Safety Data Sheet
Losartan Potassium-Hydrochlorothiazide Tablets

Strength: 50-12.5 mg Tablets **Pack Size:** 30, 90, 1,000 and 5,000 Tablets per bottle
Strength: 100-25 mg Tablets **Pack Size:** 30, 90, 1,000 and 4,000 Tablets per bottle **Revision No.:** 02

EMERGENCY OVERVIEW

Each Losartan potassium hydrochlorothiazide Tablets intended for oral administration contains Losartan potassium, hydrochlorothiazide and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

Section 1. Identification

Identification of the product

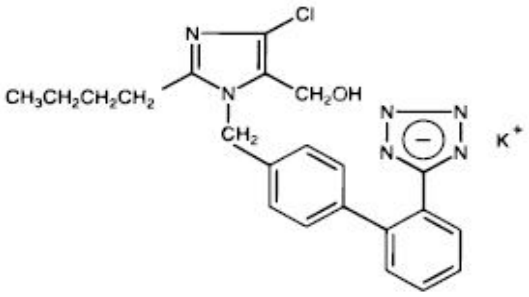
Product name: Losartan Potassium Hydrochlorothiazide Tablets

Formula: Losartan Potassium ($C_{22}H_{22}ClKN_6O$) &
Hydroclorothiazide ($C_7H_8ClN_3O4S_2$)

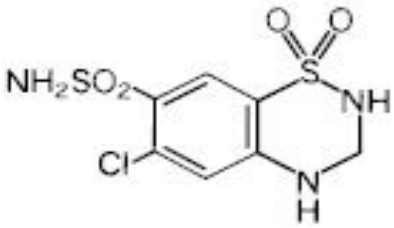
Chemical Name:

Losartan Potassium :
2-butyl-4-chloro-1-[*p*-(*o*-1*H*-tetrazol-5- ylphenyl) benzyl] imidazole-5-methanol mono potassium salt.

Hydroclorothiazide:
6-chloro-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide



Losartan potassium



Hydrochlorothiazide

Manufacturer / supplier identification

Company:	**Cadila Healthcare Ltd. Ahmedabad, India**
Address:	Sarkhej – Bavla. N.H. 8A, Moraiya. Tal. Sanand. Dist. Ahmedabad – 382210. State: Gujarat. India
Contact for information:	Tel.: +91 79 6868100 Fax: +91 79 3750319
Emergency Telephone No.	Tel.: +91 79 6868100
Recommended use / Therapeutic Category	Losartan potassium is an angiotensin II receptor (type AT_1) antagonist Hydrochlorothiazide is a diuretic.
Restriction on Use / Contraindications:	Losartan potassium-hydrochlorothiazide tablets are Contraindicated in patients who are hypersensitive to any component of this product. Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

Section 2. Hazard(s) Information

Dose and Administration

Hypertension:
Dosing must be individualized. The usual starting dose of losartan is 50 mg once daily, with 25 mg recommended for patients with intravascular volume depletion. Losartan can be administered once or twice daily at total daily doses of 25 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.

Hydrochlorothiazide is effective in doses of 12.5 to 50 mg once daily and can be given at doses of 12.5 to 25 mg as losartan potassium-hydrochlorothiazide tablets.

To minimize dose-independent side effects, it is usually appropriate to begin combination therapy only after a patient has failed to achieve the desired effect with monotherapy.

Adverse Effects

Losartan potassium-hydrochlorothiazide tablets may cause the following side effects that may be serious:
- Injury or death of unborn babies.
- Allergic reaction. Symptoms of an allergic reaction are swelling of the face, lips, throat, or tongue.

- Low blood pressure (hypotension). Low blood pressure may cause you to feel faint or dizzy.
- A new or worsening condition called systemic lupus erythematosus (Lupus; SLE)

If you have liver problems, you may see a worsening in how well your liver works. The most common side effects of losartan potassium-hydrochlorothiazide tablets in people with high blood pressure are:

- "colds" (upper respiratory infection)
- dizziness
- stuffy nose
- back pain
- fast or irregular heartbeat (palpitations)
- rash

Over Dose Effect

Losartan Potassium:

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.

Hydrochlorothiazide:

The oral LD_{50} of hydrochlorothiazide is greater than 10g/kg in both mice and rats. The most common signs and symptoms observed are those caused by electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration resulting from excessive diuresis. If digitalis has also been administered, hypokalemia may accentuate cardiac arrhythmias. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established.

Medical Conditions

Impaired Hepatic Function:

Losartan Potassium and Hydrochlorothiazide:

Losartan potassium and hydrochlorothiazide tablets are not recommended for patients with hepatic impairment who require titration with losartan. The lower starting dose of losartan recommended for use in patients with hepatic impairment cannot be given using losartan potassium and hydrochlorothiazide tablets.

Hydrochlorothiazide:

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Hypersensitivity Reaction:

Hypersensitivity reactions to hydrochlorothiazide may occur in patients with or without a history of allergy or bronchial asthma, but are more likely in patients with such a history.

Systemic Lupus Erythematosus:

Thiazide diuretics have been reported to cause exacerbation or activation of systemic lupus erythematosus.

Lithium Interaction:

Lithium generally should not be given with thiazides. Monitor serum lithium levels in patients receiving lithium and hydrochlorothiazide.

Acute Myopia and Secondary Angle-Closure Glaucoma

Hydrochlorothiazide, a sulfonamide, can cause an idiosyncratic reaction, resulting in acute transient myopia and acute angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to weeks of drug initiation. Untreated acute angle-closure glaucoma can lead to permanent vision loss. The primary treatment is to discontinue hydrochlorothiazide as rapidly as possible. Prompt medical or surgical treatments may need to be considered if the intraocular pressure remains uncontrolled. Risk factors for developing acute angle-closure glaucoma may include a history of sulfonamide or penicillin allergy.

Contraindications

Losartan potassium-hydrochlorothiazide tablets are Contraindicated in patients who are hypersensitive to any component of this product.

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

Pregnancy Comments

Fetal/Neonatal Morbidity and Mortality:

Drugs that act directly on the renin-angiotensin system can cause fetal and neonatal morbidity and death when administered to pregnant women. Several dozen cases have been reported in the world literature in patients who were taking angiotensin converting enzyme inhibitors. When pregnancy is detected, losartan potassium-hydrochlorothiazide tablets should be discontinued as soon as possible.

The use of drugs that act directly on the renin-angiotensin system during the second and third trimesters of pregnancy has been associated with fetal and neonatal injury, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Oligohydramnios has also been reported, presumably resulting from decreased fetal renal function; oligohydramnios in this setting has been associated with fetal limb contractures, craniofacial deformation, and hypoplastic lung development. Prematurity, intrauterine growth

retardation, and patent ductus arteriosus have also been reported, although it is not clear whether these occurrences were due to exposure to the drug.
These adverse effects do not appear to have resulted from intrauterine drug exposure that has been limited to the first trimester.

Mothers whose embryos and fetuses are exposed to an angiotensin II receptor antagonist only during the first trimester should be so informed. Nonetheless, when patients become pregnant, physicians should have the patient discontinue the use of losartan potassium- hydrochlorothiazide tablets as soon as possible.

Rarely (probably less often than once in every thousand pregnancies), no alternative to an angiotensin II receptor antagonist will be found. In these rare cases, the mothers should be apprised of the potential hazards to their fetuses, and serial ultrasound examinations should be performed to assess the intra-amniotic environment.

If oligohydramnios is observed, losartan potassium-hydrochlorothiazide tablets should be discontinued unless it is considered life-saving for the mother. Contraction stress testing (CST), a non-stress test (NST), or biophysical profiling (BPP) may be appropriate, depending upon the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury.

Infants with histories of in utero exposure to an angiotensin II receptor antagonist should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion. Exchange transfusion or dialysis may be required as means of reversing hypotension and/or substituting for disordered renal function.

Pregnancy Category Pregnancy Categories C (first trimester) and D (second and third trimesters)

Section 3. Composition / information on ingredients

Component	Exposure Limit	CAS No.
Principle Component :		
Losartan Potassium	Not Found	124750-99-8
Hydrochlorothiazide	Not Found	58-93-5

Inactive Ingredients :

Lactose monohydrate	Not Found	64044-51-5
Magnesium stearate	Not Found	557-04-0
Maize starch	Not Found	9005-25-8
Microcrystalline cellulose	Not Found	9004-34-6
Polyethylene glycol	Not Found	25322-68-3
Sodium starch glycolate	Not Found	9063-38-1
Talc	Not Found	14807-96-6
Titanium dioxide.	Not Found	13463-67-7

Section 4. First - aid measures

General Remove from exposure. Remove contaminated Clothing. Person developing serious hypersensitivity reaction must receive medical attention

Overdose Treatment If symptomatic hypotension should occur, supportive treatment should be instituted.

Neither losartan nor its active metabolite can be removed by hemodialysis.

Section 5. Fire - fighting measures

Flash point	Not Found	**Upper Flammable Limit:**	Not Found
Auto-Ignition Temperature:	Not Found	**Lower Flammable Limit:**	Not Found
Extinguishing Media	Water Spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and material.	**Fire and Explosion Hazard**	This material is assumed to be combustible. As with all dry powders it is advisable to ground mechanical equipment in contact with the dry material to dissipate the potential build-up of static electricity.

Fire Fighting Procedure	As with all fires, evacuate personnel to a safe area. Fire fighter should use self- contained breathing equipment and protective clothing.

Section 6. Accidental Release Measures

Spill Response	Wear approved respiratory protection, chemically compatible gloves and protective clothing. Wipe up spillage or collect spillage using high efficiency vacuum cleaner. Avoid breathing dust. Place spillage in appropriately labelled container for disposal. Wash spill site.

Section 7. Handling and Storage

Storage	Store at 20° to 25°C (68° to 77°F)) [See USP Controlled Room Temperature]. Keep container tightly closed. Protect from light
Incompatibilities:	No data available.

Section 8. Exposure controls / personal protection

Respiratory Protection	Protection from inhalation is not normally necessary. If ventilation is inadequate or dust is likely to generate, use of suitable dust mask would be appropriate.
Skin Protection	Skin protection is not normally necessary, however it is good practice to avoid contact with chemical to use suitable gloves when handling.
Eye protection	Eye protection is not normally necessary. If concerned wear protective goggles or glasses. Wash hands prior to touching eye and in particular handling contact lenses.
Protective Clothing	Protective clothing is not normally necessary, however it is good practice to use apron.
Engineering Control	Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Section 9. Physical and chemical properties

Appearance	Losartan Potassium-Hydrochlorothiazide 50-12.5 mg Tablets, are white to off-white, capsule-shaped, film-coated tablets debossed with “ZD18” on one side and plain on other side. Losartan Potassium-Hydrochlorothiazide 100-25 mg Tablets, are white to off-white, capsule-shaped, film-coated tablets debossed with “ZD19” on one side and plain on other side.

Solubility in water	No Data Available	**Odour**	Odourless
Boiling point	No Data Available	**Melting Point**	No Data Available
Evaporation rate	No Data Available	**Vapour density**	No Data Available
Reactivity in water	No Data Available	**Evaporation rate**	No Data Available
% Volatile by volume	No Data Available	**Specific gravity**	No Data Available
		Vapour pressure	No Data Available

Other information Losartan potassium is off-white to creamish-yellow powder with a molecular weight of 461.01. It is soluble in water.

Hydrochlorothiazide is a white or practically white, practically odorless crystalline powder with a molecular weight of 297.74. It is slightly soluble in water; freely soluble in sodium hydroxide solution, in n-butylamine, and in dimethylformamide, sparingly soluble in methanol; insoluble in ether, in chloroform, and in dilute mineral acids.

Section 10. Stability and Reactivity

Condition to avoid	Avoid exposure to extreme heat, light and moisture.	**Stable**	Stable under normal ambient and anticipated storage and handling conditions.
Decomposition Products	No Data Available	**Hazardous Reaction**	No data available.
Incompatibilities:	No data available.		

Section 11. Toxicological information

General Handling of formulated product is not expected to cause any toxicological affects. The data pertains to the ingredient in formulations, rather than this specie formulation.

Target organ Refer contraindication and adverse effect.

Other Not Available

Section 12. Ecological information

Do not allow product to enter drinking water supplies, waste water or soil

Section 13. Disposal Consideration

Dispose the waste in accordance with all applicable Federal, State and local laws.

Section 14. Transport Information

The product is not hazardous when shipping via air (IATA), ground (DOT), or sea (IMDG).

Section 15. Regulatory Information

Generic Medicine. Approved by USFDA & the ANDA Number is 078385

Section 16. Other information

None

Date of issue: 28/05/2015 **Supersedes edition of:** 01

The information contained herein is based on the state of our knowledge. It Characterises the product with regard to the appropriate safety precautions. It does not represent a guarantee of the properties of the product.