SUMMARY OF PRODUCT CHARACTERISTIC

1. Trade name of the medical product

Losartan Potassium and Hydrochlorothiazide Tablets USP

2. Pharmaceutical dosage form & Strength

Tablets

Each film coated tablet contains:

Losartan Potassium USP	50 mg
Hydrochlorothiazide BP	12.5 mg
Excipients	Q.S.

Color: Lake of Quinoline Yellow & Titanium Dioxide BP

3. Presentation

3 x 10 Tablets in Alu-Alu Blister pack

4. Qualitative and Quantitative composition

Sr. No.	Ingredients	Specifications	Quantity/ Tablet (mg)
SIFTING & MIXING			
1.	Losartan Potassium (A)	USP	50.00
2.	Hydrochlorothiazide (A)	BP	12.50
3.	Microcrystalline Cellulose (Ph 102)	BP	63.00
4.	Croscarmellose Sodium	USP(NF)	2.500
LUBRICATION			
5.	Magnesium Stearate	BP	1.500
6.	Purified Talc	BP	3.000
7.	Sodium Starch Glycolate	BP	2.500
Theoretical standard average weight (Core)			135.0
COATING			
8.	Hydroxy Propyl Methyl Cellulose 5 Cps	BP	2.170
9.	Titanium Dioxide	BP	0.150
10.	Color Quinoline Yellow Lake	In-house	0.500
11.	Propylene Glycol	BP	0.250
12.	Dichloro Methane(#)	BP	40.00
13.	Isopropyl Alcohol(#)	BP	25.00
Theoretical standard average weight (Coated)			138.0

Note:

- (A) = Quantity of the active ingredient to be calculated on the 100% assay and on anhydrous basis
- (#) = This will not remain in final product.

5. Pharmacological Class

Angiotensin II Antagonists with Thiazide Diuretics

6. **Therapeutic indication**

Losartan potassium and Hydrochlorothiazide Tablets are indicated for the treatment of hypertension and Reduced risk of stroke in hypertensive patients with left ventricular hypertrophy.

7. Dosage and directions for use:

Hypertension:

The usual starting and maintenance dose is 1 tablet once daily for most patients. For patients who do not respond adequately, the dosage may be increased to 2 tablets once daily. The maximum dose is 2 tablets once daily.

Reduction in the risk of stroke in hypertensive patients with left ventricular hypertrophy:

The usual maintenance dose of Losartan potassium and Hydrochlorothiazide is one tablet of Losartan potassium and Hydrochlorothiazide 50mg/12.5mg (Losartan 50mg/HCTZ 12.5mg) once daily. For patients who do not respond adequately to Losartan potassium and Hydrochlorothiazide 50mg/12.5mg, the dosage may be increased to one tablet of Losartan potassium and Hydrochlorothiazide 100mg/25mg (Losartan 100mg/HCTZ 25mg) once daily. The maximum dose is one tablet of Losartan potassium and Hydrochlorothiazide 100mg/25mg once daily. In general, the antihypertensive effect is attained within three to four weeks after initiation of therapy.

8. Contraindication(s)

Losartan potassium and Hydrochlorothiazide Tablets are contraindicated in the following situations:

Patients with hypersensitivity to any component of the formulation.

Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

9. Special warnings and precautions

In patients who are intravascularly volume-depleted (e.g., those treated with diuretics), symptomatic hypotension may occur after initiation of therapy with Losartan potassium and Hydrochlorothiazide Tablets.

Losartan that act on the angiotensin system can cause injury and death to the developing fetus when used in the second and third trimesters. When pregnancy is detected, discontinue the therapy as soon as possible.

Hypersensitivity reactions to hydrochlorothiazide may occur in patients with or without a history of allergy or bronchial asthma.

Angioedema, including swelling of the larynx and glottis, causing airway obstruction and/or swelling of the face, lips, pharynx, and/or tongue has been reported rarely in patients treated with losartan.

Hepatic and renal impairment: Losartan potassium / Hydrochlorothiazide is not recommended for patients with hepatic impairment or moderate to severe renal impairment.
Pregnancy: Category C (first trimester); Category D (second and third trimester).
Lactation: It is not known whether losartan is excreted in human milk. Hydrochlorothiazide appears in human milk. Losartan potassium and Hydrochlorothiazide Tablets are not recommended in nursing woman. If required, use with caution.

10. Interactions with other drugs and other substances

Losartan potassium:

Lithium— Plasma levels of lithium may be elevated, increasing the risk of toxicity.
Rifamycins (eg, rifampin): May lead to reduced plasma Losartan levels, decreasing the antihypertensive effects.
Amifostine: Antihypertensives may enhance the hypotensive effect of Amifostine.
Fluconazole: May decrease the metabolism of Losartan.

Hydrochlorothiazide:

When given concurrently, the following drugs may interact with Hydrochlorothiazide:
Alcohol, barbiturates, or narcotics—potentiating of orthostatic hypotension may occur.
Antidiabetic drugs (oral agents and insulin)—dosage adjustment of the ant diabetic drug may be required.
Other antihypertensive drugs—there may be an additive effect.
Cholestyramine and colestipol resins— Absorption of hydrochlorothiazide may be impaired.
Corticosteroids, ACTH- there may be intensified electrolyte depletion, particularly hypokalaemia.
Nondepolarizing skeletal muscle relaxants (eg, turbocurarine) — Responsiveness to muscle relaxant may be increased.
Lithium— Plasma levels of lithium may be elevated, increasing the risk of toxicity.
Non-steroidal anti-inflammatory drugs— Antihypertensive, diuretic, and natriuretic effects of hydrochlorothiazide may be reduced.

11. Adverse effects

Cardiovascular: Chest pain, orthostatic hypotension
Central nervous system: Fatigue
Endocrine& metabolic: Hypoglycemia, Hypokalemia
Gastrointestinal: Diarrhea, Anorexia, epigastric distress
Genitourinary: Urinary tract infection
Hematologic: Anemia
Neuromuscular & skeletal: Weakness, back pain
Respiratory: Cough
Dermatologic: Photosensitivity

12. Pharmacological Action

Losartan potassium:

Angiotensin II [formed from angiotensin I in a reaction catalyzed by angiotensin converting enzyme (ACE, kininase II)], is a potent vasoconstrictor, the primary

vasoactive hormone of the renin-angiotensin system and an important component in the pathophysiology of hypertension. It also stimulates aldosterone secretion by the adrenal cortex. Angiotensin II binds to the AT1 receptor found in many tissues (e.g. vascular smooth muscle, adrenal gland, kidneys, and the heart) and elicits several important biological actions, including vasoconstriction and the release of aldosterone. Losartan and its principal active metabolite block the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor. Affinity of losartan for the AT1 receptor is 1000 times greater than the AT2 receptor. Losartan increases urinary flow rate and in addition to being natriuretic and kaliuretic, increases excretion of chloride, magnesium, uric acid, calcium, and phosphate.

Hydrochlorothiazide:
Hydrochlorothiazide inhibits reabsorption of sodium and chloride in ascending loop of Henle and early distal tubules causing increased excretion of sodium and water as well as potassium and hydrogen ions.

13. Pharmacokinetic

Losartan potassium:
Losartan is well absorbed and undergoes first-pass metabolism, forming an active carboxylic acid metabolite and other inactive metabolites. The systemic bioavailability of losartan tablets is approximately 33%. Mean peak concentrations of losartan and its active metabolite are reached in 1 hour and in 3-4 hours, respectively. Both losartan and its active metabolite are ≥ 99% bound to plasma proteins, primarily albumin. The volume of distribution of losartan is 34 L. About 14% of an orally-administered dose of losartan is converted to its active metabolite (carboxylosartan) by CYP2C9 and CYP3A4. When losartan is administered orally, about 4% of the dose is excreted unchanged in the urine, and about 6% of the dose is excreted in the urine as active metabolite. Plasma concentrations of losartan and its active metabolite decline polyexponentially with a terminal half-life of about 2 hours and 6-9 hours, respectively.

Hydrochlorothiazide:
Hydrochlorothiazide is rapidly absorbed from the gastrointestinal tract. It is reported to have a bioavailability of about 65 to 70%. It has been estimated to have a plasma half-life of between about 5 and 15 hours. Hydrochlorothiazide is widely distributed in body tissue. Hydrochlorothiazide appears to be preferentially bound to red blood cells. Protein binding is about 68%. Its apparent volume of distribution is 3.6 to 7.8 L/kg. Hydrochlorothiazide is not metabolized but is eliminated rapidly by the kidney. Hydrochlorothiazide is excreted mainly unchanged (up to 61% of dose administered) in the urine. Elimination half-life of about 5.6-14.8 hr.

14. Shelf-life
36 months

15. Special precautions for storage
Store below 30°C. Protect from light.

16. Condition of Prescription
Prescription Medicine