xxxxxxxxx-5343

LOSARTAN POTASSIUM

50 mg & 100 mg Film-Coated Tablet
Angiotensin II Receptor Blocker

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

CLINICAL PHARMACOLOGY

PHARMACODYNAMICS:
Losartan potassium, representing the first of a new class of antihypertensives, is a specific angiotensin-II receptor (type AT1) antagonist. Angiotensin II is a potent vasoconstrictor and the primary active hormone of the renin-angiotensin-aldosterone system, playing a major part in the pathophysiology of hypertension. The cardiovascular homeostatic effects of angiotensin II are elicited through the AT1 receptor.
Losartan is a potent, synthetic orally active compound, which binds selectively to the AT1 receptor. In vitro and in vivo, both Losartan and its pharmacologically active metabolite, E-3174 block all physiologically relevant actions of angiotensin II including vasoconstriction, sodium and water retention and sympathetic stimulation. This leads to reduction in the blood pressure. Losartan does not have agonist effects and does not bind or block other hormone receptors or ion channels important in cardiovascular regulation.

PHARMACOKINETICS:
Following oral administration, Losartan Potassium is well absorbed and undergoes substantial first-pass metabolism; the systemic bioavailability is approximately 33%. It undergoes first-pass metabolism to form an active carboxylic acid metabolite E-3174 (EXP-3174), which has greater pharmacological activity than losartan. 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 an 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 is used in the management of hypertension and may have a role in patients who are unable to tolerate ACE inhibitors. It has also been tried in heart failure and in myocardial infarction

CONTRAINDICATIONS:
Losartan is contraindicated in patients who are hypersensitive to any component of this product. Losartan is also contraindicated in pregnancy and if pregnancy is detected, Losartan should be discontinued immediately.

PRECAUTIONS:
Intravascular volume depletion: In patients who are intravascularly volume depleted (eg. those treated with high-dose diuretics), symptomatic hypotension may occur. Such a condition should be corrected prior to administration of Losartan , or a lower starting dose should be used.
Hepatic impairment: Based on pharmacokinetic data, which demonstrate significantly increased plasma concentrations of Losartan, or a lower starting dose should be considered for patients with history of hepatic impairment.
Renal artery stenosis: Other drugs that affect the renin-angiotensin-aldosterone system may increase blood urea and serum creatinine in patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney. While not confirmed, this potentially may occur with angiotensin-II receptor antagonists.
Use in Pregnancy, Nursing mothers and Children
Pregnancy: Although there is no experience with the use of Losartan in pregnant women, animal studies with Losartan have demonstrated fetal and neonatal injury and death, the mechanism of which is believed to be its effects on the renin-angiotensin-aldosterone system. In humans, fetal renal perfusion, which is dependent upon the development of the renin-angiotensin-aldosterone system, begins in the second trimester. When used in pregnancy during the second trimester, drugs that act directly on the renin-angiotensin-aldosterone-system can cause injury and even death in developing fetus. Losartan is contraindicated in pregnancy, and if pregnancy is detected, Losartan should be discontinued immediately.
Nursing mothers: It is not known whether Losartan is excreted in human milk. Because of the potential for the adverse effects on the nursing infant, a decision should be made whether to discontinue breast-feeding or discontinue the drug, taking into account the importance of the drug to the mother.
Children: Safety and efficacy in children have not been established.

ADVERSE REACTIONS:
Adverse effects with Losartan have usually been mild and transient in nature and have not required discontinuation of therapy. The overall incidence of adverse effects reported with Losartan was comparable to placebo.
In controlled clinical trials of essential hypertension, dizziness was the only drug related adverse effect that occurred with an incidence greater than placebo in 1% or more of patients treated with Losartan. In addition, dose-related orthostatic effects were seen in less than 1% of patients. Rarely, rash was reported, although the incidence in controlled clinical trials was less than placebo. In contrast to ACE inhibitors, Losartan is not found to cause accumulation of bradykinin and so incidence of cough observed with Losartan is significantly less as compared to ACE inhibitors and is not more than that observed with placebo in several clinical trials.

DRUG INTERACTIONS:
No drug interactions of clinical significance have been identified with Losartan. Compounds which have been studied in clinical pharmacokinetic trials include hydrochlorothiazide, digoxin, warfarin, cimetidine and phenobarbitone.

DOSAGE & ADMINISTRATION:
The starting and maintenance dose of Losartan is 25 or 50mg once daily for most patients, with or without food. The maximal antihypertensive effect is attained 0-6 weeks after initiation of therapy. Some patients may receive an additional benefit by increasing the dose up to 100mg once daily, in one or two divided doses, or as prescribed by the physician.
Use in elderly:
Patients up to 75 years: No initial dosage adjustment is necessary for this group of patients, or as prescribed by the physician.
Patients over 75 years: At present there is limited clinical experience in this group; a lower starting dose of 25mg once daily is recommended. Or as prescribed by the physician.
Use in renal impairment: No initial dosage adjustment is necessary in patients with mild renal impairment (eg. creatinine clearance 20-50mL/min). For patients with moderate to severe renal impairment (eg. creatinine clearance <20mL/min) or patients on dialysis, lower starting dose of 25 mg once daily is recommended. Or as prescribed by the physician.
Intravascular volume depletion: In patients who are intravascularly volume depleted (eg. those treated with high-dose diuretics), symptomatic hypotension may occur. Such a condition should be corrected prior to administration of Losartan, or a lower starting dose should be used. Or as prescribed by the physician.

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

STORAGE CONDITION
Store at temperatures not exceeding 30^{o}C. Protect from moisture.

AVAILABILITY
Losartan Potassium 50 mg Film-Coated Tablet - In Alu/PVC/PVDC blister pack of 10's (box of 50's & 100's)
Losartan Potassium 100 mg Film-Coated Tablet - In Alu/ white opaque PVC/LDPE/PVDC blister packs of 10's (Box of 30's)

torrent PHARMA

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA

Imported and Distributed by :
TORRENT PHARMA PHILIPPINES INC.
Unit 601, 6/F, ITC Building, 337 Sen. Gil Puyat Avenue,
Makati City, PHILIPPINES

PRODUCT NAME :	Losartan Potassium	**COUNTRY :** Philippines	**LOCATION :** Indrad		**Supersedes A/W No.:**		
ITEM / PACK :	Insert	**NO. OF COLORS:** 1	**REMARK : Folded Size 30 mm**				
DESIGN STYLE :	-	**PANTONE SHADE NOS.:**	**SUBSTRATE :**				
CODE :	xxxxxxx-5343	Black	**Activities**	**Department**	**Name**	**Signature**	**Date**
DIMENSIONS (MM) :	150 x 180		Prepared By	**Pkg.Dev**			
ART WORK SIZE :	S/S		Reviewed By	**Pkg.Dev**			
DATE :	10-10-2014		Reviewed By	**RA**			
			Approved By	**CQA**			