LOTAN
Losartan Potassium 25/50

GENERIC NAME: Losartan Potassium

PHARMALOGICAL CATEGORY: Angiotensin II Receptor Antagonist

THERAPEUTIC CATEGORY: Antihypertensive

COMPOSITION AND PRESENTATION:

LOTAN 25

Composition:

Each film coated tablet contains Losartan potassium 25 mg.

Presentation:

30 Tablets x 5 Blisters

LOTAN 50

Composition:

Each film coated tablet contains Losartan potassium 50 mg.

Presentation:

30 Tablets x 5 Blisters

MECHANISM OF ACTION:

Angiotensin II (formed from angiotensin I in a reaction catalyzed by angiotensin converting enzyme, ACE) is a very potent chemical that causes the muscles surrounding the blood vessels to contract, which thereby narrows the blood vessels. This narrowing increases the pressure within the vessels and can cause high blood pressure (hypertension). It is also the primary vasoactive hormone of the renin-angiotensin system which is an important component in the pathophysiology of hypertension. It also stimulates aldosterone secretion by the adrenal cortex. These all effects of Angiotensin II cause high blood pressure.

Angiotensin receptor blockers (ARBs) are medications that block the vasoconstriction and aldosteron secreting action of angiotensin II by selectively blocking the binding of angiotensin II to the Angiotensin I receptor found in many tissues, (e.g., vascular smooth muscle, adrenal gland). The lower blood pressure makes it easier for the heart to pump blood and can improve heart failure. In addition, the progression of kidney disease due to high blood pressure or diabetes is slowed.

There is also an AT2 receptor found in many. Both losartan and its principal active metabolite do not exhibit any partial agonist activity at the AT1 receptor and have much greater affinity (about 1000-fold) for the AT1 receptor than for the AT2 tissues but it is not known to be associated with cardiovascular homeostasis receptor. As a result, the blood vessels dilate and the blood pressure is reduced.

INDICATIONS:

- For controlling high blood pressure, can be used alone or with combination other antihypertensive agents including diuretics.

- For Hypertensive Patients with Left Ventricular Hypertrophy to reduce the risk of stroke. (But there is evidence that this benefit does not apply to Black patients.)
- For treating heart failureFor preventing kidney failure in people with diabetes or high blood pressure.
- For treating 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.

NOTE: Since these medications have effects that are similar to those of ACE inhibitors, they are often used when an ACE inhibitor cannot be tolerated by patients.

DOSE:
Lotan may be given with or without food.

For hypertension in adults: 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); but with history of hepatic impairment patients the dose once or twice daily with total daily doses ranging from 25 mg to 100 mg.
The effect of losartan is substantially present within one week but in some studies the maximal effect occurred in 3-6 weeks
NOTE: If blood pressure is not controlled by LOTAN alone, a low dose of a diuretic may be added. Hydrochlorothiazide has been shown to have an additive effect.

For hypertension in pediatric 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. For pediatric patients of less than 6yrs , the drug is not recommended.

For 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 should be increased to 100 mg once daily followed by an increase in hydrochlorothiazide to 25 mg once daily based on blood pressure

For Nephropathy in Type 2 Diabetic Patients: The usual starting dose is 50 mg once daily. The dose should be increased to 100 mg once daily based on blood pressure response. LOTAN may be administered with insulin and other commonly used hypoglycemic agents (e.g., sulfonylureas, glitazones and glucosidase inhibitors).

PHARMACOKINETIC:

- Well absorbed orally,
- Undergoes substantial first pass metabolism by cytochrome P450 enzymes.
- Bioavailability is approximately 33%
- About 40% of an orally administered dose is converted to an active carboxylic acid metabolite in the liver by cytochrome P450 enzymes that is responsible for most of the drug activity in addition several inactive metabolites are also formed.

- Excretion is biliary, about 35% of the dose is recovered in the urine and 65% in the faeces. About 4% of the dose is excreted unchanged in the urine and about 6% is excreted in urine as active metabolite.
- Onset of Action: Peak Plasma concentration is 1hr and its metabolite is 3-4hrs.
- Duration of Action: Terminal half life is about 2hrs and its metabolite is 6-9hrs.
- 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.
- A meal slows absorption of losartan.

ADVERSE EFFECTS EFFECTS:

The most common side effects are as follows:

- Cough,
- Elevated potassium levels,
- Low blood pressure,
- Dizziness,
- Headache,
- Drowsiness,
- Diarrhea,
- Abnormal taste sensation (metallic or salty taste), and rash.
- The most serious, but rare, side effects are
- Kidney failure,
- Liver failure,
- Allergic reactions,
- A decrease in white blood cells, and
- Swelling of tissues (angioedema).

CONTRAINDICATIOIN:

Pregnanant Patients:

It is not prescribed for pregnant patients because they may cause birth defects. When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus.

Nursing Mothers:

Lotan is contraindicated in Nursing mothers.

Kidney Problem Patients:

It is not prescribed for those individuals with severe kidney problems.

Liver Problem:

Reduction in dose by 50% is suggested in patients with impaired liver function.

Hypersensitivity:

It is not prescribed to those patients who have had a severe reaction to ARBs, probably should avoid them.

Children:
Losartan's safety and efficacy in children has not been established.

DRUG INTERACTIONS:

- **With Potassium**:
  May increase blood levels of potassium. Therefore, the use of potassium supplements, salt substitutes (which often contain potassium), or other drugs that increase potassium may result in excessive blood potassium levels.
- **With Lithium**:
  May also increase the blood concentration of lithium and lead to an increase in side effects from lithium.
- **With Rifampin**:
  Rifampin reduces the blood levels of losartan and reduces the effect of Losartan.
- **With Fluconazole**:
  Fluconazole reduces the conversion of losartan to its active form. This effect could decrease the effects of Losartan.
- **With Inhibitors of Cytochrome P450:**
  Inhibitors of cytochrome p450 such as ketoconazole (Nizoral) have been shown in lab studies to inhibit the formation of the active drug metabolite. Therefore, caution should be used when adding losartan to a patient taking Nizoral, as reduced activity of losartan would be expected.

For further information, please contact:
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