commonly reported medicinal-product related adverse effect. The most commonly reported adverse reactions overall were headache, asthma and upper respiratory tract infections; however, none were significantly different in frequency between the treatment groups.

Reporting of suspected adverse reactions

Healthcare professionals are asked to report any suspected adverse reactions via the Pharmacy and Poisons Board, Pharmacovigilance Electronic Reporting System (PvERS): https://pv.pharmacyboardkenya.org

4.9 Overdose

Symptoms of overdose may include drowsiness in adults and, initially, agitation and restlessness followed by drowsiness in children.

5. Pharmacological properties

5.1 Pharmacodynamic properties

This is a combination of two medicines: Levocetirizine and Montelukast which treat sneezing and runny nose due to allergies.

Mechanism of action

Montelukast :

Montelukast selectively antagonizes leukotriene D4 (LTD4) thecysteinylleukotriene receptor, CysLT1, in the human airway. Montelukast inhibits the actions of LTD4 at the CysLT1 receptor, preventing airway edema, smooth muscle contraction, and enhanced secretion of thick, viscous mucus.

Levocetirizine

Levocetirizine, the active enantiomer of cetirizine, is an anti-histamine; its principal effects are mediated via selective inhibition of H1 receptors. The antihistaminic activity of levocetirizine has been documented in a variety of animal and human models. In vitro binding studies revealed that levocetirizine has an affinity for the human H1-receptor 2-fold higher than that of cetirizine (Ki = 3 nmol/L vs. 6 nmol/L, respectively). This increased affinity has unknown clinical relevance.

5.2 Pharmacokinetic properties

Montelukast – absorption

After administration of a 10 mg tablet to fasted adults, the mean peak plasma concentration (Cmax) is achieved in 3 to 4 hours (Tmax). The mean oral bioavailability is 64%. Oral bioavailability and Cmax are not influenced by a standard meal taken in the morning.

Montelukast – distribution

Montelukast is more than 99% bound to plasma proteins. The steady-state volume of distribution averages 8 to 11 litres.

Montelukast – metabolism

Montelukast is extensively metabolised. In studies with therapeutic doses, plasma concentrations of metabolites of montelukast are undetectable at steady state in adults and paediatric patients.

Montelukast – elimination

The plasma clearance of montelukast averages 45 mL/min in healthy adults. Following an oral dose of radiolabelled montelukast, 86% of the

radioactivity was recovered in 5-day faecal collections and less than 0.2% was recovered in urine. Coupled with estimates of 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 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 substance in plasma (approximately 14%).

Levocetirizine

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 as cetirizine. No chiral inversion occurs during absorption and elimination.

Absorption: levocetirizine is rapidly and extensively absorbed following oral administration. Peak plasma concentrations are achieved 0.9 hours after dosing and 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 once-daily 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 is restrictive, with a volume of distribution of 0.4 L/kg.

Biotransformation: the extent of metabolism in humans is less than 14% of the dose, and differences resulting from genetic polymorphism or concomitant intake of enzyme inhibitors are therefore expected to be negligible. Metabolic pathways include aromatic oxidation, N- and O-dealkylation and taurine conjugation. Dealkylation pathways are primarily mediated by CYP3A4, while aromatic oxidation involves 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, interaction of levocetirizine with other substances, or vice versa, is unlikely.

Elimination: 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 its 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.

5.3 Preclinical safety data

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. In the following description of clinical trials experience, adverse reactions are listed regardless of causality assessment. The most common adverse

reactions in controlled clinical trials were: upper respiratory infection, fever, headache, pharyngitis, cough, abdominal pain, diarrhea, otitis media, influenza, rhinorrhea, sinusitis, otitis

6. Pharmaceutical Particulars

6.1 List of Excipients

Spray-dried lactose
Microcrystalline cellulose
Low-substituted hydroxypropyl cellulose
Ponceau 4R (E124)
Croscarmellose sodium
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf-Life

36 months.

6.4 Special Precautions for storage

Store in a cool, dry place below 30°C. Keep out of the reach of children.

6.5 Nature and Content of container

1 × 10 tablets packed in a carton together with the product insert.

6.6 Special precautions for disposal and other handling

[Not addressed in the submitted document.]
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder

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8. Marketing Authorization Number

H2021/CTD8346/16216

9. Date of first authorization/renewal of the authorization

2021 September 20

10. Date of revision of the text

2021 September 20