Telisartan®

Telmisartan
20mg / 40mg

DESCRIPTION:
Telisartan (Telmisartan) is a non-peptide angiotensin II receptor (type AT_1) antagonist. It is chemically described as 4'-[(1, 4'-dimethyl-2'-propyl] [2, 6'-bi-1H-benzimidazol]-1'-yl) methyl]-[1, 1'-biphenyl]-2-carboxylic acid. Its empirical formula is $C_{33}H_{30}N_4O_2$ its Molecular weight is 514.63.

TELISARTAN TABLETS ARE AVAILABLE FOR ORAL ADMINISTRATION AS:

1. TELISARTAN Tablets 20mg
Each Tablet contains:
Telmisartan USP……20mg

2. TELISARTAN Tablets 40mg
Each tablet contains:
Telmisartan USP……40mg

CLINICAL PHARMACOLOGY:
Mechanism of Action:
Angiotensin II is formed from angiotensin I in a reaction catalyzed by angiotensin-converting enzyme (ACE, kininase II). It is the principal pressor agent of the renin-angiotensin system, with effects that includes vasoconstriction, stimulation of synthesis and release of aldosterone, cardiac stimulation, and renal reabsorption of sodium. Telmisartan blocks the vasoconstrictor and aldosterone secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT_1 receptor in many tissues, such as vascular smooth muscle and adrenal gland. Its action is independent of pathways for angiotensin II synthesis. It has much greater affinity (>3,000 fold) for AT_1 receptor than for the AT_2 receptor. Blockade of renin-angiotensin system with ACE inhibitors, inhibits the biosynthesis of angiotensin II from angiotensin I and is widely used in the treatment of hypertension.

PHARMACOKINETICS:
ABSORPTION:
Peak concentrations of Telmisartan are reached in 0.5-1 hour after dosing. Food slightly reduces the bioavailability of Telmisartan. The absolute bioavailability of Telmisartan is dose dependent. Telmisartan shows bi-exponential decay kinetics with a terminal elimination half life of approximately 24 hours. Plasma concentrations of Telmisartan with once daily dosing are about 10-25% of peak plasma concentrations.

DISTRIBUTION:
Over 99% of Telmisartan is bound to plasma proteins mainly albumin and α_1-acid glycoprotein. Plasma protein binding is constant over the concentration range achieved with recommended doses. Volume of distribution is 500 liters indicating additional tissue binding.

METABOLISM:
Telmisartan is metabolized by conjugation to form a pharmacologically inactive acylglucuronide. After a single dose, the glucuronide represents approximately 11% of the measured radioactivity in plasma. The cytochrome P450 isoenzymes are not involved in metabolism of Telmisartan.

ELIMINATION:
Total plasma clearance of Telmisartan is >800mL/min. Terminal elimination half life of Telmisartan is about 24 hours and total clearance appears to be independent of dose.

Special population:
Renal Insufficiency:
In Mild to Moderate and severely renally impaired patients doubling of plasma concentrations was observed. However, lower plasma concentrations were observed in patients with renal insufficiency undergoing dialysis. The elimination half-life is not changed in patients with renal impairment. Low starting dose in renal impaired patients is 20mg.
Hepatic Insufficiency:
In such patients plasma concentrations of telmisartan are increased, and absolute bioavailability approaches 100%.

INDICATIONS:
TELISARTAN Tablets are indicated for treatment of Hypertension. It may be used alone or in combination with other anti-hypertensive agents.

DOSAGE & ADMINISTRATION:
Dosage of TELISARTAN must be individualized. The usual starting dose of TELISARTAN is 40mg once a day. Blood pressure response is dose related over the range of 20-80mg. TELISARTAN tablets may be taken with or without food.

CONTRAINDICATIONS:
TELISARTAN Tablets are contraindicated in patients
- Who are hypersensitive to any component of this product.
- During second and third trimesters of pregnancy and lactation.
- With biliary obstructive disorders.
- With severe hepatic impairment.
- With Severe renal insufficiency.
- With Hereditary fructose intolerance.

PRECAUTIONS & WARNINGS:
- Telmisartan is eliminated by biliary excretion; patients with biliary obstructive disorders can be expected to have reduced clearance.
- In patients in which renal function may depend on the activity of the renin-angiotensin-aldosterone system (e.g patients with congestive heart failure), treatment with angiotensin-converting enzyme inhibitors and angiotensin receptor antagonists has been associated with oliguria or progressive azotemia and (rarely) with acute renal failure or death.
- Dual blockade of renin-angiotensin-aldosterone system (e.g. by adding ACE inhibitor to an angiotensin II receptor antagonist) should include close monitoring of renal function.
- Patients with primary aldosteronism generally will not respond to antihypertensive medicinal products acting through inhibition of the renin-angiotensin system. Therefore the use of telmisartan is not recommended.
- Safety and effectiveness in pediatric patients have not been established.

WARNINGS:
- When pregnancy is detected, TELISARTAN tablets should be discontinued as soon as possible. Drugs that act directly on renin-angiotensin system can cause fetal and neonatal morbidity and death when administered during second and third trimesters to pregnant women.
- When driving vehicles or operating machinery it must be borne in mind that dizziness or drowsiness may occasionally occur when taking antihypertensive therapy.

DRUG INTERACTIONS:
Digoxin:
Digoxin levels must be monitored when initiating, adjusting, and discontinuing telmisartan to avoid over or under digitalization.

Warfarin:
Telmisartan decreases the mean warfarin trough plasma concentration.
- Based on experience with the use of medicinal products that effect the renin-angiotensin system, concomitant use of potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium and other medicinal products, that may increase the potassium level (heparin, immunosuppresor (cyclosporine or tacrolimus), trimethoprim, ACE inhibitors, angiotensin II receptor antagonist, NSAIDS including selective COX II inhibitors etc) may lead to an increase in serum potassium and should therefore be co administered cautiously with Telmisartan.
- Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administered of lithium with angiotensin converting enzyme inhibitors and rarely with angiotensin II antagonists. If use of the combination proves necessary, careful monitoring of serum lithium levels is recommended.

OVERDOSE:
The most likely manifestation of overdosage with telmisartan tablets would be hypotension, dizziness and tachycardia; bradycardia could occur from parasympathetic stimulation. If symptomatic hypotension occurs, supportive treatment should be initiated. Telmisartan is not removed by hemodialysis.

STORAGE AND PACKAGING:
- Store below 25ºC
- Protect from sunlight and moisture.
- Tablets should not be removed from blisters until immediately before administration.

DIRECTIONS:
Keep out of reach of children.
To be sold on prescription of a registered medical practioner only.

PACKING:
Telisartan 20mg tablets are available in alu-alu blister pack of 10's.
Telisartan 40mg tablets are available in alu-alu blister pack of 14's.

ٹیلیسارٹن®

ٹیلمی سارٹن ۲۰ ملی گرام / ۴۰ ملی گرام

خوراک:۔ یہ دوا ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔

ہدایات:۔ دوا کو ٹھنڈی (۲۵ سینٹی گریڈ درجہ حرارت سے کم) اور خشک جگہ پر رکھیں۔
دوا کو گرمی، روشنی اور نمی سے محفوظ رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

پیشکش:۔ **ٹیلیسارٹن®** ۲۰ ملی گرام (۱۰) گولیاں ایلو ایلو بلسٹر پیک میں دستیاب ہیں۔
ٹیلیسارٹن® ۴۰ ملی گرام (۱۴) گولیاں ایلو ایلو بلسٹر پیک میں دستیاب ہیں۔

Manufactured by:

Schazoo Zaka (Pvt) Ltd.
Kalalwala, 20-Km Lahore-Jaranwala Road,
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