Telsarta®

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COMPOSITION
Telsarta 20 mg Tablet
Each Tablet contains:
Telmisartan USP…….. 20 mg
Telsarta 40 mg Tablet
Each Tablet contains:
Telmisartan USP…….. 40 mg
Telsarta 80 mg Tablet
Each Tablet contains:
Telmisartan USP…….. 80 mg

(USP Specs.)

WARNING: PREGNANCY AND FETAL TOXICITY
Drugs that act directly on the renin-angiotensin system such as Telmisartan can cause injury and death in the developing fetus when taken during pregnancy. When pregnancy is detected, Telmisartan should be discontinued as soon as possible.

DESCRIPTION
TELSARTA tablets contain Telmisartan, a non-peptide angiotensin II receptor (sub-type AT1) antagonist. Telmisartan is chemically described as[1,1`-Biphenyl]-2-caboxylic acid, 4`-[(1,4`-dimethyl-2`-propyl[2,6`-bi-1H-benzimidazol]-1`-yl)methyl.
Its molecular formula is $C_{33}H_3N_4O_2$

CLINICAL PHARMACOLOGY

Mechanism of Action
Angiotensin II is formed from angiotensin 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 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 AT1 receptor in many tissues, such as vascular smooth muscle and the adrenal gland. Its action is therefore independent of the pathways for angiotensin II synthesis.
Telmisartan displaces angiotensin II with very high affinity from its binding site at the AT1 receptor subtype, which is responsible for the known actions of angiotensin II. Telmisartan does not exhibit any partial agonist activity at the AT1 receptor. Telmisartan selectively binds the AT1 receptor. The binding is long-lasting. Telmisartan does not show affinity for other receptors, including AT2 and other less characterized AT receptors.
Telmisartan does not inhibit angiotensin converting enzyme (kininase II), the enzyme which also degrades bradykinin. Therefore it is not expected to potentiate bradykinin-mediated adverse effects such as cough.

Pharmacokinetics

Absorption
Absorption of Telmisartan is rapid although the amount absorbed varies. The mean absolute bioavailability for telmisartan is about 50 %. When telmisartan is taken with food, the reduction in the area under the plasma concentration-time curve (AUC0-∞) of telmisartan varies from approximately 6 % (40 mg dose) to approximately 19 % (160 mg dose). By 3 hours after administration, plasma concentrations are similar whether telmisartan is taken during fasting or with food. The small reduction in AUC is not expected to cause a reduction in the therapeutic efficacy.

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.

Metabolism
Telmisartan is metabolized by conjugation to the glucuronide of the parent compound. No pharmacological activity has been shown for the conjugate.

Elimination
Telmisartan is characterized by bi-exponential decay pharmacokinetics with a terminal elimination half-life of >20 hours. The maximum plasma concentration (Cmax) and to a smaller extent the area under the plasma concentration-time curve (AUC), increase disproportionately with dose. There is no evidence of clinically relevant accumulation of telmisartan taken at the recommended dose.

After oral (and intravenous) administration, Telmisartan is nearly exclusively excreted with the feces, mainly as unchanged compound. Cumulative urinary excretion is <1 % of dose. Total plasma clearance (Cltot) is high (approximately 1,000 ml/min) compared with hepatic blood flow (about 1,500 ml/min).

Following either intravenous or oral administration of 14C-labeled telmisartan, most of the administered dose (>97%) was eliminated unchanged in feces via biliary excretion; only minute amounts were found in the urine (0.91% and 0.49% of total radioactivity, respectively).

INDICATIONS

Hypertension
Telmisartan is indicated in the treatment of hypertension in adults, as monotherapy or as an adjunct to other anti-hypertensive drugs. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions.

Concomitant use of Telmisartan with Aliskiren is contraindicated in diabetes mellitus and not recommended in patients with renal impairment especially in patients with creatinine clearance < 60 ml/min.

Concomitant use of Telmisartan is not recommended with ACE inhibitors.

Cardiovascular risk reduction:
Telmisartan 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 that are unable to take ACE inhibitors.
High risk for cardiovascular events can be evidenced in patients with a history of coronary artery disease, peripheral arterial disease, stroke, transient ischemic attack, or high-risk diabetes (insulin-dependent or non-insulin dependent) with evidence of end-organ damage.
Telmisartan should be used in lowering the risk of cardiovascular events, in combination with other forms of therapy (anti-platelet, anti-hyperlipidemic and/or antihyperglycemic therapies).

Limitations of use:
Patients with primary aldosteronism generally will not respond to antihypertensive effects of Telmisartan. Therefore, use of Telmisartan is not recommended in these patients

DOSAGE AND ADMINISTRATION

Hypertension
The usually starting dose of Telmisartan is 40 mg once daily. However, blood pressure response is dose-related over the range of 20-80 mg, so dosages must be individualized. Some patients may already benefit at a daily dose of 20 mg. In cases where the target blood pressure is not achieved, the dose of Telmisartan can be increased to a maximum of 80 mg once daily.
Most of the antihypertensive effect is apparent within 2 weeks and maximal reduction is generally attained after 4 weeks.
When additional blood pressure reduction beyond that achieved with 80 mg once daily of Telmisartan is required, a diuretic such as hydrochlorothiazide may be added, which has been shown to have an additive blood pressure lowering effect with Telmisartan.

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

Dose adjustment and dosing considerations in Special populations

Elderly (65 years and older)
No dosage adjustment is required in elderly patients.

Renal impairment
No dosage adjustment in needed in mild to moderate renal impairment.
Limited experience is available in patients with severe renal impairment or hemodialysis. A lower starting dose of 20 mg is recommended in these patients. Patients on dialysis may also develop orthostatic hypotension and their blood pressure should be closely monitored.

Hepatic impairment
Telmisartan is contraindicated in patients with severe hepatic impairment (Child-Pugh score > 9). In patients with mild to moderate hepatic impairment (Child-Pugh scores 5-9), the dose should not exceed 40 mg once daily.

Method of administration
The tablets must be taken orally once daily swallowed with a sufficient quantity of water and can be taken with or without food.

CONTRAINDICATIONS

- Hypersensitivity to telmisartan.
- 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 (CrCl < 60 ml/min)

WARNINGS AND PRECAUTIONS

Pregnancy and Fetal Toxicity

Use of drugs that act on the renin-angiotensin system including Angiotensin II receptor antagonists (AIIRAs) during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death.

Exposure to the fetus during pregnancy can be associated with oligohydramnios with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death.

Telmisartan should not be initiated during pregnancy. Unless continued telmisartan therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is detected, treatment with Telmisartan should be stopped immediately. (See USE IN SPECIAL POPULATIONS)

Hypotension
In patients with an activated renin-angiotensin system, such as volume- or salt-depleted patients (e.g., those being treated with high doses of diuretics), symptomatic hypotension may occur after initiation of therapy with telmisartan tablets. Either correct this condition prior to administration of telmisartan tablets, or start treatment under close medical supervision with a reduced dose.

Hyperkalemia
Hyperkalemia may occur with Telmisartan in elderly patients, in patients with advanced renal impairment, heart failure or diabetes, in patients taking potassium supplements, potassium-sparing diuretics, potassium-containing salt substitutes or other drugs that increase potassium levels. The use of drugs that affect the renin-angiotensin-aldosterone system may also predispose individuals to hyperkalemia.
Before considering the concomitant use of medications that affect the renin-angiotensin-aldosterone system; the benefit risk ratio should be evaluated. Close-monitoring of serum potassium in all patients at risk of hyperkalemia, is recommended

Renal impairment
As a consequence of inhibiting the renin-angiotensin-aldosterone system, certain changes in renal function are 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 or renal dysfunction), treatment with angiotensin-converting enzyme (ACE) 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 have been reported with Telmisartan. When Telmisartan is used in patients with existing impaired renal function, periodic monitoring of potassium and creatinine serum levels.

Dual blockade of the renin-angiotensin-aldosterone system (RAAS)
Dual blockade of the Renin-Angiotensin-Aldosterone System (RAAS) via concomitant use of ACE-inhibitors or Aliskiren in patients being treated with angiotensin II receptor blockers (such as Telmisartan), increases the risk of hypotension, hyperkalemia and decreased renal function (including acute renal failure).
Concomitant use of Telmisartan with Aliskiren is contraindicated in diabetes mellitus and not recommended in patients with renal impairment especially in patients with creatinine clearance < 60 ml/min.

Hepatic Impairment
Telmisartan is eliminated primarily by biliary excretion, patients with biliary obstructive disorders or hepatic insufficiency can be expected to have reduced clearance.
Telmisartan is not recommended for patients with cholestasis or biliary obstructive disorders and contraindicated in patients with severe hepatic impairment
In mild to moderate hepatic impairment, Telmisartan should be used with caution and initiated with a lower starting dose. Maximum dose should not exceed 40 mg once daily.

Primary aldosteronism
Patients with primary aldosteronism generally will not respond to antihypertensive drugs acting through inhibition of the renin-angiotensin system. Therefore, the use of Telmisartan is not recommended in these individuals.

Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy
Due to potential vaso-dilatory effect of Telmisartan, special caution is required in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy.

Diabetic patients treated with insulin or any antidiabetics
Telmisartan may cause hypoglycemia when used with insulin or other oral anti-diabetic agents. Blood monitoring of glucose may become essential in such patients and the dose adjustment of concomitant insulin or antidiabetic drug may be required.

Reno-vascular Implications
Telmisartan should be used with caution in patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney.

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.

ADVERSE REACTIONS

Infections and infestations
Uncommon: Upper respiratory tract infection including pharyngitis and sinusitis, urinary tract infection including cystitis
Rare: Sepsis including fatal outcome
Blood and the lymphatic system disorders
Uncommon: Anaemia
Rare: Eosinophilia, thrombocytopenia
Immune system disorders
Rare: Anaphylactic reaction, hypersensitivity
Metabolism and nutrition disorders
Uncommon: Hyperkalaemia
Rare: Hypoglycaemia (in diabetic patients)
Psychiatric disorders
Uncommon: Depression, insomnia
Rare: Anxiety
Nervous system disorders
Uncommon: Syncope
Rare: Somnolence
Eye disorders
Rare: Visual disturbance
Ear and labyrinth disorders
Uncommon: Vertigo
Cardiac disorders
Uncommon: Bradycardia
Rare: Tachycardia
Vascular disorders
Uncommon: Hypotension, orthostatic hypotension
Respiratory, thoracic and mediastinal disorders
Uncommon: Dyspnoea, cough
Very rare: Interstitial lung disease
Gastrointestinal disorders
Uncommon: Abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting
Rare: Stomach discomfort, dry mouth
Hepato-biliary disorders
Rare: Hepatic function abnormal/liver disorder
Skin and subcutaneous tissue disorders
Uncommon: Hyperhidrosis, pruritus, rash
Rare: Angioedema (also with fatal outcome), eczema, erythema, urticaria, drug eruption, toxic skin eruption
Muscoloskeletal and connective tissue disorders
Uncommon: Myalgia, back pain (e.g. sciatica), muscle spasms
Rare: Arthralgia, pain in extremity, tendon pain (tendonitis like symptoms)
Renal and urinary disorders
Uncommon: Renal impairment including acute renal failure
General disorders and administration site conditions
Uncommon: Chest pain, asthenia (weakness)
Rare: Influenza-like illness
Investigations
Uncommon: Blood creatinine increased
Rare: Blood uric acid increased, hepatic enzyme increased, blood creatine phosphokinase increased, haemoglobin decreased

DRUG INTERACTIONS

Aliskiren and ACE inhibitors
Concomitant use of Telmisartan with Aliskiren is contraindicated in diabetes mellitus and not recommended in patients with renal impairment especially in patients with creatinine clearance < 60 ml/min.
Concomitant use of Telmisartan is not recommended with ACE inhibitors due to additive effects on Renin-Angiotensin-Aldosterone System blockade.

Digoxin
When Telmisartan was co-administered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) were observed. Therefore, digoxin levels should be monitored when initiating, adjusting, and discontinuing Telmisartan for the purpose of keeping the digoxin level within the therapeutic range.

Lithium
Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin receptor blockers including Telmisartan. If use of the combination proves necessary, careful monitoring of serum lithium levels is recommended.

NSAIDs and selective COX-II inhibitors
In patients who are elderly, volume-depleted (including those with dehydration or on diuretic therapy), or with compromised renal function, co-administration of NSAIDs, including selective COX-2 inhibitors, with angiotensin II receptor antagonists, including Telmisartan, may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible. Monitor renal function periodically in patients receiving Telmisartan and NSAID therapy.

The antihypertensive effect of angiotensin II receptor antagonists, including Telmisartan may be reduced by NSAIDs including selective COX-2 inhibitors.

Potassium sparing diuretics or potassium supplements
Angiotensin II receptor antagonists such as Telmisartan, reduce 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 when used in conjunction with Telmisartan. If concomitant use is indicated because of documented hypokalemia, they should be used with caution and with frequent monitoring of serum potassium.

Diuretics (thiazides & loop diuretics)
Prior treatment with high dose diuretics such as furosemide (loop diuretic) and hydrochlorothiazide (thiazide diuretic) may result in volume depletion, and a potential risk of hypotension when initiating therapy with Telmisartan.

Corticosteroids
Reduction of anti-hypertensive effect of Telmisartan has been observed.

Other interactions
Orthostatic hypotension may be aggravated when Telmisartan is used with alcohol, barbiturates, narcotics, or antidepressants.

USE IN SPECIAL POPULATIONS

Pregnancy
US FDA Pregnancy Category D. The use of angiotensin II receptor antagonists (AIIRAs) including Telmisartan is not recommended during the first trimester of pregnancy. The use of AIIRAs including Telmisartan is contraindicated during the second and third trimesters of pregnancy.
Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Resulting oligohydramnios can be associated with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death. Unless continued AIIRA therapy is considered essential, patients planning pregnancy should be switched to alternative treatments which have an established safety profile for use in pregnancy. When pregnancy is detected, discontinue telmisartan as soon as possible.
In the unusual case that there is no appropriate alternative to therapy, the mother should be apprised of the potential risk to the fetus. Perform serial ultrasound examinations to assess the intra-amniotic environment. If oligohydramnios is observed, discontinue Telmisartan unless it is considered lifesaving for the mother. Exposed infants whose mothers have taken AIIRAs should be closely observed. Fetal testing may be appropriate. Ultrasound check of renal function and skull is recommended. If oliguria or hypotension occurs in neonates with a history of in utero exposure to Telmisartan, support of blood pressure and renal perfusion should be provided. Exchange transfusions or dialysis may be required as a means of reversing hypotension and/or substituting for disordered renal function.

Nursing Mothers
Because no information is available regarding the use of Telmisartan during breast-feeding, Telmisartan is not recommended and alternative treatments with better established safety profiles during breast-feeding are preferable, especially while nursing a newborn or preterm infant.

Pediatrics
Safety and efficacy of Telmisartan has not been established in patients <18 years of age.
Geriatrics
The pharmacokinetics of telmisartan do not differ between the elderly and those younger than 65 years

Renal Impairment
No dosage adjustment is necessary in patients with mild to moderate impairment of renal function. Caution should be exercised in patients with severe renal impairment. Telmisartan is not removed from blood by hemodialysis. The elimination half-life is not changed in patients with renal impairment. (See WARNINGS AND PRECAUTIONS and DOSAGE AND ADMINISTRATION)

Hepatic Impairment
In patients with hepatic insufficiency, plasma concentrations of telmisartan are increased, and absolute bioavailability approaches 100%. The elimination half-life is not changed in patients with hepatic impairment. Telmisartan is contraindicated in patients with severe liver impairment while for mild to moderate liver disease; dose of 40 mg should not be exceeded. (See DOSAGE AND ADMINISTRATION and WARNINGS AND PRECAUTIONS)

OVERDOSAGE

There is limited information available with regards to overdose in humans.

Symptoms
The most prominent manifestations of Telmisartan overdose are hypotension and tachycardia; bradycardia and dizziness. Increase in serum creatinine, and acute renal failure have also been reported.

Management of overdose
Telmisartan is not removed by hemodialysis. Over dosed patients 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 over dosage. Serum electrolytes and creatinine should be monitored frequently. If hypotension occurs, the patient should be placed in a supine position, with salt and volume replacement given quickly.

PRESENTATION
Telsarta 20mg: Pack of 10 tablets.
Telsarta 40mg: Pack of 10 tablets.
Telsarta 80mg: Pack of 10 tablets.

INSTRUCTIONS
Use as advised by the physician.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Protect from light, heat and moisture.
Store below 30°C.
For suspected adverse drug reaction, email us at reports@pharmevo.biz

For more information on our products
call PharmAssist helpline 0800-82222
Monday to Friday 9:00 am to 6:00 pm
or email us at : pharmassist@pharmevo.biz

ہدایات:
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یا ہمیں pharmassist@pharmevo.biz پر ای میل کریں

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Our dream, a healthier society

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