Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

EPIMO-L TABLET (Montelukast 10mg & Levocetirizine 5mg) Tablet.

2. Qualitative and quantitative composition

Each Film coated tablet contains:

Montelukast Sodium BP	
Eq to Montelukast	10 mg.
Levocetirizine Dihydrochloride USP	5 mg.
Lactose	
Excipients	Q.S.
Colour: Titanium Dioxide BP	

3. Pharmaceutical form

A white coloured, round shaped, Biconvex, film coated tablet.

4. Clinical particulars

4.1 Therapeutic indications

EPIMO-L TABLET Tablets are indicated for the symptomatic treatment of allergic rhinitis (seasonal and perennial) in adults only.

4.2 Posology and method of administration

Oral: Adults: 1 tablet to be administered once daily. Epimon-L Tablets can be administered regardless of food. Or, as prescribed by the physician.

4.3 Contraindications

EPIMO-L Tablets are contraindicated in following conditions:

- Known hypersensitivity to levocetirizine or other piperazine derivatives or to montelukast or to any component of the formulation.
- End stage renal disease (ESRD) patients (creatinine clearance)

4.4 Special warnings and precautions for use

Montelukast 1 Acute Asthma: Montelukast is not indicated for use in the reversal of bronchospasm in acute asthma attacks, including status asthmatics. Patients should be advised to have appropriate rescue medication available. Patients who have exacerbations of asthma after exercise should have a short-acting inhaled β-agonist available as rescue medication. Concomitant Corticosteroid Use: While the dose of inhaled corticosteroid may be reduced gradually under medical supervision, montelukast should not be abruptly substituted for inhaled or oral corticosteroids. Aspirin Sensitivity: Patients with known aspirin sensitivity should continue avoidance of aspirin or non-steroidal anti-inflammatory agents while taking montelukast. Although montelukast is effective in improving airway function in asthmatics with documented aspirin sensitivity, it has not been shown to truncate bronchoconstrictor response to aspirin and other non-steroidal anti-inflammatory drugs in aspirin-sensitive asthmatic patients. Hereditary Problems: Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take montelukast. Eosinophilic Conditions: In rare cases, patients on therapy with anti-asthma agents including 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 cases usually, but not always, have been associated with the reduction or withdrawal of oral corticosteroid therapy. The possibility that leukotriene receptor antagonists may be associated with emergence of Churg Strauss syndrome can neither be excluded nor established. Physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. Patients who develop these symptoms should be reassessed and their treatment regimens evaluated. Neuropsychiatric Events: Neuropsychiatric events have been reported in adult, adolescent, and pediatric patients taking montelukast. Post-marketing reports with montelukast use include agitation, aggressive behavior or hostility, anxiousness, depression, disorientation, disturbance in attention, dream abnormalities, hallucinations, insomnia, irritability, memory impairment, restlessness, somnambulism, suicidal thinking and behavior (including suicide), and tremor. The clinical details of some post-marketing reports involving montelukast appear consistent with a drug-induced effect. Patients and prescribers should be alert for neuropsychiatric events. Patients should be instructed to notify their prescriber if these changes occur. Prescribers should carefully evaluate the risks and benefits of continuing treatment with montelukast if such events occur.

Levocetirizine.

Levocetirizine Somnolence: 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 after ingestion of levocetirizine. Concurrent use of levocetirizine with alcohol or other central nervous system depressants should be avoided because additional reductions in alertness and additional impairment of central nervous system performance may occur. 2 Urinary Retention: Urinary retention has been reported with levocetirizine. Levocetirizine should be used with caution in patients with predisposing factors of urinary retention (e.g., spinal cord lesion, prostatic hyperplasia) as levocetirizine may increase the risk of urinary retention. Discontinue levocetirizine if urinary retention occurs.

4.5 Interaction with other medicinal products and other forms of interaction

Montelukast

Theophylline, prednisone, prednisolone, oral contraceptives (ethinyl estradiol/ norethindrone 35 mcg/1mg), terfenadine, digoxin, and

warfarin: The recommended clinical dose of montelukast did not have clinically important effects on the pharmacokinetics of these drugs. CYP 450 inducers such as phenytoin, phenobarbital, and rifampicin: The area under the plasma concentration curve (AUC) for montelukast was decreased approximately 40% in subjects with co-administration of phenobarbital. Since montelukast is metabolised by CYP 3A4, 2C8, and 2C9, caution should be exercised, particularly in children, when montelukast is co-administered with inducers of CYP 3A4, 2C8, and 2C9, such as phenytoin, phenobarbital and rifampicin. Paclitaxel, rosiglitazone, and repaglinide: In vitro studies have shown that montelukast is a potent inhibitor of CYP 2C8. However, data from a clinical drug-drug interaction study involving montelukast and rosiglitazone (a probe substrate representative of medicinal products primarily metabolized by CYP 2C8) demonstrated that montelukast does not inhibit CYP 2C8 in vivo. Therefore, montelukast is not anticipated to markedly alter the metabolism of medicinal products metabolised by this enzyme (e.g., paclitaxel, rosiglitazone, and repaglinide). Gemfibrozil: In vitro studies have shown that montelukast is a substrate of CYP 2C8, and to a less significant extent of 2C9, and 3A4. In a clinical drug-drug interaction study involving montelukast and gemfibrozil (an inhibitor of both CYP 2C8 and 2C9) gemfibrozil increased the systemic exposure of montelukast by 4.4-fold. No routine dosage adjustment of montelukast is required upon co-administration with gemfibrozil or other potent inhibitors of CYP 2C8, but the physician should be aware of the potential for an increase in adverse reactions. Trimethoprim: Based on in vitro data, clinically important drug interactions with less potent inhibitors of CYP 2C8 (e.g., trimethoprim) are not anticipated. Itraconazole: Co-administration of montelukast with itraconazole, a strong inhibitor of CYP 3A4, resulted in no significant increase in the systemic exposure of montelukast.

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.

4.6 Pregnancy and Lactation

Pregnant Women

Montelukast: Pregnancy Category B; Levocetirizine: Pregnancy Category B. Animal studies with individual agents do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development. However, there are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this product should be used during pregnancy only if clearly needed.

Lactating Women

Studies in rats have shown that montelukast is excreted in milk. It is not known if montelukast is excreted in human milk. Cetirizine has been reported to be excreted in human breast milk. Levocetirizine is also expected to be excreted in human milk. Thus, use of this product in nursing mothers is not recommended.

4.7 Effects on ability to drive and use machines

Dizziness may occur in some individual 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 after ingestion of this product.

4.8 Undesirable effects

Montelukast

Clinical Trials Experience

The most common adverse reactions (incidence ≥ 5% and greater than placebo) in controlled clinical trials were upper respiratory infection, fever, headache, pharyngitis, cough, abdominal pain, diarrhea, otitis media, influenza, rhinorrhea, and sinusitis. Adverse experiences occurring in ≥ 1% of patients with an incidence greater than that in patients treated with placebo were:

- Body as a whole: Asthenia/fatigue, fever, trauma.
- Digestive system disorders: Dyspepsia, pain (abdominal), gastroenteritis (infectious).
- Nervous system/psychiatric: Headache, dizziness.
- Respiratory system disorders: Influenza, cough, congestion (nasal).
- Skin/skin appendages disorder: Rash.
- Abnormal laboratory tests: Increase in ALT, increase in AST, pyuria.

Post-Marketing Experience

The following adverse reactions have been identified during post-approval use of montelukast. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to

drug exposure. • Blood and lymphatic system disorders: Increased bleeding tendency, thrombocytopenia.
• Immune system disorders: Hypersensitivity reactions including anaphylaxis, hepatic eosinophilic infiltration.
• Psychiatric disorders: Agitation including aggressive behavior or hostility, anxiousness, depression, disorientation, disturbance in attention, dream abnormalities, hallucinations, insomnia, irritability, memory impairment, restlessness, somnambulism, suicidal thinking and behavior (including suicide), and tremor.
• Nervous system disorders: Drowsiness, paraesthesia/hypoesthesia, seizures.
• Cardiac disorders: Palpitations.
• Respiratory, thoracic and mediastinal disorders: Epistaxis, pulmonary eosinophilia.
• Gastrointestinal disorders: Diarrhea, dyspepsia, nausea, pancreatitis, vomiting. • Hepatobiliary disorders: Cases of cholestatic hepatitis, hepatocellular liver-injury, and mixed-pattern liver injury have been reported in patients treated with montelukast. Most of these occurred in combination with other confounding factors, such as use of other medications, or when montelukast was administered to patients who had underlying potential for liver disease such as alcohol use or other forms of hepatitis.
• Skin and subcutaneous tissue disorders: Angioedema, bruising, erythema multiforme, erythema nodosum, pruritus, Stevens-Johnson syndrome/toxic epidermal necrolysis, urticaria.
• Musculoskeletal and connective tissue disorders: Arthralgia, myalgia including muscle cramps.
• General disorders and administration site conditions: Edema.

Levocetirizine Clinical

Trials Experience

Common adverse reactions reported with levocetirizine in clinical trials were somnolence, fatigue, asthenia (physical weakness), dry mouth, headache, abdominal pain, nasopharyngitis/pharyngitis, and urinary retention. Most of these side effects were mild to moderate in intensity.

Post-Marketing Experience

In addition to the adverse reactions reported during clinical studies and listed above, very rare cases of the following adverse drug reactions have been reported in post-marketing experience.
• Immune system disorders: Hypersensitivity, including anaphylaxis.
• Psychiatric disorders: Aggression, agitation.
• Nervous system disorders: Convulsions.
• Eye disorders: Visual disturbances.
• Cardiac disorders: Palpitations.
• Respiratory, thoracic, and mediastinal disorders: Dyspnea.

- Gastrointestinal disorders: Nausea.
- Hepatobiliary disorders: Hepatitis.
- Skin and subcutaneous tissue disorders: Angioneurotic oedema, fixed drug eruptions, pruritus, rash, urticaria.
- Musculoskeletal, connective tissue, and bone disorders: Myalgia.
- Investigations: Increased weight, abnormal liver function tests.

4.9 Overdose

There are no published reports on overdose of this combination product. However, overdose has been reported with individual components of this product as follows:

Montelukast Symptoms:

There have been reports of acute overdose in post-marketing experience and clinical studies with montelukast. These include reports in adults and children with a dose as 6 high as 1000 mg. The clinical and laboratory findings observed were consistent with the safety profile in adults and pediatric patients. There were no adverse experiences in the majority of overdose 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. Treatment: No specific information is available on the treatment of overdose with montelukast. Should overdose occur, symptomatic or supportive treatment is recommended. It is not known whether montelukast is dialysable by peritoneal or haemodialysis.

Levocetirizine Symptoms:

Symptoms of overdose may include drowsiness in adults and initially agitation and restlessness, followed by drowsiness in children. Treatment: There is no known specific antidote to levocetirizine. Should overdose occur, symptomatic or supportive treatment is recommended. Gastric lavage should be considered following short-term ingestion. Levocetirizine is not effectively removed by haemodialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Montelukast

Pharmacotherapeutic group: Leukotriene receptor antagonist

ATCcode: R03D C03

The cysteinyl leukotrienes (LTC4, LTD4, LTE4) are products of arachidonic acid metabolism and are released from various cells, including mast cells and eosinophils. These eicosanoids bind to cysteinyl leukotriene (CysLT) receptors. The CysLT type-1 (CysLT1) receptor is found in the human airway (including airway smooth muscle cells and airway macrophages) and on other pro-inflammatory cells (including eosinophils and certain myeloid stem cells). CysLTs have been correlated

with the pathophysiology of asthma and allergic rhinitis. In asthma, leukotriene-mediated effects include airway edema, smooth muscle contraction, and altered cellular activity associated with the inflammatory process. In allergic rhinitis, CysLTs are released from the nasal mucosa after allergen exposure during both early-and late-phase reactions and are associated with symptoms of allergic rhinitis. Montelukast is an orally active compound that binds with high affinity and selectivity to the CysLT1 receptor (in preference to other pharmacologically important airway receptors, such as the prostanoid, cholinergic, or β-adrenergic receptor). Montelukast inhibits the physiologic actions of LTD4 at the CysLT1 receptor without any agonist activity.

Levocetirizine.

Pharmacotherapeutic group: antihistamine for systemic use, piperazine derivatives, **ATCcode: R06A E09**.
Mechanism of action: Levocetirizine, the (R) enantiomer of cetirizine, is a potent and selective antagonist of peripheral H1-receptors. Binding studies revealed that levocetirizine has high affinity for human H1-receptors (Ki = 3.2 nmol/l). Levocetirizine has an affinity 2-fold higher than that of cetirizine (Ki = 6.3 nmol/l). Levocetirizine dissociates from H1-receptors with a half-life of 115 ± 38 min. After single administration, levocetirizine shows receptor occupancy of 90% at 4 hours and 57% at 24 hours. 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.

5.2 Pharmacokinetic properties

Montelukast:

Absorption: Montelukast is rapidly absorbed following oral administration. For the 10 mg film-coated tablet, the mean peak plasma concentration (Cmax) is achieved 3 hours (Tmax) after administration in adults in the fasted state. The mean oral bioavailability is 64%. The oral bioavailability and Cmax are not influenced by a standard meal. Safety and efficacy were demonstrated in clinical trials where the 10 mg film-coated tablet was administered without regard to the timing of food ingestion.

Distribution:
Montelukast is more than 99% bound to plasma proteins. The steady-state volume of distribution of montelukast averages 8-11 litres. Studies in rats with radiolabelled montelukast indicate minimal distribution across the blood-brain barrier. In addition, concentrations of radiolabelled material at 24 hours post-dose were minimal in all other tissues.

Biotransformation:
Montelukast is extensively metabolised. In studies with therapeutic doses, plasma concentrations of metabolites of

montelukast are undetectable at steady state in adults and children. Cytochrome P450 2C8 is the major enzyme in the metabolism of montelukast. Additionally, CYP 3A4 and 2C9 may have a minor contribution, although itraconazole, an inhibitor of CYP 3A4, was shown not to change pharmacokinetic variables of montelukast in healthy subjects that received 10 mg montelukast daily. Based on in vitro results in human liver microsomes, therapeutic plasma concentrations of montelukast do not inhibit cytochromes P450 3A4, 2C9, 1A2, 2A6, 2C19, or 2D6. The contribution of metabolites to the therapeutic effect of montelukast is minimal.

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 is 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%).

Characteristics in patients:

No dosage adjustment is necessary for the elderly or mild to moderate hepatic insufficiency. Studies in patients with renal impairment have not been undertaken. Because montelukast and its metabolites are eliminated by the biliary route, no dose adjustment is anticipated to be necessary in patients with renal impairment. There are no data on the pharmacokinetics of montelukast in patients with severe hepatic insufficiency (Child-Pugh score>9). With high doses of montelukast (20- and 60-fold the recommended adult dose), decrease in plasma theophylline concentration was observed. This effect was not seen at the recommended dose of 10 mg once daily

Levocetirizine dihydrochloride:

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. In adults, peak plasma concentrations are achieved 0.9 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, neither concerning the passage of levocetirizine through the blood brain-barrier. In rats and dogs, the highest tissue levels are found in liver and kidneys, the lowest in the CNS compartment. 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.
Elimination: The plasma half-life in adults is 7.9 ± 1.9 hours. The half-life is shorter in small children. The mean apparent total body clearance in adults 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.
Special population:
Renal impairment:
The apparent body clearance of levocetirizine is correlated to the creatinine clearance. It is therefore recommended to adjust the dosing intervals of levocetirizine, based on creatinine clearance in patients with moderate and severe renal impairment. In anuric end stage renal disease subjects, the total body clearance is decreased by approximately 80% when compared to normal subjects. The amount of levocetirizine removed during a standard 4-hour hemodialysis procedure was < 10%.
Paediatric population:
Data from a paediatric pharmacokinetic study with oral administration of a single dose of 5 mg levocetirizine in 14 children age 6 to 11 years with body weight ranging between 20 and 40 kg show that Cmax and AUC values are about 2-fold greater than that reported in healthy adult subjects in a cross-study comparison. The mean Cmax was 450 ng/ml, occurring at a mean time of 1.2 hours, weight-normalized, total body clearance was 30% greater, and the elimination half-life 24% shorter in this paediatric population than in adults. Dedicated pharmacokinetic studies have not been conducted in paediatric patients younger than 6

years of age. A retrospective population pharmacokinetic analysis was conducted in 323 subjects (181 children 1 to 5 years of age, 18 children 6 to 11 years of age, and 124 adults 18 to 55 years of age) who received single or multiple doses of levocetirizine ranging from 1.25 mg to 30 mg. Data generated from this analysis indicated that administration of 1.25 mg once daily to children 6 months to 5 years of age is expected to result in plasma concentrations similar to those of adults receiving 5 mg once daily.

Elderly:

Limited pharmacokinetic data are available in elderly subjects. Following once daily repeat oral administration of 30 mg levocetirizine for 6 days in 9 elderly subjects (65–74 years of age), the total body clearance was approximately 33% lower compared to that in younger adults. The disposition of racemic cetirizine has been shown to be dependent on renal function rather than on age. This finding would also be applicable for levocetirizine, as levocetirizine and cetirizine are both predominantly excreted in urine. Therefore, the levocetirizine dose should be adjusted in accordance with renal function in elderly patients.

Gender:

Pharmacokinetic results for 77 patients (40 men, 37 women) were evaluated for potential effect of gender. The half-life was slightly shorter in women (7.08 ± 1.72 hr) than in men (8.62 ± 1.84 hr); however, the body weight-adjusted oral clearance in women (0.67 ± 0.16 ml/min/kg) appears to be comparable to that in men (0.59 ± 0.12 ml/min/kg). The same daily doses and dosing intervals are applicable for men and women with normal renal function. Race: The effect of race on levocetirizine has not been studied. As levocetirizine is primarily renally excreted, and there are no important racial differences in creatinine clearance, pharmacokinetic characteristics of levocetirizine are not expected to be different across races. No race-related differences in the kinetics of racemic cetirizine have been observed.

Hepatic impairment:

The pharmacokinetics of levocetirizine in hepatically impaired subjects have not been tested. Patients with chronic liver diseases (hepatocellular, cholestatic, and biliary cirrhosis) given 10 or 20 mg of the racemic compound cetirizine as a single dose had a 50% increase in half-life along with a 40% decrease in clearance compared to healthy subjects. **Pharmacokinetic / pharmacodynamic relationship:**

The action on histamine-induced skin reactions is out of phase with the plasma concentrations.

5.3 Preclinical safety data

Montelukast:

In animal toxicity studies, minor serum biochemical alterations in ALT, glucose, phosphorus and triglycerides were observed which were

transient in nature. The signs of toxicity in animals were increased excretion of saliva, gastro-intestinal symptoms, loose stools and ion imbalance. These occurred at dosages which provided>17-fold the systemic exposure seen at the clinical dosage. In monkeys, the adverse effects appeared at doses from 150 mg/kg/day (>232-fold the systemic exposure seen at the clinical dose). In animal studies, montelukast did not affect fertility or reproductive performance at systemic exposure exceeding the clinical systemic exposure by greater than 24-fold. A slight decrease in pup body weight was noted in the female fertility study in rats at 200 mg/kg/day (>69fold the clinical systemic exposure). In studies in rabbits, a higher incidence of incomplete ossification, compared with concurrent control animals, was seen at systemic exposure>24-fold the clinical systemic exposure seen at the clinical dose. No abnormalities were seen in rats. Montelukast has been shown to cross the placental barrier and is excreted in breast milk of animals. No deaths occurred following a single oral administration of montelukast sodium at doses up to 5000 mg/kg in mice and rats (15,000 mg/m2 and 30,000 mg/m2 in mice and rats, respectively), the maximum dose tested. This dose is equivalent to 25,000 times the recommended daily adult human dose (based on an adult patient weight of 50 kg). Montelukast was determined not to be phototoxic in mice for UVA, UVB or visible light spectra at doses up to 500 mg/kg/day (approximately>200-fold based on systemic exposure). Montelukast was neither mutagenic in in vitro and in vivo tests nor tumorigenic in rodent species.

Levocetirizine:

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6. Pharmaceutical Particulars

6.1 List of Excipients

Batch Formula:
Batch Size: 1,00,000 Tablets

Sr. No.	Name of Ingredients	Spec.	Qty In mg / Tablet	Overages. %	Qty in mg/ Tablet with overages	Qty In Kg. For Std. Batch Size	Function
GRANULATION							
3	**Micro Crystalline Cellulose	BP	20.00	NA	20.00	2.000 KG	Diluent
4	Lactose	BP	64.60	NA	64.60	6.460 KG	Diluent
5	Cross Carmellose Sodium	BP	5.00	NA	5.00	0.500 KG	Disintegrant
6	Magnesium Stearate	BP	1.00	NA	1.00	0.100 KG	Lubricant
7	Colloidal silicon Dioxide	BP	1.00	NA	1.00	0.100 KG	Absorbent
LUBRICATION							
9	Magnesium Stearate	BP	2.00	NA	2.00	0.200 KG	Lubrication
10	Talcum	BP	1.00	NA	1.00	0.100 KG	Glidant
					110.00	**11.00 KG**	
COATING							
12	Isopropyl Alcohol	BP	2.00 ml	NA	2.00 ml	2.00 ltr	Solvent
13	Ready mix of white	IH	0.334 mg	NA	0.334 mg	0.334	Coating agent
14	Methylene Chloride	BP	3.50 ml	NA	3.50 ml	3.50 ltr	Solvent
	TOTAL				113.000	11.300 KG	

Note: * Compensate the qty of Actives with microcrystalline cellulose to maintain th average weight.

6.2 Incompatibilities
Not applicable

6.3 Shelf-Life
36months

6.4 Special Precautions for storage
STORE UPTO 30°C.
KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and Content of container

10 X 1 X 10 Alu/Alu Blister pack

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder

Relax Biotech Pvt. Ltd.

8. Marketing Authorization Number

CTD10751

9. Date of first authorization/renewal of the authorization

06/10/2023

10. Date of revision of the text

May 29TH , 2025