F4322B-Phl

Rx TELMISARTAN + HYDROCHLOROTHIAZIDE

TELSITAN-H

40 mg/12.5 mg Film-Coated Tablet

ANGIOTENSIN II ANTAGONIST/DIURETICS

Formulation:
Each film-coated tablet contains:
Telmisartan BP .....40 mg
Hydrochlorothiazide USP .....12.5 mg

Pharmacology:
Angiotensin II is formed from angiontensin I in a reaction catalyzed by angiotensin converting enzyme (ACE, kininase II). Angiotensin II is the principal pressor agent of the renin-angiotensin system, with effects that include vasoconstriction, stimulation of the 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, receptor in many tissues, such as vascular smooth muscle and the adrenal gland. Hydrochlorothiazide is a thiazide diuretic.Thiazides affect the renal tubular mechanisms of electrolyte reabsorption, directly increasing excretion of sodium salt and chloride in approximately equivalent amounts. Indirectly, the diuretic action of hydrochlorothiazide reduces plasma volume, with consequent increases in plasma renin activity, increases in aldosterone secretion, increases in urinary potassium loss, and decreases in serum potassium.

Pharmacokinetic Properties
Absorption
Following oral administration, peak concentrations (C_{max}) of Telmisartan are reached in 0.5-1.0 hour after dosing. Food slightly reduces the bioavailability of Telmisartan. The absolute bioavailability of telmisartan is dose dependent. At 40 and 160 mg the bioavailability was 42% and 58%, respectively.
Metabolism
Telmisartan is metabolized by conjugation to form a harmacologically inactive acylglucuronide; the glucuronide of the parent compound is the only metabolite that has been identified in human plasma and urine. After a single dose, the glucuronide represents approximately 11% of the measured radioactivity in plasma. The cytochrome P450 isoenzymes are not involved in the metabolism of Telmisartan. Total plasma clearance of Telmisartan is >800mL / min. Terminal half-life and total clearance appear to be independent of dose.
Distribution
Telmisartan is highly bound to plasma proteins (>99.5%), mainly albumin and a, acid glycoprotein. Plasma protein binding is constant over the concentration range achieved with recommended doses. The volume of distribution for Telmisartan is approximately 500 liters indicating additional tissue binding.

Indications:
Telmisartan/hydrochlorothiazide is indicated for the treatment of hypertension. The fixed dose combination is not indicated for initial therapy.

Dosage and Method of Administration:
The usual starting dose of Telmisartan tablet is 40 mg once a day. Blood pressure response is dose related over the range of 20 - 80 mg or as prescribed by the physician. Patients with biliary obstructive disorders or hepatic insufficiency should have treatment started under dose medical supervision.
Hydrochlorothiazide is effective in doses or 12.5 mg to 50 mg once daily.To minimize dose-independent side effects, it is usually appropriate to begin combination therapy only after a patient has failed to achieved the desired effect with monotherapy.

Contraindications:
Telmisartan/hydrochlorothiazide is contraindicated in patients who arc hypersensitive to any component of this product. Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

Drug Interactions:
Telmisartan
Digoxin: When Telmisartan was coadministered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) were observed. It is, therefore, recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing telmisartan to avoid possible over or under-digitalization.
Warfarin: Telmisartan administered for 10 days slightly decreased the mean warfarin trough plasma concentration; this decrease did not result in a change in International Normalized Ratio (INR).
Other Drugs: Coadministration of telmisartan did not result in a clinically significant interaction with acetaminophen, amlodipine, glibenclamide, simvastatin, hydrochlorothiazide or ibuprofen. Telmisartan is not metabolized by the cytochrome P450 system and had no effects in vitro on cytochrome P450 enzymes, except for some inhibition of CYP2CI9. Telmisartan is not expected to interact with drugs that inhibit cytochrome P450 enzymes; It is also not expected to interact with drugs metabolized by cytochrome P450 enzymes, except for possible inhibition of the metabolism of drugs metabolized by CYP2CI9.

Hydrochlorothiazide
When administered concurrently, the following drugs may interact with thiazide *diuretics:*
Alcohol, barbiturates, or narcotics: Potentiation of orthostatic hypotension may occur.
Antidiabetic drugs (oral agents and insulin): Dosage adjustment of the antidiabetic drug may be required.
Other hypertensitive drugs: Additive effector potentiation. 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 gastrointestinal tract by up to 85% and 43%, respectively.
Corticosteroids, ACTH: Intensified electrolyte depletion, particularly hypokalemia.
Pressor amines (e.g. norepinephrine): Possible decreased response to pressor amines but not sufficient to preclude their use.
Skeletal muscle relaxants, non depolarizing (e.g. tubocurarine): Possible increased responsiveness to the muscle relaxant.
Lithium: Should not generally be given with diuretics.
Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Refer to the package insert of lithium preparations before use of sure preparations with Telmisartan/hydrochlorothiazide.
Non-steroidal anti-inflammatory drugs: In some patients, the administration of a non-steroidal anti-inflammatory agent can reduce the diuretic, natriuretic, and antihypersensitive effects of loop, potassiumsparing and thiazide diuretics. Therefore, when Temisartan/ Hydrochlorothiazide and non-steroidal anti-inflammatory agents are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

Over Dosage
Telmisartan
Limited data are available with regard to over dosage in humans. The most likely manifestation of over dosage with Telmisartan tablets would be hypotension, dizziness and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted. Telmisartan is not removed by hemodialysis.

Hydrochlorothiazide
The most common symptoms observed in patients are those caused by electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration resulting from excessive dieresis. If digitalis has also been administered, hypokalemia
may accentuate cardiac arrhythmias. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established.

Adverse Effects
Telmisartan
Adverse experiences that have been reported with Telmisartan, without regard to causality, are listed below:
Autonomic Nervous System: impotence, increased sweating, flushing.
Body as a Whole: allergy, fever, leg pain, malaise.
Cardiovascular: palpitation, dependent edema, angina
pectoris, tachycardia, leg edema, abnormal ECG, hypertension, peripheral edema
CNS: insomnia, somnolence, migraine, vertigo, paresthesia, involuntary muscle contractions, hypoaesthesia.
Gastrointestinal: flatulence, constipation, gastritis, dry mouth, hemorrhoids, gastroenteritis, enteritis, gastroesophageal reflux, toothache, non-specific gastrointestinal disorders.
Metabolic: gout, hypercholesterolemia, diabetes mellitus.
Musculoskeletal: arthritis, arthralgia, leg cramps, myalgia.
Psychiatric: anxiety, depression, nervousness.
Resistance Mechanism: infection, fungal infection, abscess, otitis media.
Respiratory: asthma, rhinitis, dyspnea, epistaxis Skin: dermatitis, eczema, pruritus.
Urinary: micturition frequency, cystitis.
Vascular: cerebrovascular disorder.
Special Senses: abnormal vision, conjunctivitis, tinnitus, earache.

Hydrochlorothiazide
Adverse experiences that have been reported with hydrochlorothiazide, without regard to causality, are listed below:
Body as a whole: weakness.
Digestive: Pancreatitis, jaundice (intrahepatic cholestatic jaundice), sialadenitis, cramping, gastric irritation.
Hematologic: Aplastic anemia, agranulocytosis, leucopenia, hemolytic anemia, thrombocytopenia.
Hypersensitivity: purpura, photosensitivity, urticaria, necrotizing angitis (vasculitis and cutaneous vasculitis), fever, respiratory distress including pneumonitis and pulmonary edema, anaphylactic reactions.
Metabolic: hyperglycemia, glycosuria, hyperuricemia
Musculoskeletal: muscle spasm.
Nervous System/Psychiatric: restlessness.
Renal: renal failure, renal dysfunction, interstitial nephritis.
Skin: erythema multiforme including Stevens-Johnson syndrome, exfoliative dermatitis including toxic epidermal necrolysis.
Special Senses: transient blurred vision, xanthopsia.

Special Precautions:
Pregnancy
Pregnancy Categories C (first trimester) and D (second and third trimesters).
Nursing Mothers
It is not known whether Telmisartan is excreted in human milk, but telmisartan was shown to be present in the milk of lactating rats. Thiazides appear in human milk. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue nursing or discontinue drug, taking into account the importance of the drug to the mother.
Impaired Hepatic Function
As the majority of Telmisartan is eliminated by biliary excretion, patients with biliary obstructive disorders or hepatic insufficiency can be expected to have reduced clearance. Telmisartan/hydrochlorothiazide should therefore be used with caution in these patients.
Renal impairment
As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients whose renal function may depend on the activity of the renin-angiotensin-aldosterone system (e.g., patients with severe congestive heart failure), treatment with angiotensin- converting enzyme inhibitors and angiotensin receptor antagonists has been associated with oliguria and/or progressive azotemia and (rarely) with acute renal failure and/or death. Similar results may be anticipated in patients treated with tablets.

REPORTING OF SUSPECTED ADVERSE REACTIONS:
- To allow continued monitoring of the benefit/risk balance of the medicinal product, reporting of suspected adverse reactions is necessary.
- Healthcare professionals are encouraged to report any suspected adverse reaction/s directly to the importer/distributor and/or to FDA: www.fda.gov.ph.
- Patients are advised to seek immediate medical attention at the first sign/s of adverse reactions.

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

Storage Conditions:
Store at temperature not exceeding 30°C.
Protect from light, heat and moisture.
Keep away from the reach of children.

Availability:
Alu/Alu blister pack x 14's (Box of 28 tablets)
Alu/Alu blister pack x 10's (Box of 100 tablets)

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