1.4.1

Prescribing Information (Summary of Product Characteristics)

1.4.1.1 Name of the medicinal Product

Losartan Potassium Tablets USP 50 mg

1.4.1.1.1 Strength

50 mg/tablet

1.4.1.1.2 Pharmaceutical Form

Oral Tablets

1.4.1.2 Qualitative and Quantitative Composition

1.4.1.2.1 Qualitative declaration

Losartan Potassium USP

1.4.1.2.2 Quantitative declaration

Sr. No.	Ingredients Chemical Name	Specification	Standard Quantity (mg/Tablet)	Reason for Inclusion
01	Losartan Potassium	USP-NF	50.00	Anti-Hypertensive
02	Microcrystalline Cellulose (pH 102)	BP	58.00	Diluent
03	Lactose Monohydrate	USP-NF	36.00	Diluent
04	Croscarmellose Sodium	USP-NF	10.00	Disintegrant
05	Magnesium Stearate	BP	3.000	Lubricant
06	Colloidal Anhydrous Silica (Aerosil)	BP	3.000	Glidant
07	Colour Erythrosin Pink SC-SP-2006	IHS	4.000	Coating agent
08	Isopropyl Alcohol	BP	32.00	Solvent
09	Dichloromethane	BP	48.00	Solvent

1.4.1.3 Pharmaceutical Form

Oral Tablets

Pink coloured, round shaped, biconvex, film coated tablet, plain on both sides.

1.4.1.4 Clinical Particulars

1.4.1.4.1 Therapeutic Indications

It is indicated for the treatment of Hypertension: It may be used alone or in combination with other antihypertensive agents, including diuretics. Hypertensive patients with left ventricular hypertrophy: It is indicated to reduce the risk of stroke in patients with hypertension and left ventricular hypertrophy, but there is evidence that this benefit does not apply to Black patients and in Nephropathy in Type 2 diabetic patients: It is indicated for the treatment of diabetic nephropathy with an elevated serum creatinine and proteinuria (urinary albumin to creatinine ratio ≥300 mg/g) in patients with type 2 diabetes and a history of hypertension. In this population, losartan reduces the rate of progression of nephropathy as measured by the occurrence of doubling of serum creatinine or end stage renal disease (need for dialysis or renal transplantation).

1.4.1.4.2 Posology and Method of Administration

Method of administration: For oral use only. Patients can take this medicine with or without food. Losartan Potassium should be swallowed with a glass of water or as directed by physician. Take your normal dose immediately and continue taking your tablets at the usual time of day, do not take a double dose to make up for the missed dose.

The usual recommended doses: Adult Hypertensive Patients: Losartan may be administered with other antihypertensive agents, and with or without food. Dosing must be individualized. The usual starting dose is 50 mg once daily, with 25 mg used in patients with possible depletion of intravascular volume (e.g., patients treated with diuretics) and patients with a history of hepatic impairment. It can be administered once or twice daily with total daily doses ranging from 25 mg to 100 mg. If the antihypertensive effect measured at trough using once-a-day dosing is inadequate, a twice-a-day regimen at the same total daily dose or an increase in dose may give a more satisfactory response. The effect of losartan is substantially present within one week but in some studies the maximal effect occurred in 3-6 weeks. If blood pressure is not controlled by Losartan potassium alone, a low dose of a

diuretic may be added. Hydrochlorothiazide has been shown to have an additive effect. No initial dosage adjustment is necessary for elderly patients or for patients with renal impairment, including patients on dialysis.

Pediatric population use: Above one month of age: Limited pharmacokinetic data are available in hypertensive children above one month of age. Losartan is not recommended for use in children under 6 years old. Children and adolescents aged 6-18 years old: There are limited data on the efficacy and safety of Losartan Potassium children and adolescents aged 6-18 years old for the treatment of hypertension. **Pediatric Hypertensive Patients ≥6 years of age:** The usual recommended starting dose is 0.7 mg/kg once daily (up to 50 mg total) administered as a tablet or a suspension. Dosage should be adjusted according to blood pressure response. Doses above 1.4 mg/kg (or in excess of 100 mg) daily have not been studied in pediatric patients.

It is not recommended in pediatric patients <6 years of age or in pediatric patients with glomerular filtration rate <30 mL/min/1.73 m2.

Hypertensive Patients with Left Ventricular Hypertrophy: The usual starting dose is 50 mg once daily. Hydrochlorothiazide 12.5 mg daily should be added and/or the dose of Losartan potassium should be increased to 100 mg once daily followed by an increase in hydrochlorothiazide to 25 mg once daily based on blood pressure response.

Use in Elderly: Although consideration should be given to initiating therapy with 25 mg in patients over 75 years of age, dosage adjustment is not usually necessary for the elderly.

1.4.1.4.3 Contraindications

It is contraindicated in patient with known hypersensitivity to losartan or to any of excipients. It is also contra-indicated during pregnancy and lactation. Losartan Potassium should be discontinued as soon as possible, when pregnancy is suspected. Do not co-administer aliskiren with losartan in patients with diabetes.

1.4.1.4.4 Special Warnings and Special Precautions for Use

Hypotension Volume-Depleted Patients: In patients who are intravascularly volume-depleted (e.g., those treated with diuretics), symptomatic hypotension may occur after initiation of therapy with losartan. These conditions should be corrected prior to administration of losartan, or a lower starting dose should be used. Potassium Supplements:

A patient receiving losartan should be told not to use potassium supplements or salt substitutes containing potassium without consulting the prescribing physician.

Electrolyte Imbalance: Electrolyte imbalances are common in patients with renal impairment, with or without diabetes, and should be addressed. In a clinical study conducted in type 2 diabetic patients with proteinuria, the incidence of hyperkalemia was higher in the group treated with losartan as compared to the placebo group; however, few patients discontinued therapy due to hyperkalemia.

Impaired hepatic function: Based on pharmacokinetic data which demonstrate significantly increased plasma concentrations of losartan in cirrhotic patients, a lower dose should be considered for patients with impaired liver function.

Impaired renal function: As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function have been reported in susceptible individuals treated with losartan; in some patients, these changes in renal function were reversible upon discontinuation of therapy. In patients whose renal function may depend on the activity of the renin-angiotensin-aldosterone system (e.g., patients with severe congestive heart failure), treatment with angiotensin converting enzyme inhibitors has been associated with oliguria and/or progressive azotemia and (rarely) with acute renal failure and/or death. Similar outcomes have been reported with losartan. In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen (BUN) have been reported. Similar effects have been reported with losartan; in some patients, these effects were reversible upon discontinuation of therapy. Pediatric Use: **Above one month of age:** Limited pharmacokinetic data are available in hypertensive children above one month of age. Losartan is not recommended for use in children under 6 years old.

Children and adolescents aged 6-18 years old: There are limited data on the efficacy and safety of Losartan Potassium children and adolescents aged 6-18 years old for the treatment of hypertension. Losartan is also not recommended in children with hepatic impairment.

Geriatric Use: No overall differences in effectiveness or safety were observed in controlled clinical studies between geriatric patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Pregnancy and breast-feeding: Before taking any medicine for advice consult to direction of physician.

Pregnancy: It is contra-indicated pregnancy therefore it should not be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Use in breast-feeding: Tell your doctor if you are breast-feeding or about to start breast-feeding. It is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed, especially if your baby is a new-born or born prematurely.

Excipients with known effect: Each film coated tablet contains lactose monohydrate, patients with rare hereditary problems of galactose intolerance, total-lactase deficiency or glucose-galactose malabsorption should not take this medicine. Talk to your physician.

1.4.1.4.5 Interaction with other medicinal products and other forms of interaction

Tell your physician if you are taking potassium supplements, potassium-containing salt substitutes, potassium-sparing medicines such as certain diuretics (amiloride, triamteren, spironolactone), or other medicines that may increase serum potassium (e.g., heparin, trimethoprim-containing medicines), as the combination with losartan potassium is not advisable. Take particular co-administered with losartan potassium: other blood pressure lowering medicines as they may additionally reduce your blood pressure. Blood pressure may also be lowered by class of drugs: tricyclic antidepressants, antipsychotics, baclofen, amifostine, non-steroidal anti-inflammatory drugs such as indomethacin, including Cox-2-inhibitors (medicines that reduce inflammation, and can be used to help relieve pain) as they may reduce the blood pressure lowering effect of losartan. If patients are taking an ACE–inhibitor or aliskiren if your kidney function is impaired, the concomitant use of these medicines may lead to a worsening of the kidney function. Lithium containing medicines should not be taken in combination with losartan without close supervision by your physician. Special precautionary measures (e.g. blood tests) may be appropriate.

1.4.1.4.6 Pregnancy and Lactation

Pregnancy: It is contra-indicated pregnancy therefore it should not be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation : Tell your doctor if you are breast-feeding or about to start breast-feeding. It is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed, especially if your baby is a new-born or born prematurely.

1.4.1.4.7 Effects on ability to Drive and use Machines

Not applicable

1.4.1.4.8 Undesirable Effects

Dizziness, low blood pressure (especially after excessive loss of water from the body within blood vessels e.g. in patients with severe heart failure or under treatment with high dose diuretics), dose-related orthostatic effects such as lowering of blood pressure appearing when rising from a lyingor sitting position, debility, fatigue, too little sugar in the blood (hypoglycaemia), too much potassium in the blood (hyperkalaemia), changes in kidney function including kidney failure, reduced number of red blood cells (anaemia), increase in blood urea, serum creatinine and serum potassium in patients with heart failure. *Uncommon:* somnolence, headache, sleep disorders, feeling of increased heart rate (palpitations), severe chest pain (angina pectoris), shortness of breath (dyspnoea), abdominal pain, obstipation, diarrhoea, nausea, vomiting, hives (urticaria), itching (pruritus), rash, localised swelling (oedema), cough. *Rare:* Hypersensitivity, angioedema, inflammation of blood vessels (vasculitis including Henoch-Schönlein purpura), numbness or tingling sensation (paraesthesia), fainting (syncope), very rapid and irregular heartbeat (atrial fibrillation), brain attack (stroke), inflammation of the liver (hepatitis), elevated blood alanine aminotransferase (ALT) levels, usually resolved upon discontinuation of treatment. *Not known:* reduced number of thrombocytes, migraine,liver function abnormalities, muscle and joint pain, flu-like symptoms, back pain and urinary tract infection, increased sensitivity to the sun (photosensitivity), unexplained muscle pain with dark (tea-coloured) urine (rhabdomyolysis), impotence, inflammation of the pancreas (pancreatitis), low levels of sodium in the blood (hyponatraemia), depression, generally feeling unwell (malaise), ringing, buzzing, roaring, or clicking in the ears (tinnitus) disturbed taste (dysgeusia).Side effects in children are similar to those seen in adults.

1.4.1.4.9 Overdose

Significant lethality was observed in mice and rats after oral administration of 1000 mg/kg and 2000 mg/kg, respectively, about 44 and 170 times the maximum recommended human dose on a mg/m2 basis. Limited data are available in regard to overdosage in humans. The most likely manifestation of overdosage would be hypotension and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should

occur, supportive treatment should be instituted. Neither losartan nor its active metabolite can be removed by hemodialysis.

1.4.1.5 Pharmacological Properties

1.4.1.5.1 Pharmacodynamics Properties

Losartan is a non-peptide angiotensin II receptor antagonist with high affinity and selectivity for the AT1 receptor, without binding to or blocking other hormone receptors or ion channels important in cardiovascular regulation. Angiotensin II is a potent vasoconstrictor, a primary active hormone of the renin-angiotensin system and a major determinant of the pathophysiology of hypertension. Losartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by inhibiting the binding of angiotensin II to the AT1 receptor.

1.4.1.5.2 Pharmacokinetic Properties

Absorption: Following oral administration, losartan is well absorbed (based on absorption of radiolabeled losartan) and undergoes substantial first-pass metabolism; the systemic bioavailability of losartan is approximately 33%. About 14% of an orally-administered dose of losartan is converted to the active metabolite. Mean peak concentrations of losartan and its active metabolite are reached in 1 hour and in 3-4 hours, respectively. While maximum plasma concentrations of losartan and its active metabolite are approximately equal, the AUC of the metabolite is about 4 times as great as that of losartan. A meal slows absorption of losartan and decreases its Cmax but has only minor effects on losartan AUC or on the AUC of the metabolite (about 10% decreased)

Distribution: The volume of distribution of losartan and the active metabolite is about 34 liters and 12 liters, respectively. Both losartan and its active metabolite are highly bound to plasma proteins, primarily albumin, with plasma free fractions of 1.3% and 0.2%, respectively. Plasma protein binding is constant over the concentration range achieved with recommended doses.

Metabolism: Losartan is an orally active agent that undergoes substantial first-pass metabolism by cytochrome P450 enzymes. It is converted, in part, to an active carboxylic acid metabolite that is responsible for most of the angiotensin II receptor antagonism that follows losartan treatment. Losartan metabolites have been identified in human plasma and urine. In addition to the active carboxylic acid metabolite, several inactive metabolites are

formed. Following oral administration of 14C-labeled losartan potassium, circulating plasma radioactivity is primarily attributed to losartan and its active metabolite. The pharmacokinetics of losartan and its active metabolite are linear with oral losartan doses up to 200 mg and do not change over time. Neither losartan nor its metabolite accumulates in plasma upon repeated once-daily dosing.

Elimination: Total plasma clearance of losartan and the active metabolite is about 600 mL/min and 50 mL/min, respectively, with renal clearance of about 75 mL/min and 25 mL/min, respectively. After single doses of losartan administered orally, about 4% of the dose is excreted unchanged in the urine and about 6% is excreted in urine as active metabolite. Biliary excretion contributes to the elimination of losartan and its metabolites. Following oral 14C-labeled losartan, about 35% of radioactivity is recovered in the urine and about 60% in the feces. Half life: The terminal half-life of losartan is about 2 hours and of the metabolite is about 6-9 hours.

1.4.1.5.3 Preclinical Safety Data

Preclinical data reveal no special hazard for humans based on conventional studies of general pharmacology, genotoxicity and carcinogenic potential. In repeated dose toxicity studies, the administration of losartan induced a decrease in the red blood cell parameters (erythrocytes, haemoglobin, haematocrit), a rise in urea-N in the serum and occasional rises in serum creatinine, a decrease in heart weight (without a histological correlate) and gastrointestinal changes (mucous membrane lesions, ulcers, erosions, haemorrhages). Like other substances that directly affect the renin-angiotensin system, losartan has been shown to induce adverse effects on the late foetal development, resulting in foetal death and malformations.

1.4.1.6 Pharmaceutical Particulars

1.4.1.6.1 List of Excipients

Microcrystalline Cellulose (pH 102)

Lactose Monohydrate

Croscarmellose Sodium

Magnesium Stearate

Colloidal Anhydrous Silica

Dichloromethane

Isopropyl Alcohol

Colour Erythrosine SC-SP-2006

1.4.1.6.2 Incompatibilities

Not applicable.

1.4.1.6.3 Shelf Life

36 months

1.4.1.6.4 Special Precautions for Storage

Store below 30°C. Protect from Light & Moisture.

1.4.1.6.5 Nature and Contents of Container

10 Tablets are in Alu-Alu Blister Pack. Such 3 Alu-Alu blisters are packed in a printed carton along with packing insert

1.4.1.6.6 Special precaution for disposal and other handling

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

1.4.1.7 Marketing Authorization Holder and Manufacturing Site Addresses

1.4.1.7.1 Name and Address of Marketing Authorization Holder

Lincoln Pharmaceuticals Limited

Trimul Estate, Khatraj, Taluka: Kalol,

District: Gandhinagar Gujarat, India.

Telephone no.: +91-79-41078096

Fax: +91-79-41078062

E-mail: hiren@lincolnpharma.com;

Web site: www.lincolnpharma.com

1.4.1.7.2 Name and Address of manufacturing site(s)

Lincoln Pharmaceuticals Limited

Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
E-mail: hiren@lincolnpharma.com;
Web site: www.lincolnpharma.com

1.4.1.8 Marketing Authorization Number

To be included after obtaining first registration.

1.4.1.9 Date of First <Registration> / Renewal of The <Registration>

It will be applicable after registration of this product.

1.4.1.10 Date of Revision of the Text

02,Febuary 2023

1.4.1.11 Dosimetry (If Applicable)

Not Applicale

1.4.1.12 Instructions for preparation of radiopharmaceuticals (if Applicable)

Not Applicable