Co-Telisartan®

14 Tablets

Telmisartan U.S.P 40mg + Hydrochlorothiazide U.S.P 12.5mg

Anti-hypertensive & Diuretic

COMPOSITION:

Each tablet contains:
Telmisartan U.S.P……..40mg
Hydrochlorothiazide U.S.P……12.5mg

DESCRIPTION:

Co-Telisartan (Telmisartan + hydrochlorothiazide) is a combination of Telmisartan, is a non-peptide angiotensin II receptor (type AT_1) antagonist, and hydrochlorothiazide, a diuretic. Telmisartan 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 $C_{33}H_{30}NO_4O_2$. Its Molecular weight is 514.63.

Hydrochlorothiazide is chemically described as 6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide. Its empirical formula is $C_7H_8ClN_3O_4S_2$, and its Molecular weight is 297.74.

CLINICAL PHARMACOLOGY:

Mechanism of action:
Telmisartan:
Telmisartan is an orally effective and specific angiotensin II receptor subtype 1 (AT_1) antagonist. 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.
Hydrochlorothiazide:
Hydrochlorothiazide is a Thiazide diuretic. Thiazides affect the renal tubular mechanisms of electrolyte reabsorption, directly increasing excretion of sodium and chloride in approximately equivalent amounts.

Pharmacokinetics:
1. Telmisaratn:
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.
Distribution:
Over 99% of Telmisartan is bound to plasma proteins mainly albumin and α1-acid glycoprotein. Plasma protein binding is constant over the concentration range achieved with recommended doses.
Metabolism and elimination:
Telmisartan is metabolized by conjugation to form a pharmacologically inactive acylglucuronide. After a single dose, the glucuronide represents approximately 11%.
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.
2. Hydrochlorothiazide:
Absorption:
Hydrochlorothiazide is fairly rapidly absorbed from the gastrointestinal tract. It is reported to have a bioavailability of about 65-70%. Peak plasma concentrations of hydrochlorothiazide are reached in approximately 1 to 2.5 hours after dosing. It has been estimated to have a plasma half life of between about 5 and 15 hours and appears to be preferentially bound to red blood cells.
Distribution:
Hydrochlorothiazide crosses the placental barrier but not the blood brain barrier and is excreted in breast milk.
Metabolism and elimination:
Hydrochlorothiazide is not metabolized but is eliminated rapidly by the kidney. At least 61% of the oral dose is eliminated unchanged within 24 hours.

Special population:
➢ Renal Impairment
Telmisartan:
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.

Hydrochlorothiazide:
In patient with impairment renal function the rate of hydrochlorothiazide elimination is reduced. In functionally anephric patients the elimination half life is about 34 hours.

➢ Hepatic Impairment:
Telmisartan:
In such patients plasma concentrations of Telmisartan are increased, and absolute Bioavailability approaches 100%.
Hydrochlorothiazide:
Thiazide diuretics should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alteration of fluid and electrolyte balance may precipitate hepatic coma.

INDICATIONS:

Co-Telisartan is indicated for the treatment of hypertension. This fixed dose combination is not indicated for initial therapy.

DOSAGE AND ADMINISTRATION:

It is usually appropriate to begin combination therapy only after a patient has failed to achieve the desired effect with monotherapy.
Co-Telisartan (Telmisartan + Hydrochlorothiazide) may be taken with or without food.
Co-Telisartan (Telmisartan + Hydrochlorothiazide) may be administered with other anti-hypertensive agents.
Usually effective dose of telmisartan is 40mg once a day. Blood pressure response is dose related over the range of 20-80mg. Some patients may already benefit at a daily dose of 20mg.
Hydrochlorothiazide is effective in doses of 12.5 to 50 mg once daily
Renal Impaired patients:
The usual regimens of therapy with Co-Telisartan (Telmisartan + Hydrochlorothiazide) may be followed as long as the patient's creatinine clearance is > 30ml/min. In patients with more severe renal impairment it is not recommended to use thiazide.
Hepatic Impaired patients: In patient with mild to moderate hepatic impairment the dosage should not exceed 40mg+12.5mg once daily.

ADVERSE REACTIONS:

Adverse reactions occurring with both Telmisartan + hydrochlorothiazide include:
Common: Dizziness
Uncommon: Hypokalemia, anxiety, syncope, paraesthesia, vertigo, tachycardia, arrhythmias, hypotension, orthostatic hypotension, dyspnoea, diarrhea, dry mouth, flatulence, back pain, muscle spasms, myalgia, erectile dysfunction, chest pain and blood uric acid increase.

As with other angiotensin II antagonists isolated case of angioneurotic edema, urticaria and other related reactions have been reported.
Replacement Therapy: The combination may be substituted for the titrated components.

CONTRA-INDICATIONS:

Co-Telisartan (Telmisartan + Hydrochlorothiazide) is contraindicated
In patients who are hypersensitive to this drug or to any component of this product.
This product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs, Due to hydrochlorothiazide.
In patients Refractory Hypokalemia and hypercalcemia.
During the second and third trimesters of pregnancy and lactation.
In patients with cholestasis and biliary obstructive disorders.
In patients with severe hepatic impairment.
In patients with severe renal impairment.

PRECAUTIONS AND WARNINGS:

WARNINGS:
USE IN PREGNANCY: When pregnancy is detected, Co-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.
PRECAUTIONS:
Hepatic Impairment: Co-Telisartan (Telmisartan + Hydrochlorothiazide) should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alteration of fluid and electrolyte balance may precipitate hepatic coma.
Renal Impairment and kidney transplantation: There is less experience in patients with mild to moderate Renal Impairment, therefore, periodic monitoring of potassium, creatinine and uric acid serum level is recommended. Thiazide diuretic-associated azotemia may occur in patients with impaired renal function.
Symptomatic Hypotension: A patient receiving Co-Telisartan (Telmisartan + Hydrochlorothiazide) should be cautioned that lightheadedness can occur, especially during the first days of therapy and it should be informed to the physician. The patients should be told that if syncope occurs, Co-Telisartan should be discontinued until the physician has been consulted. All patients should be cautioned that inadequate fluid intake, excessive perspiration, diarrhea or vomiting can lead to an excessive fall in blood pressure, with the same consequences of lightheadedness and possible syncope.
Potassium Supplements: A patient receiving Co-Telisartan (Telmisartan + Hydrochlorothiazide) should be told not to use potassium supplements or salt substitutes containing potassium without consulting the prescribing physician.

DRUG INTERACTIONS:

Telmisartan:
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.
Co-administration of Telmisartan did not result in a clinically significant interaction with acetaminophen, amlodipine, glibenclamide, simvastatin, hydrochlorothiazide or ibuprofen. Telmisartan is not significantly metabolized by the cytochrome P_{450} system and had no effects on invitro on cytochrome P_{450} enzymes, except for some inhibition of CYP_2C_{19}.Telmisartan is not expected to interact with drugs that inhibit cytochrome P_{450} enzymes; it is also not expected to interact with drugs metabolized by cytochrome P_{450} enzymes, except for possible inhibition of the metabolism of drug metabolized by CYP_2C_{19}.
Hydrochlorothiazide:
When administered concurrently the following drugs may interact with thiazide diuretics: Alcohol, barbiturates, or narcotics: Potentiation of orthostatic hypotension may occur. Anti diabetic drugs (oral agents and insulin): Dosage adjustment of the antidiabetic drug may be required.
Cholestyramine and colestipol resins: Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins. Single doses of either cholestyramine or colestipol resins bind the hydrochlorothiazide and reduce its absorption from the gastrointestinal tract by up to 85 and 43 percent respectively.
Corticosteroids, ACTH (AdrenoCortic Tropic Hormone): Intensified electrolyte depletion, particularly hypokalemia.
Skeletal muscle relaxants, nondepolarizing (e.g, tubocurarine): Possible increased responsiveness to the muscle relaxant.
Lithium: Generally should not be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity.
Non-steroidal Anti-inflammatory Drugs: Administration of a non-steroidal anti-inflammatory agent can reduce the diuretic, natriuretic and antihypertensive effects of loop, potassium-sparing and thiazide diuretics.
Nursing mothers:
Telmisartan + Hydrochlorothiazide is contraindicated during lactation since it is not known whether Telmisartan is excreted in human milk. Thiazides appear in human milk and may inhibit lactation.

Pediatric Use:
Telmisartan pharmacokinetics have not been investigated in patients < 18 years of age.
Safety and effectiveness in pediatric patients have not been established.

OVERDOSAGE:

The most likely manifestation of Telmisartan overdose are expected to be hypotension and tachycardia; bradycardia might also occur. Overdose with hydrochlorothiazide is associated with electrolyte depletion and dehydration resulting from excessive diuresis.
The patient should be closely monitored. Management depends on the time since ingestion and severity of the symptoms. Suggested measures include induction of emesis and gastric levage. Serum electrolytes and creatinine should be monitored frequently.

STORAGE:

Store below 25°C.
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: CO-Telisartan tablets are available in alu-alu blister pack of 14´s.

کو۔ٹیلیسارٹن®

ٹیلمی سارٹن ۴۰ ملی گرام + ہائیڈروکلوروتھیاذائیڈ ۱۲.۵ ملی گرام

خوراک:۔ یہ دواڈاکٹر 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:۔ کو۔ٹیلیسارٹن® ۴۰ ملی گرام + ۱۲.۵ ملی گرام (۱۴) گولیاں ایلو ایلو بلسٹر پیک میں دستیاب ہیں۔

Manufactured by:

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