Telarb® Tablets

(Telmisartan)

WARNING: AVOID USE IN PREGNANCY

When used in pregnancy, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing foetus. When pregnancy is detected, tablets should be discontinued as soon as possible.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Telarb® 20mg Tablet
Each film coated tablet contains:
Telmisartan USP..... 20mg

Telarb® 40mg Tablet
Each film coated tablet contains:
Telmisartan USP..... 40mg

Telarb® 80mg Tablet
Each film coated tablet contains:
Telmisartan USP..... 80mg

PHARMACEUTICAL FORM

Tablet

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS:

Hypertension: Treatment of essential hypertension in adults. It may be used alone or in combination with other antihypertensive agents.

Cardiovascular Prevention/ Risk Reduction: Reduction of cardiovascular morbidity in adults with manifest atherothrombotic cardiovascular disease (history of coronary heart disease, stroke, or peripheral arterial disease) or type 2 diabetes mellitus with documented target organ damage.
Cardiovascular Risk Reduction is indicated for reduction of the risk of myocardial infarction, stroke, or death from cardiovascular causes in patients 55 years of age or older at high risk of developing major cardiovascular events who are unable to take ACE inhibitors.

Telarb® can be used in addition to other needed treatment (such as antihypertensive, antiplatelet or lipid-lowering therapy). Use of telmisartan with an ACE inhibitor is not recommended.

POSOLOGY AND METHOD OF ADMINISTRATION:

Posology: Dosage must be individualized. The usual starting dose is 40mg once a day. Blood pressure response is dose-related over the range of 20 to 80mg

Treatment of Essential Hypertension: The usually effective dose is 40mg once daily. Some patients may already benefit at a daily dose of 20mg. In cases where the target blood pressure is not achieved, dose can be increased to a maximum of 80mg once daily.
Alternatively, telmisartan may be used in combination with thiazide type diuretics such as hydrochlorothiazide which has been shown to have an additive blood pressure lowering effect with telmisartan. When considering raising the dose, it must be borne in mind that the maximum antihypertensive effect is generally attained four to eight weeks after the start of treatment.

Cardiovascular Prevention/ Risk reduction: Recommended dose is 80mg once daily. It is not known whether doses lower than 80mg of telmisartan are effective in reducing cardiovascular morbidity. When initiating telmisartan therapy for the reduction of cardiovascular morbidity, close monitoring of blood pressure is recommended, and if appropriate adjustment of medications that lower blood pressure may be necessary.

Special Populations

Patients with renal impairment: Limited experience is available in patients with severe renal impairment or haemodialysis. A lower starting dose of 20mg is recommended in these patients. No posology adjustment is required for patients with mild to moderate renal impairment.

Patients with hepatic impairment: Telmisartan is contraindicated in patients with severe hepatic impairment. In patients with mild to moderate hepatic impairment the posology should not exceed 40mg once daily.

Elderly patients: No dose adjustment is necessary for elderly patients.

Paediatric Population: The safety and efficacy of telmisartan in children and adolescents aged below 18 years have not been established.

Method of administration: Telarb® tablets are for once-daily oral administration and should be taken with liquid, with or without food.

CONTRAINDICATIONS:

- Hypersensitivity to the active substance or to any of the excipients.
- Second and third trimester of pregnancy.
- Biliary obstructive disorders.
- Severe hepatic impairment.

The concomitant use of telmisartan 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: Angiotensin II receptor antagonists should not be initiated during pregnancy. When pregnancy is diagnosed, treatment with angiotensin II receptor antagonists should be stopped immediately, and, if appropriate, alternative therapy should be started.

Hepatic impairment: Not to be given to patients with cholestasis, biliary obstructive disorders or severe hepatic impairment. Should be used only with caution in patients with mild to moderate hepatic impairment.

Renovascular hypertension: Increased risk of severe hypotension and renal insufficiency in bilateral renal artery stenosis.

Renal impairment and kidney transplantation: In patients with impaired renal function, periodic monitoring of potassium and creatinine serum levels is recommended. No experience regarding the administration of this medicinal product in patients with recent kidney transplantation.

Intravascular hypovolaemia: Symptomatic hypotension, especially after the first dose, may occur in patients who are volume and/or sodium depleted by vigorous diuretic therapy, dietary salt restriction, diarrhoea or vomiting. Such conditions should be corrected before the administration of telmisartan. Volume and/or sodium depletion should be corrected prior to administration of telmisartan.

Dual blockade of the renin-angiotensin-aldosterone system (RAAS): Concomitant use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren increases the risk of hypotension, hyperkalaemia and decreased renal function (including acute renal failure). 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 whose vascular tone and renal function depend predominantly on the activity of the renin angiotensin-aldosterone system (e.g. patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis), treatment with medicinal products that affect this system such as telmisartan has been associated with acute hypotension, hyperazotaemia, oliguria, or rarely acute renal failure.

Primary aldosteronism: Use of telmisartan is not recommended in primary aldosteronism.

Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy: Special caution is indicated in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy.

Diabetic patients treated with insulin or antidiabetics: Hypoglycaemia may occur under telmisartan treatment. Therefore, appropriate blood glucose monitoring should be considered, a dose adjustment of insulin or antidiabetics may be required, when indicated.

Hyperkalaemia: The use of medicinal products that affect the renin-angiotensin-aldosterone system may cause hyperkalaemia. In the elderly, in patients with renal insufficiency, in diabetic patients, in patients concomitantly treated with other medicinal products that may increase potassium levels, and/or in patients with intercurrent events, hyperkalaemia may be fatal. Before considering the concomitant use of medicinal products that affect the renin- angiotensin aldosterone system, the benefit risk ratio should be evaluated.
Medicinal products or therapeutic classes of medicinal products that may provoke hyperkalaemia are salt substitutes containing potassium, potassium-sparing diuretics, ACE inhibitors, angiotensin II receptor antagonists, non-steroidal anti-inflammatory medicinal products (NSAIDS, including selective COX-2 inhibitors), heparin, immunosuppressive agents (cyclosporin or tacrolimus), and trimethoprim.
Intercurrent events, in particular dehydration, acute cardiac decompensation, metabolic acidosis, worsening of renal function, sudden worsening of the renal condition (e.g. infectious diseases), cellular lysis (e.g. acute limb ischaemia, rhabdomyolysis, extend trauma). Close-monitoring of serum potassium in at risk patients is recommended.

Ethnic differences: As observed for angiotensin converting enzyme inhibitors, telmisartan and the other angiotensin II receptor antagonists are apparently less effective in lowering blood pressure in black people than in non-blacks, possibly because of higher prevalence of low-renin states in the black hypertensive population.

Other: As with any antihypertensive agent, excessive reduction of blood pressure in patients with ischaemic cardiopathy or ischaemic cardiovascular disease could result in a myocardial infarction or stroke.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:
Digoxin: Plasma concentration of digoxin is known to be increased when telmisartan was co administered with digoxin therefore, when initiating, adjusting, and discontinuing telmisartan, monitor digoxin levels in order to maintain levels within the therapeutic range. As with other medicinal products acting on the RAAS, telmisartan may provoke hyperkalaemia.

Concomitant use not recommended: Potassium sparing diuretics or potassium supplements ;Angiotensin II receptor antagonists such as telmisartan, attenuate diuretic induced potassium loss. Potassium sparing diuretics e.g. spironolactone, eplerenone, triamterene, or amiloride, potassium supplements, or potassium containing salt substitutes may lead to a significant increase in serum potassium. If concomitant use is indicated because of documented hypokalaemia, they should be used with caution and with frequent monitoring of serum potassium.

Lithium: Reversible increases in serum lithium concentrations and toxicity is known to occur.

Concomitant use requiring caution: Non-steroidal anti-inflammatory medicinal products: NSAIDs may reduce the antihypertensive effect of angiotensin II receptor antagonists. Co-administration of angiotensin II receptor antagonists and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution, especially in the elderly.
Diuretics (thiazide or loop diuretics): Prior treatment with high dose diuretics such as furosemide (loop diuretic) and hydrochlorothiazide (thiazide diuretic) may result in volume depletion, and in a risk of hypotension when initiating therapy with telmisartan.

To be taken into account with concomitant use
Other antihypertensive agents: The blood pressure lowering effect can be increased by concomitant use of other antihypertensive medicinal products. Based on their pharmacological properties it can be expected that the 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.

Corticosteroids (systemic route): Reduction of the antihypertensive effect.

FERTILITY, PREGNANCY AND LACTATION:
Fertility: No effects on male and female fertility were known to occur.

Pregnancy: Pregnancy Categories C (first trimester) and D (second and third trimesters). The use of angiotensin II receptor antagonists is contraindicated during the second and third trimesters of pregnancy.

Breast-feeding: Not recommended and alternative treatments with better established safety profiles during breastfeeding are preferable, especially while nursing a new born or preterm infant.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
When driving vehicles or operating machinery it should be taken into account that dizziness or drowsiness may occasionally occur when taking antihypertensive therapy such as telmisartan.

UNDESIRABLE EFFECTS:
The most frequent 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.

OVERDOSE:
The most prominent manifestations of overdose were hypotension and tachycardia; bradycardia, dizziness, increase in serum creatinine, and acute renal failure have also been reported.
Patient should be closely monitored, and the treatment should be symptomatic and supportive. Suggested measures include induction of emesis and / or gastric lavage. Activated charcoal may be useful in the treatment of over dosage. Serum electrolytes and creatinine should be monitored frequently.

PHARMACOLOGICAL PROPERTIES
PHARMACODYNAMIC PROPERTIES:
Pharmacotherapeutic group: Angiotensin II Antagonists, plain.
ATC Code: C09CA07.

Mechanism of action: Orally active and specific angiotensin II receptor (type AT_1) antagonist; displaces angiotensin II with very high affinity from its binding site at the AT_1 receptor subtype, which is responsible for the known actions of angiotensin II; selectively binds the AT_1 receptor. The binding is long-lasting. In human, an 80mg dose almost completely inhibits the angiotensin II evoked blood pressure increase. The inhibitory effect is maintained over 24 hours and still measurable up to 48 hours.

PHARMACOKINETIC PROPERTIES
Absorption: Absorption is rapid although the amount absorbed varies. Mean absolute bioavailability is about 50%. When taken with food, the reduction in the area under the plasma concentration time curve ($AUC_{0-\infty}$) varies from approximately 6% (40mg dose) to approximately 19% (160mg dose). By 3 hours after administration, plasma concentrations are similar whether telmisartan is taken fasting or with food.

Distribution: Telmisartan is largely bound to plasma protein (>99.5 %), mainly albumin and alpha-1 acid glycoprotein. The mean steady state apparent volume of distribution (Vdss) is approximately 500 L.

Biotransformation: Metabolised by conjugation to the glucuronide of the parent compound. No pharmacological activity has been shown for the conjugate.

Elimination: Telmisartan is characterised by biexponential decay pharmacokinetics with a terminal elimination half-life of >20 hours. After oral (and intravenous) administration, telmisartan is nearly exclusively excreted with the faeces, mainly as unchanged compound.
Cumulative urinary excretion is <1% of dose. Total plasma clearance (Cl_{tot}) is high (approximately 1,000 ml/min) compared with hepatic blood flow (about 1,500 ml/min).

SPECIAL POPULATIONS:
- **Renal impairment:** In patients with mild to moderate and severe renal impairment, doubling of plasma concentrations is known to occur. However, lower plasma concentrations were observed in patients with renal insufficiency undergoing dialysis. Telmisartan is highly bound to plasma protein in renal-insufficient patients and cannot be removed by dialysis. The elimination half-life is not changed in patients with renal impairment.
- **Hepatic impairment:** Pharmacokinetic studies in patients with hepatic impairment showed an increase in absolute bioavailability up to nearly 100 %. The elimination half-life is not changed in patients with hepatic impairment.

SHELF LIFE
See expiry on the pack.

AVAILABILITY
Telarb® 20mg tablet in a pack of 14's
Telarb® 40mg tablet in a pack of 14's
Telarb® 80mg tablet 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® ٹیبلٹ
(ٹیلمیسارٹن)

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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