LOSARTAN POTASSIUM

NEOSARTAN®

50 mg Film-coated Tablet
100 mg Film-coated Tablet

ANGIOTENSIN II RECEPTOR BLOCKER (ARB)

FORMULATION:
Each film-coated tablet contains:
Losartan potassium..... 50mg & 100mg

DESCRIPTION:
Losartan potassium (Neosartan®) 50mg Tablet is a white to off-white, oblong, biconvex, film-coated tablet, plain on both sides.
Losartan potassium (Neosartan®) 100mg Tablet is a white to off-white, oval, biconvex, film-coated, plain on both sides.

PHARMACODYNAMICS:
Losartan inhibits the pressor effect of angiotensin II (as well as angiotensin I) infusions. A dose of 100 mg inhibits the pressor effect by about 85% at peak with 25-40% inhibition persisting for 24 hours. Removal of the negative feedback of angiotensin II causes a doubling to tripling in plasma renin activity and consequent rise in angiotensin II plasma concentration in hypertensive patients. Losartan does not affect the response to bradykinin, whereas ACE inhibitors increase the response to bradykinin. Aldosterone plasma concentrations fall following losartan administration. In spite of the effect of losartan on aldosterone secretion, very little effect on serum potassium was observed.

The effect of losartan is substantially present within one week but in some studies the maximal effect occurred in 3-6 weeks. In long-term follow-up studies (without placebo control) the effect of losartan appeared to be maintained for up to a year. There is no apparent rebound effect after abrupt withdrawal of losartan. There was essentially no change in average heart rate in losartan-treated patients in controlled trials.

PHARMACOKINETICS:
Losartan potassium is an angiotensin II receptor antagonist with antihypertensive activity due mainly to selective blockage of AT_1 receptors and the consequent reduced pressure effect on angiotensin II.

Losartan potassium is readily absorbed from the gastrointestinal tract following oral administration, with an oral bioavailability of about 33%. It undergoes first-pass metabolism to form an active carboxylic acid metabolite E-3174 (EXP-3174), which has greater pharmacological activity than Losartan and some inactive metabolites. Metabolism is primarily by cytochrome P450 isoenzyme CYP2C9 and CYP3A4. Peak plasma concentrations of Losartan and E-3174 occur about 1 hour and 3 to 4 hours respectively, after an oral dose. Both Losartan and E-3174 are more than 98% bound to plasma proteins.
Losartan is excreted in the urine and in the feces via bile, as unchanged drug and metabolites. Following oral dosing, about 35% of the dose is excreted in the urine, and about 60% in the feces. The terminal elimination half-lives of Losartan and E-3174 are about 1.5 to 2.5 hours and 3 to 9 hours respectively.

INDICATIONS:
Losartan potassium is used in the management of hypertension and may have role in patients who develop cough with ACE inhibitors. Management of diabetic nephropathy.

PRECAUTIONS:
Losartan potassium should be used with care, if at all, during breast feeding. It should be used with caution in patients with renal artery stenosis. Reduced doses may be required in patients with renal or hepatic impairment. Patients with volume depletion may experience hypotension.
Vulnerable group: No dosage adjustment needed for renal failure and elderly. Decrease the dosage in hepatic insufficiencies. Medication error.

CONTRAINDICATION:
Losartan potassium is contraindicated in pregnancy. Hypersensitivity.

PREGNANCY AND LACTATION:
Pregnancy Category D
Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Resulting oligohydramnios can be associated with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death. When pregnancy is detected, discontinue losartan as soon as possible. These adverse outcomes are usually associated with use of these drugs in the second and third trimester of pregnancy. Most epidemiologic studies examining fetal abnormalities after exposure to antihypertensive use in the first trimester have not distinguished drugs affecting the renin-angiotensin system from other antihypertensive agents.

Appropriate management of maternal hypertension during pregnancy is important to optimize outcomes for both mother and fetus.

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 (Neosartan®), unless it is considered lifesaving 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 (Neosartan®) 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.

Nursing Mothers
It is not known whether losartan is excreted in human milk, but significant levels of losartan and its active metabolite were shown to be present in rat milk. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

ADVERSE EFFECTS:
Nervous System Disorders: dizziness, headache
Vascular Disorders: dosed-related orthostatic hypotension particularly in patients with volume depletion (for example those who received high-dose diuretics)
Respiratory Tract Disorders: dyspnea, cough
Gastrointestinal Disorders: abdominal pain, constipation, diarrhea, nausea, vomiting
Blood and Lymphatic System Disorders: neutropenia
Skin and Subcutaneous Disorders: rash, pruritus, urticaria, angioedema
Renal Disorders: impaired renal function
Musculoskeletal Disorders: myalgia
General Disorders: fatigue, back pain
Investigational: Hyperkalemia in patients with renal disease, elevated liver enzymes

OVERDOSE AND TREATMENT:
Regarding the overdosage there are limited data available. The most likely sign and symptoms of overdosage would be hypotension and tachycardia; bradycardia may occur from parasympathetic (vagal) stimulation. If symptomatic hypotension occur, the supportive treatment should be made.

DRUG INTERACTIONS:
The antihypertensive effects of losartan may be potentiated by drugs or other agents that lower blood pressure. An additive hyperkalemic effect is possible; supplements, potassium-sparing diuretics or other drugs that can cause hyperkalemia; losartan and potassium-sparing diuretics should not generally be given together. NSAIDs should be used with caution in patients taking losartan as the risk of renal impairment may be increased, particularly in those who are adequately hydrated; use of NSAIDs may also attribute to hypotensive effect of losartan. Losartan and some other angiotensin II receptor antagonist are metabolized by cytochrome P450 isoenzymes and interactions may occur with drugs that affect these enzymes.

DOSAGE AND ADMINISTRATION:
Adult Hypertension:
Usual Dose: 50 mg once daily.
This dose may be increased if necessary to 100 mg daily as a single dose or in two divided doses.
Use in Elderly:
An initial dose of 25 mg once daily may be used in the elderly over 76 years.
Use in Patients with Renal Impairment:
An initial dose of 25 mg once daily may be used for patients with moderate to severe renal impairment (creatinine clearance less than 20 mL per minute).
Use in Patients with Intravascular Volume Depletion:
An initial dose of 25 mg once daily may be used for patients with intravascular fluid depletion.
Or as prescribed by a physician.

WARNING:
Should be discontinued when pregnancy is diagnosed.

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph
Patient should seek medical attention immediately at the first sign of any adverse drug reaction.

Store at temperatures not exceeding 30°C.

AVAILABILITY:
50mg Film-coated Tablet – Alu-White PVC Blister Pack x 10's
(Box of 30's & 300's)-DR-XY37290
100mg Film-coated Tablet – Alu-White PVC Blister Pack x 10's
(Box of 30's)-DR-XY36844

KEEP OUT OF REACH OF CHILDREN.

DATE OF FIRST AUTHORIZATION:
50mg Film-coated Tablet – January 4, 2010
100mg Film-coated Tablet – October 20, 2009

DATE OF REVISION OF PACKAGE INSERT:
October 2021

NEOSARTAN® is a registered mark of **GX INTERNATIONAL, INC.**

Manufactured by:
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For:
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RMG Corporate Center
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