Losartan Potassium

Doxar

50 mg Film-Coated Tablet

ANGIOTENSIN II RECEPTOR BLOCKER

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

PRODUCT DESCRIPTION:
White to off-white, Oblong, biconvex, film-coated tablet.

PHARMACODYNAMICS AND PHARMACOKINETICS:
Losartan potassium is a long-acting antihypertensive, nonpeptide angiotensin II type I-receptor (AT1 receptor) antagonist. Losartan reduces risk of stroke and cardiovascular death due to myocardial infarction and heart failure in hypertensive patients with left ventricular hypertrophy. Losartan provides renal protection for type 2 diabetic patients with proteinuria. Losartan is used in the management of hypertension, particularly in patients who develop cough with ACE inhibitors.

Renin, secreted within the kidney, catalyzes the formation of angiotensin I from angiotensinogen. Angiotensin converting enzyme (ACE) then converts angiotensin I to angiotensin II, the effector molecule of the renin-angiotensin system, and a major determinant of the pathophysiology of hypertension. 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, which results in increased blood pressure. Angiotensin II contributes to the development of nephropathy through several mechanisms, including constriction of the glomerular arteries leading to increased microcirculatory pressure and abnormal albumin secretion. In addition to its hemodynamic effects, angiotensin II can cause glomerular damage.

Losartan is a potent, orally active compound that binds selectively to the AT1 receptor. The maximum hypotensive effect is achieved in about 3 to 6 weeks after starting treatment. It does not bind to or block other hormone receptors or ion channels important in cardiovascular regulation. Furthermore, losartan does not inhibit ACE, the enzyme that degrades bradykinin.
Consequently, effects not directly related to blocking the AT1 receptor, such as the potentiation of bradykinin-mediated effects (e.g., cough) or the generation of edema are not associated with losartan. Angiotensin II may be synthesized through other pathways, so ACE-inhibitors may not be able to completely block angiotensin II effects.
Losartan and its potent metabolite are able to completely inhibit the physiologic effects of angiotensin II, reducing blood pressure and retarding the development of nephropathy.

Following oral administration, losartan is readily absorbed from the gastrointestinal tract. Food has minimal effect on its absorption. About 14% of an orally administered dose of losartan is converted to the active metabolite that is responsible for most of the angiotensin II receptor antagonism caused by losartan. Losartan undergoes substantial first-pass hepatic metabolism via cytochrome P-450 (CYP) isoenzymes to an active 5-carboxylic acid metabolite designated EXP-3174. This active metabolite has more potent pharmacological activity than losartan and some inactive metabolites. Losartan has a peak plasma concentration of about one hour while the metabolite E-3174 reaches peak plasma concentration in three to four hours. Plasma half-lives of losartan and EXP-3174 are 2.5 and 6 to 9 hours respectively. Both losartan and its active metabolite are highly bound to plasma proteins, primarily albumin. About 35% of the oral dose of losartan is excreted in the urine and about 60% in the feces. About 6% is excreted in urine as the active metabolite. Biliary excretion also contributes to the elimination of losartan and its metabolites.

INDICATIONS:
It is used in the management of hypertension particularly in patients who develop cough with ACE inhibitors and to reduce the risk of stroke in patients with left ventricular hypertrophy and in the treatment of diabetic nephropathy.

DOSAGE AND ADMINISTRATION:
Losartan may be administered with or without food and together with other antihypertensive agents.

The usual dose for hypertension is 50 mg once daily for most patients. The maximal antihypertensive effect is attained 3-6 weeks after initiation of therapy. Dose may be increased to 100 mg once daily or in two divided doses. A low dose of a diuretic may be added if blood pressure is not controlled by losartan alone.
Hydrochlorothiazide has been shown to have an additive effect.

It may be prudent to start with 25 mg once daily in patients with possible intravascular volume depletion (e.g., patients treated with diuretics), and in patients with hepatic impairment. Similar reduction may be appropriate in patients with hepatic or renal impairment.

In the elderly over 75 years and for patients with moderate to severe renal impairment (creatinine clearance less than 20 mL per minute), the dose is started at 25 mg once daily.

Or as prescribed by the physician.

CONTRAINDICATIONS/PRECAUTIONS/WARNINGS:
Losartan is contraindicated in patients who are hypersensitive to any component of the product.

Symptomatic hypotension may occur after losartan intake in patients who have intravascular volume depletion.

This condition should be corrected prior to administration of losartan, or a lower starting dose should be used.

As a result of losartan's effect on the renin-angiotensin system, increased blood urea and serum creatinine have been reported in patients with bilateral renal artery stenosis, or renal artery stenosis in a solitary kidney, and renal failure in susceptible individuals.

Electrolyte imbalances are common in patients with renal impairment, and should be corrected. Serum potassium levels should be monitored in type II diabetic patients with proteinuria. Therapy with losartan in patients with hyponatremia, renal insufficiency volume depletion or in those treated aggressively with diuretics should be initiated at a reduced dosage as these patients are at greater risk of hypertension or deterioration of renal function.

A lower dose should be considered for patients with history of hepatic impairment, because of data demonstrating increased losartan levels in patients with cirrhosis.

PREGNANCY AND LACTATION:
Losartan is contraindicated in pregnancy since it has been associated with fetal toxicity in animal studies and other drugs that act on the renin-angiotensin system, such as ACE inhibitors, have been associated with fetal toxicity in humans.

Losartan must be discontinued as soon as pregnancy is detected. Drugs that act directly on the renin-angiotensin system can cause injury and even death in the developing fetus, particularly during the second and third trimesters. Fetal renal perfusion, which is dependent upon the development of the renin-angiotensin system, begins in the second trimester.

Losartan should be used with caution during breast-feeding as it is not known whether it is excreted in human milk.

Safety and effectiveness in children have not been established.

DRUG INTERACTIONS:
Like other angiotensin II receptor antagonists, losartan may cause hyperkalemia in patients taking potassium supplements or potassium-sparing drugs. Losartan enhances the blood pressure-lowering action of other antihypertensive drugs so the dosage of the drug has to be adjusted.

Despite the biotransformation of losartan by CYP isoenzymes, no pharmacokinetic or pharmacodynamic interactions with warfarin or digoxin have been reported.

ADVERSE REACTIONS:
Losartan is generally well-tolerated. Adverse effects are usually mild and transient. Dizziness was the most common adverse effect reported. Other reported effects are headache, fatigue, neutropenia, asthenia, upper respiratory tract infection, back pain, gastrointestinal disturbances and dose-related orthostatic hypotension. Hypotension was seen in patients particularly in those with volume depletion (i.e., patients on high-dose diuretics).

Losartan may cause hyperkalemia in patients with chronic renal failure and in those receiving potassium-sparing diuretics or potassium supplements. Serum potassium and renal function must be monitored.

Rhabdomyolysis, anaphylactic reactions, angioedema with swelling of the larynx and glottis causing airway obstruction and/or swelling of the face, lips, pharynx and/or tongue have been reported rarely in patients treated with losartan.
The drug appears less likely to cause cough and angioneurotic edema than ACE inhibitors.

Losartan has a uricosuric effect after single or multiple doses in salt-depleted or salt-loaded normotensive patients, sodium-depleted patients with essential hypertension, and hypertensive patients with intrinsic renal disease.

OVERDOSE AND TREATMENT:
Symptoms of losartan overdose include extremely low blood pressure, dizziness, increased heartbeat and fainting.

If overdose is suspected, patients should be immediately brought to the emergency room for proper care and prompt management.

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

AVAILABILITY:
Blister pack x 10’s (Box of 100’s)

DR-XY35051

STORE AT TEMPERATURES NOT EXCEEDING 30oC.

For suspected adverse drug reaction, report to the FDA:www.fda.gov.ph

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