For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory xxxxxxxx-5253

TOZAAR 50MG TABLET
TOZAAR 25MG TABLET

(Losartan Potassium Tablet 25mg/50mg)

COMPOSITION:
TOZAAR 25MG TABLET
Each film coated tablet contains:
Losartan Potassium Ph.Eur. …….. 25 mg
TOZAAR 50MG TABLET
Each film coated tablet contains:
Losartan Potassium Ph.Eur. …….. 50 mg
DESCRIPTION:
TOZAAR 25MG TABLET:
White colour, oval shaped, biconvex film coated tablet with break line on both sides with thickness: 3.00mm, length: 8.25mm. and width: 4.50mm.
TOZAAR 50MG TABLET:
White colour, oval shaped, biconvex film coated tablet break line on both the sides with thickness: 3.70mm, length: 10.45mm. and width: 5.60mm.
PHARMACOLOGICAL ACTION:
Tozaar (losartan potassium is the first of a new class of antihypertensive, a nonpeptide angiotensin II (AII) receptor antagonist. This novel agent binds competitively and selectively to the AII subtype I (ATI receptor) thereby blocking AII-induced physiological effect.
The active metabolite, E3174, bind to the ATI receptor with 10-fold greater affinity than the parent compound, and is about 15 to 20 times more potent in inhibiting angiotensin II-induced pressor and contractile responses. Tozaar (losartan potassium) is orally active. In patients with hypertension, once-daily administration of losartan decrease blood pressure throughout a 24-hour period without affecting the heart rate.
Losartan potassium in dose 50 to 100 mg daily as monotherapy has reduces diastolic blood pressure (DBP) by about 8 to 13 mmHg in patients with mild to moderate hypertension, and has shown equivalent effectiveness to enalapril, atenolol or extended release felodipine. The addition of thiazide diuretic to losartan reduces larger blood pressure reductions than occur with either drug alone.
Pharmacokinetics:
Absorption
Following oral administration, losartan is well absorbed and undergoes first-pass metabolism, forming an active carboxylic acid metabolite and other inactive metabolites. The systemic bioavailability of losartan tablets is approximately 33%. Mean peak concentrations of losartan and its active metabolite are reached in 1 hour and in 3-4 hours, respectively. There was no clinically significant effect on the plasma concentration profile of losartan when the drug was administered with a standardized meal.
Distribution
Both losartan and its active metabolite are ≥99% bound to plasma proteins, primarily albumin. The volume of distribution of losartan is 34 litres. Studies in rats indicate that losartan crosses the blood-brain barrier poorly, if at all.
Biotransformation
About 14% of an intravenously or orally-administered dose of losartan is converted to its active metabolite. Following oral and intravenous administration of ^{14}C-labelled losartan potassium, circulating plasma radioactivity primarily is attributed to losartan and its active metabolite.
In addition to the active metabolite, inactive metabolites are formed, including two major metabolites formed by hydroxylation of the butyl side chain and a minor metabolite, an N-2 tetrazole glucuronide.
Elimination
Plasma clearance of losartan and its active metabolite is about 600 ml/min and 50 ml/min, respectively. Renal clearance of losartan and its active metabolite is about 74 ml/min and 26 ml/min, respectively. When losartan is administered orally, about 4% of the dose is excreted unchanged in the urine, and about 6% of the dose is excreted in the urine as active metabolite. The pharmacokinetics of losartan and its active metabolite are linear with oral losartan potassium doses up to 200 mg.
Following oral administration, plasma concentrations of losartan and its active metabolite decline polyexponentially with a terminal half-life of about 2 hours and 6-9 hours, respectively. During once-daily dosing with 100 mg, neither losartan nor its active metabolite accumulates significantly in plasma.
Both biliary and urinary excretion contributes to the elimination of losartan and its metabolites. Following an oral dose of ^{14}C-labelled losartan in man, about 35% of radioactivity is recovered in the urine and 58% in the faeces.
Characteristics in patients
Following oral administration in patients with mild to moderate alcoholic cirrhosis of the liver, plasma concentrations of losartan and its active metabolite were, respectively, 5-fold and 1.7-fold greater than those seen in young male volunteers.
Neither losartan nor the active metabolite can be removed by haemodialysis.
INDICATIONS:
Hypertension
'Tozaar' (Losartan potassium) tablet is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents, including diuretics.
Hypertensive Patients with Left Ventricular Hypertrophy
'Tozaar' (Losartan potassium) tablet is indicated to reduce the risk of stroke in patients with hypertension and left ventricular hypertrophy, but there is evidence that this benefit does not apply to Black patients.
Nephropathy in Type 2 Diabetic Patients
'Tozaar' (Losartan potassium) tablet is indicated for the treatment of 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. In this population, 'Tozaar' (Losartan potassium) tablet reduces the rate of progression of nephropathy as measured by the occurrence of doubling of serum creatinine or end stage renal disease (need for dialysis or renal transplantation).
CONTRA-INDICATIONS:
'Tozaar' is contraindicated in pregnancy and in patients who are hypersensitive to any component of this product.
DOSAGE AND DIRECTIONS FOR USE:
Tozaar may be administered with or without food.
Tozaar may be administered with other antihypertensive agents.
Hypertension
The usual starting and maintenance dose is 50 mg once daily for most patients. The maximal antihypertensive effect is attained 3-6 weeks after initiation of therapy. Some patients may receive an additional benefit by increasing the dose to 100 mg once daily.
For patients with intravascular volume-depletion (e.g. those treated with high-dose diuretics), a starting dose of 25mg once daily should be considered.
No initial dosage adjustment is necessary for elderly patients or for patients with renal impairment, including patients on dialysis. A lower dose should be considered for patients with a history of hepatic impairment.
Hypertensive Patients with Left Ventricular Hypertrophy
The usual starting dose is 50 mg of Tozaar once daily. A low dose of hydrochlorothiazide should be added and/or the dose of Tozaar should be increased to 100 mg once daily based on blood pressure response.
Renal Protection in Type 2 Diabetic Patients with Proteinuria and Hypertension
The usual starting dose is 50 mg once daily. The dose may be increased to 100 mg once daily based on blood pressure response. Tozaar may be administered with other antihypertensive agents (e.g., diuretics, calcium channel blockers, alpha or beta blockers, and centrally acting agents) as well as with insulin and other commonly used hypoglycemic agents (e.g., sulfonylureas, glitazones and glucosidase inhibitors).
Mode of Administration: Oral
INTERACTION WITH OTHER MEDICAMENTS:
Thiazide type diuretics: If losartan is administered together with thiazide type diuretic, the blood-pressure-lowering effect are additive. Tozaar should not be used with potassium-sparing diuretic.
SIDE-EFFECTS
Dizziness, headache, asthenia/fatigue, cough, diarrhea, dyspepsia, cramp muscle, myalgia, pain back, pain leg, insomnia, nasal congestion, upper respiratory infection, serious disorder and sinusitis. These adverse events, whether or not attributed to the treatment, occurring at least 1% patients.
SPECIAL WARNINGS AND PRECAUTIONS:
Hypersensitivity:
Angioedema.
The use of 'Tozaar' in patients with haemodynamically significant obstructive valvular disease or cardiomyopathy has not been adequately studied.
Hypotension and electrolyte/fluid imbalance
In patients who are intravascularly volume depleted (e.g. those treated with high-dose diuretics), symptomatic hypotension may occur. These conditions should be corrected prior to administration of 'Tozaar', or a lower starting dose should be used.
Electrolyte imbalances are common in patients with renal impairment, with or without diabetes, and should be addressed. In a clinical study conducted in type 2 diabetic patients with nephropathy, the incidence of hyperkalaemia was higher in the group treated with 'Tozaar' as compared to the placebo group.
Liver function impairment
Based on pharmacokinetic data which demonstrate significantly increased plasma concentrations of losartan in cirrhotic patients, a lower dose should be considered for patients with a history of hepatic impairment.
Renal function impairment
As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function including renal failure have been reported (in particular, in patients whose renal function is dependent on the renin-angiotensin-aldosterone system such as those with severe cardiac insufficiency or pre-existing renal dysfunction).
As with other drugs that affect the renin-angiotensin-aldosterone system, increases in blood urea and serum creatinine have also been reported in patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney; these changes in renal function may be reversible upon discontinuation of therapy.
Caution is required in patients with significant renal disease and renal transplant recipients as there have been reports of anaemia developing in such patients treated with 'Tozaar'.
Race (Black patients):
There is no evidence that Losartan reduces the risk of stroke in black patients with hypertension and left ventricular hypertrophy.
PREGNANCY AND LACTATION:
Use during pregnancy
Although there is no experience with the use of 'Tozaar' in pregnant women, animal studies with losartan potassium have demonstrated foetal and neonatal injury and death, the mechanism of which is believed to be pharmacologically mediated through effects on the renin-angiotensin-aldosterone system.
In humans, foetal renal perfusion, which is dependent upon the development of the renin-angiotensin-aldosterone system, begins in the second trimester; thus, risk to the foetus increases if 'Tozaar' is administered during the second or third trimesters of pregnancy.
When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin-aldosterone system can cause injury and even death in the developing foetus. 'Tozaar' should not be used in pregnancy, and if pregnancy is detected 'Tozaar' should be discontinued as soon as possible.
Use during lactation
It is not known whether losartan is excreted in human milk. However, significant levels of losartan and the 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 breast-feeding or discontinue the drug, taking into account the importance of the drug to the mother.
OVERDOSAGE AND THEIR MANAGEMENT:
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.
Neither Losartan nor the active metabolite can be removed by haemodialysis.
STORAGE INSTRUCTIONS:
Store below 30^{O}C.
PRESENTATION:
Tozaar tablets 25 mg and 50 mg are packed in Blister pack using a white opaque triplex film PVC/LDPE/PVdC film of 10 tablets. Such blisters containing 10 tablets are packed into a carton of 10's, 30's and 100's.
Not all presentations may be available locally.
DATE OF REVISION:
18, September, 2019

torrent PHARMA

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

PRODUCT NAME :	Tozaar	**COUNTRY :** Malaysia	**LOCATION :** Indrad		**Supersedes A/W No.:**			
ITEM / PACK :	Insert	**NO. OF COLORS:** 1	**REMARK :**					
DESIGN STYLE :	Front / Back	**PANTONE SHADE NOS.:**	**SUBSTRATE :**					
CODE :	xxxxxxxxxx-5253		**Activities**	**Department**	**Name**	**Signature**	**Date**	
DIMENSIONS (MM) :	150 x 240		Prepared By	**Pkg.Dev**				
ART WORK SIZE :	S/S		Reviewed By	**Pkg.Dev**				
DATE :	18-09-2019	Black	Approved By	**Quality**				

This colour proof is not colour binding. Follow Pantone shade reference for actual colour matching.