Telarb®-H Tablets

(Telmisartan + Hydrochlorothiazide)

WARNING: FETAL TOXICITY

When pregnancy is detected, discontinue telmisartan/hydrochlorothiazide as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Telarb®-H Tablet 40mg/12.5mg
Each bilayered tablet contains:
Telmisartan USP.....40mg
Hydrochlorothiazide BP.....12.5mg

Telarb®-H Tablet 80mg/12.5mg
Each bilayered tablet contains:
Telmisartan USP.....80mg
Hydrochlorothiazide BP.....12.5mg

PHARMACEUTICAL FORM

Tablet

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS:

Treatment of Essential Hypertension: Telmisartan/hydrochlorothiazide fixed dose combination (40mg telmisartan/12.5mg hydrochlorothiazide) and (80mg telmisartan/12.5mg hydrochlorothiazide) is indicated in adults whose blood pressure is not adequately controlled on telmisartan alone.

POSOLOGY AND METHOD OF ADMINISTRATION:

Posology: Should be taken in patients whose blood pressure is not adequately controlled by telmisartan alone. Individual dose titration with each of the two components is recommended before changing to the fixed dose combination. When clinically appropriate, direct change from monotherapy to the fixed combination may be considered.
Telmisartan/hydrochlorothiazide 80mg/12.5mg may be administered once daily in patients whose blood pressure is not adequately controlled by telmisartan 80mg.

Special populations:

Patients with renal impairment: Periodic monitoring of renal function is advised.
Patients with hepatic impairment: In patients with mild to moderate hepatic impairment the posology should not exceed 40mg/12.5mg once daily. Not indicated in patients with severe hepatic impairment.
Elderly patients: No dose adjustment is necessary.
Paediatric population: The safety and efficacy in children and adolescents aged below 18 have not been established. No data are available.

Method of administration: Once daily oral administration. Should be taken with liquid, with or without food.

CONTRAINDICATIONS:

- Hypersensitivity to the active substances or to any of the excipients. Hypersensitivity to other sulphonamide-derived substances (since hydrochlorothiazide is a sulphonamide-derived medicinal product).
- Second and third trimesters of pregnancy.
- Cholestasis and biliary obstructive disorders.
- Severe hepatic impairment. Severe renal impairment (creatinine clearance <30 ml/min).
- Refractory hypokalaemia, hypercalcaemia.
- The concomitant use of telmisartan/hydrochlorothiazide with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m^2).

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

Pregnancy: Should not be initiated during pregnancy.
Hepatic impairment: Should be used with caution in patients with impaired hepatic function.
Renal impairment: Not be used in patients with severe renal impairment (creatinine clearance < 30 ml/min). Experience with telmisartan/hydrochlorothiazide is modest in the patients with mild to moderate renal impairment.
Intravascular hypovolaemia: Symptomatic hypotension, especially after the first dose, may occur in patients, such conditions should be corrected before the administration of telmisartan/hydrochlorothiazide.
Dual blockade of the renin-angiotensin-aldosterone system (RAAS): Dual blockade of RAAS through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is therefore not recommended. ACE-inhibitors and angiotensin II receptor blockers should not be used concomitantly in patients with diabetic nephropathy.
Other conditions with stimulation of the renin-angiotensin-aldosterone system: In patients e.g. with severe congestive heart failure or underlying renal disease, including renal artery stenosis, treatment with medicinal products that affect this system has been associated with acute hypotension, hyper azotaemia, oliguria, or rarely acute renal failure.
Primary Aldosteronism: The use of telmisartan/hydrochlorothiazide is not recommended.
Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy: Special caution is indicated in such patients.
Metabolic and endocrine effects: Thiazide therapy may impair glucose tolerance, therefore, blood glucose monitoring should be considered; An increase in cholesterol and triglyceride levels has been associated with thiazide diuretic therapy; hyperuricaemia may occur or frank gout may be precipitated in some patients receiving thiazide therapy.
Electrolyte imbalance: Thiazides, including hydrochlorothiazide, can cause fluid or electrolyte imbalance. Observe for clinical signs of fluid or electrolyte imbalance.
Non-melanoma skin cancer: An increased risk of non-melanoma skin cancer (NMSC) [basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)] with increasing cumulative dose of hydrochlorothiazide (HCTZ) exposure is known to occur.
Ethnic differences: Telmisartan is apparently less effective in lowering blood pressure in black patients than in non-blacks, possibly because of higher prevalence of low renin states in the black hypertensive population.
Other: Excessive reduction of blood pressure in patients with ischaemic cardiopathy or ischaemic cardiovascular disease could result in a myocardial infarction or stroke.
General: Hypersensitivity reactions to hydrochlorothiazide may occur in patients with or without a history of allergy or bronchial asthma. Exacerbation or activation of systemic lupus erythematosus is known to occur with the use of thiazide diuretics. Photosensitivity reactions are known to occur with thiazide diuretics.
Choroidal effusion, acute myopia and angle-closure glaucoma: Hydrochlorothiazide can cause an idiosyncratic reaction, resulting in choroidal effusion with visual field defect acute transient myopia and acute angle closure glaucoma. The primary treatment is to discontinue hydrochlorothiazide as rapidly as possible.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:

Lithium: Reversible increases in serum lithium concentrations and toxicity are known to occur.
Medicinal products associated with potassium loss and hypokalaemia: (e.g. other kaliuretic diuretics, laxatives, corticosteroids, ACTH, amphotericin, carbenoxolone, penicillin G sodium, salicylic acid and derivatives). If prescribed with the telmisartan/hydrochlorothiazide combination, monitoring of potassium plasma levels is advised.
Medicinal products that may increase potassium levels or induce hyperkalaemia: (e.g. ACE inhibitors, potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, cyclosporin or other medicinal products such as heparin sodium). Not recommended.
Medicinal products affected by serum potassium disturbances: Periodic monitoring of serum potassium and ECG is recommended when telmisartan/hydrochlorothiazide is administered with medicinal products affected by serum potassium disturbances (e.g. digitalis glycosides, antiarrhythmics) and the following torsades de pointes inducing medicinal products (which include some antiarrhythmics), hypokalaemia being a predisposing factor to torsades de pointes;

- Class Ia antiarrhythmics (e.g. Quinidine, hydroquinidine, disopyramide)
- Class III antiarrhythmics (e.g. Amiodarone, sotalol, dofetilide, ibutilide)
- Some antipsychotics (e.g. Thioridazine, chlorpromazine, levomepromazine, trifluoperazine, cyamemazine, sulpiride, sultopride, amisulpride, tiapride, pimozide, haloperidol, droperidol)
- Others (e.g. Bepridil, cisapride, diphemanil, erythromycin IV, halofantrin, mizolastin, pentamidine, sparfloxacine, terfenadine, vincamine IV).

Digitalis glycosides: Thiazide-induced hypokalaemia or hypomagnesaemia favours the onset of digitalis-induced arrhythmia.
Digoxin: Monitor digoxin levels in order to maintain levels within the therapeutic range.
Other antihypertensive agents: Telmisartan may increase the hypotensive effect of other antihypertensive agents.
Antidiabetic medicinal products (oral agents and insulin): Dose adjustment may be required.
Metformin: Risk of lactic acidosis induced by a possible functional renal failure linked to hydrochlorothiazide.
Cholestyramine and colestipol resins: Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins.
Non-steroidal anti-inflammatory medicinal products (NSAIDs): i.e. acetylsalicylic acid may reduce diuretic, natriuretic, and antihypertensive effects; increase the risk of renal impairment. Therefore, the combination should be administered with caution, especially in the elderly.
Medicinal products used in the treatment for gout: (e.g. probenecid, sulfinpyrazone and allopurinol). Dose adjustment of uricosuric medicinal products may be necessary.

Calcium salts: Thiazide diuretics may increase serum calcium levels due to decreased excretion. serum calcium levels should be monitored and calcium dose adjusted accordingly.
Beta-blockers and Diazoxide: May increase the risk of hyperglycaemia.
Amantadine: Thiazides may increase the risk of adverse events caused by amantadine.
Cytotoxic agents (e.g. cyclophosphamide, methotrexate): Thiazides may reduce the renal excretion of cytotoxic medicinal products and potentiate their myelosuppressive effects.
Following medicinal products may potentiate the hypotensive effects of all antihypertensives including telmisartan: Baclofen, amifostine. Furthermore, orthostatic hypotension may be aggravated by alcohol, barbiturates, narcotics or antidepressants.

PREGNANCY AND LACTATION:
Pregnancy: Category D. The use of angiotensin II receptor antagonists is not recommended during the first trimester of pregnancy; contraindicated during the second and third trimesters of pregnancy. No adequate data from the use of telmisartan/hydrochlorothiazide in pregnant women.
Lactation: The use of hydrochlorothiazide during breast feeding is not recommended.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
Can have influence on the ability to drive and use machines. Dizziness or drowsiness may occasionally occur when taking telmisartan/hydrochlorothiazide.

UNDESIRABLE EFFECTS:
The most frequently spontaneously reported events include:
- Headache, dizziness, asthenia, coughing, nausea, fatigue, weakness, edema, face edema, lower limb edema, angioneurotic edema, urticaria, hypersensitivity, sweating increased, erythema.
- Chest pain, atrial fibrillation, congestive heart failure, myocardial infarction, blood pressure increased, hypertension aggravated, hypotension (including postural hypotension), hyperkalemia, syncope.
- Dyspepsia, diarrhoea, pain, urinary tract infection, erectile dysfunction, back pain, abdominal pain, muscle cramps (including leg cramps), myalgia, bradycardia, eosinophilia, thrombocytopenia.
- Uric acid increased, abnormal hepatic function/liver disorder, renal impairment including acute renal failure, anemia, increased CPK, anaphylactic reaction, tendon pain (including tendonitis, tenosynovitis), drug eruption (toxic skin eruption mostly reported as toxicoderma, rash, and urticaria), hypoglycemia (in diabetic patients), and angioedema (with fatal outcome). Rare cases of rhabdomyolysis have been reported in patients receiving angiotensin II receptor blockers.

Creatinine, Blood Urea Nitrogen (BUN): No patient discontinued treatment due to an increase in BUN or creatinine (≥11.2mg/dL) and serum creatinine (≥ 0.5mg/dL)
Liver Function Tests: Occasional elevations of liver enzymes and/or serum bilirubin have occurred. No telmisartan/hydrochlorothiazide treated patients discontinued therapy due to abnormal hepatic function.

OVERDOSE:
Overdose with hydrochlorothiazide is associated with electrolyte depletion, resulting from excessive diuresis. Hypokalaemia may result in muscle spasms and/or accentuate arrhythmia associated with the concomitant use of digitalis glycosides or certain anti-arrhythmic medicinal products.
Telmisartan is not removed by haemodialysis. The patient should be closely monitored, and the treatment should be symptomatic and supportive. Management depends on the time since ingestion and the severity of the symptoms. Suggested measures include induction of emesis and/or gastric lavage. Activated charcoal may be useful in the treatment of overdose. Serum electrolytes and creatinine should be monitored frequently.

PHARMACOLOGICAL PROPERTIES:
PHARMACODYNAMIC PROPERTIES:
Pharmacotherapeutic group: Agents acting on the renin-angiotensin system; angiotensin II antagonists and diuretics,
ATC code: C09DA07
Telmisartan/hydrochlorothiazide is a combination of an angiotensin II receptor antagonist, telmisartan, and a thiazide diuretic, hydrochlorothiazide.

Mechanism Of Action: Telmisartan is an orally active and specific angiotensin II receptor (type AT_1) antagonist;
Hydrochlorothiazide is a thiazide diuretic; The mechanism of the antihypertensive effect of thiazide diuretics is not fully known. Thiazides have an effect on the renal tubular mechanisms of electrolyte reabsorption, directly increasing excretion of sodium and chloride in approximately equivalent amounts. The diuretic action of hydrochlorothiazide reduces plasma volume, increases plasma renin activity, increases aldosterone secretion, with consequent increases in urinary potassium and bicarbonate loss, and decreases in serum potassium.

PHARMACOKINETIC PROPERTIES:
Absorption: Following oral administration, peak concentrations of telmisartan are reached in 0.5-1.5 h after dosing; absolute bioavailability at 40mg and 160mg was 42% and 58%, respectively.
Following oral administration of telmisartan/hydrochlorothiazide, peak concentrations of hydrochlorothiazide are reached in approximately 1.0-3.0 hours after dosing. Based on cumulative renal excretion of hydrochlorothiazide the absolute bioavailability is known to be about 60%.
Distribution: Telmisartan is highly bound to plasma proteins (>99.5%). Hydrochlorothiazide is 68% protein bound in the plasma and its apparent volume of distribution is 0.83-1.14l/kg.
Biotransformation: Metabolised by conjugation to form a pharmacologically inactive acylglucuronide. The cytochrome P450 isoenzymes are not involved in the metabolism of telmisartan. Hydrochlorothiazide is not metabolised in man.
Elimination: ***Telmisartan:*** Most of the administered dose (>97%) was eliminated in faeces via biliary excretion. Total plasma clearance after oral administration is >1500 ml/min. Terminal elimination half-life was >20 hours.
Hydrochlorothiazide: Is excreted almost entirely as unchanged substance in urine. About 60 % of the oral dose is eliminated within 48 hours. Renal clearance is about 250-300 ml/min. The terminal elimination half-life of hydrochlorothiazide is 10-15 hours.
Elderly: Pharmacokinetics do not differ between the elderly and those younger than 65 years.
Gender: Plasma concentrations of telmisartan are generally 2-3 times higher in females than in males.
Renal impairment: Renal excretion does not contribute to the clearance of telmisartan. Based on modest experience in patients with mild to moderate renal impairment (creatinine clearance of 30-60 ml/min, mean about 50 ml/min) no dose adjustment is necessary in patients with decreased renal function.
Hepatic impairment: The elimination half-life is not changed in patients with hepatic impairment.

SHELF LIFE
See expiry on the pack.

AVAILABILITY
Telarb®-H tablet 40mg/12.5mg in a pack of 14's
Telarb®-H tablet 80mg/12.5mg in a pack of 14's

INSTRUCTIONS
Dosage: As advised by the physician.
To be sold on the prescription of registered medical practitioner.
Keep out of reach of children.
Avoid exposure to heat, light and humidity.
Store between 15 to 30°C.
Improper storage may deteriorate the medicine.

ٹیل آرب®-ایچ ٹیبلٹ

(ٹیلمیسارٹن + ہائیڈروکلوروتھائیزائیڈ)

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو گرمی، روشنی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری
سینٹی گریڈ کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی۔

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SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com
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