Safety Data Sheet
LOSARTAN POTASSIUM TABLETS, USP

Strength: 25mg **Pack Size:** 30, 90, 1000 and 10,000 Tablets per bottle
Strength: 50mg **Pack Size:** 90,100, 1000 and 10, 000 Tablets per bottle
Strength: 100mg **Pack Size:** 90,100, 1000 and 5000 Tablets per bottle **Revision No.:** 02

EMERGENCY OVERVIEW

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

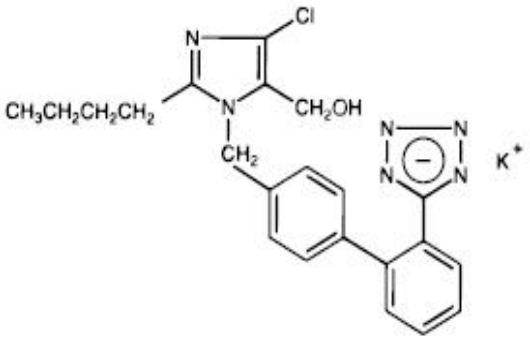
Section 1. Identification

Identification of the product

Product name: **Losartan Potassium Tablets, USP**

Formula: $C_{22}H_{22}ClKN_6O$

Chemical Name: 2-butyl-4-chloro-1-[*p*-(*o*-1*H*-tetrazol-5-ylphenyl) benzyllimidazole-5-methanol monopotassium salt.



Manufacturer / supplier identification

Company: **Cadila Healthcare Ltd. Ahmedabad, India**

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Recommended use / Therapeutic Category Losartan potassium is an angiotensin II receptor (type AT_1) antagonist.

Restriction on Use / Contraindications:	Losartan potassium tablets are contraindicated in patients who are hypersensitive to any component of this product.

Section 2. Hazard(s) Information

Dose and Administration	**Adult Hypertensive Patients:** Losartan potassium tablets may bead ministered withother antihypertensive agents, and with or without food. Dosing must be individualized. The usual starting dose of losartan potassium tablets is 50 mg once daily, with 25 mg used in patients with possible depletion of intravascular volume and patients with a history of hepatic impairment . Losartan potassium tablets can be administered once or twice daily with total daily doses ranging from 25 mg to 100 mg. **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.
Adverse Effects	**Body as a Whole:** Facial edema, fever, orthostatic effects, Cardiovascular: Angina pectoris, second degree AV block, CVA, hypotension, myocardial infarction, arrhythmias including atrial fibrillation, palpitation, sinus bradycardia, tachycardia, ventricular tachycardia, ventricular fibrillation **Digestive:** Anorexia, constipation, dental pain, dry mouth, flatulence, gastritis, vomiting **Hematologic:** Anemia **Metabolic:** Gout **Musculoskeletal:** Arm pain, hip pain, joint swelling, knee pain, musculoskeletal pain, shoulder pain, stiffness, arthralgia, arthritis, fibromyalgia, muscle weakness **Nervous System/Psychiatric:** Anxiety, anxiety disorder, ataxia, confusion, depression, dream abnormality, hypesthesia, decreased libido, memory impairment, migraine, nervousness, paresthesia, peripheral neuropathy, panic disorder, sleep disorder, somnolence, tremor, vertigo **Respiratory:** Dyspnea, bronchitis, pharyngeal discomfort, epistaxis, rhinitis, respiratory congestion **Skin:** Alopecia, dermatitis, dry skin, ecchymosis, erythema, flushing, photosensitivity, pruritus, rash, sweating, urticaria **Special Senses:** Blurred vision, burning/stinging in the eye, conjunctivitis, taste perversion, tinnitus, decrease in visual acuity **Urogenital:** Impotence, nocturia, urinary frequency, urinary tract infection

Over Dose Effect	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.
Medical Conditions	In the unusual case that there is no appropriate alternative to therapy with drugs affecting the renin-angiotensin system for a particular patient, apprise the mother of the potential risk to the fetus. Perform serial ultrasound examinations to assess the intra-amniotic environment. If oligohydramnios is observed, discontinue losartan potassium, unless it is considered life-saving for the mother. Fetal testing may be appropriate, based on the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury. Closely observe infants with histories of *in utero* exposure to losartan potassium for hypotension, oliguria, and hyperkalemia. Losartan potassium has been shown to produce adverse effects in rat fetuses and neonates, including decreased body weight, delayed physical and behavioral development, mortality and renal toxicity. With the exception of neonatal weight gain (which was affected at doses as low as 10 mg/kg/day), doses associated with these effects exceeded 25 mg/kg/day (approximately three times the maximum recommended human dose of 100 mg on a mg/m^2 basis). These findings are attributed to drug exposure in late gestation and during lactation. Significant levels of losartan and its active metabolite were shown to be present in rat fetal plasma during late gestation and in rat milk. **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 potassium tablets. These conditions should be corrected prior to administration of losartan potassium tablets, or a lower starting dose should be used
Contraindications	Losartan potassium tablets are contraindicated in patients whare hypersensitive to any component of this product.

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 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 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 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.

Losartan potassium has been shown to produce adverse effects in rat fetuses and neonates, including decreased body weight, delayed physical and behavioral development, mortality and renal toxicity. With the exception of neonatal weight gain (which was affected at doses as low as 10 mg/kg/day), doses associated with these effects exceeded 25 mg/kg/day (approximately three times the maximum recommended human dose of 100 mg on a mg/m2 basis). These findings are attributed to drug exposure in late gestation and during lactation. Significant levels of losartan and its active metabolite were shown to be present in rat fetal plasma during late gestation and in rat milk.

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
Inactive Ingredients :		
Colloidal Silica Anhydrous	Not Found	99439-28-8
Hydroxypropyl Cellulose (Low Substituted)	Not Found	9004-64-2
Hypromellose	Not Found	9004-65-3
Lactose Monohydrate	Not Found	64044-51-5

Maize Starch	Not Found	9005-25-8
Microcrystalline Cellulose	Not Found	9004-34-6
Polyethylene Glycol	Not Found	25322-68-3
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) 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 Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Section 9. Physical and chemical properties

Appearance Losartan Potassium Tablets USP, 25 mg are white to off-white, capsule-shaped, film-coated tablets debossed with the logo of “Z” on one side and “2”on other side

Losartan Potassium Tablets USP, 50 mg are white to off-white, capsule-shaped, film-coated tablets debossed with the logo of “Z16” on one side and plain on other side.

Losartan Potassium Tablets USP, 100 mg are white to off-white, capsule-shaped,film-coated tablets debossed with the logo of "Z18" 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. Oxidation of the 5-hydroxymethyl group on the imidazole ring results in the active metabolite of losartan.

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 078243

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.