TELEXA®- 80

PRODUCT DESCRIPTION

TELEXA® 80 Tablets:

Each tablet contains,
Telmisartan – 80 mg

Rx only
Prescribing Information

USE IN PREGNANCY

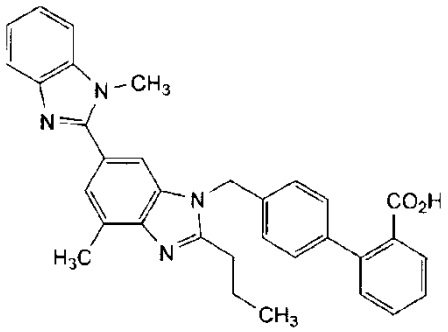
When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus.

When pregnancy is detected, TELEXA® 80 tablets should be discontinued as soon as possible. **See WARNINGS: Fetal/Neonatal Morbidity and Mortality**

DESCRIPTION

Telmisartan:

Structural formula:



Molecular formula: $C_{33}H_{30}N_4O_2$

Chemical name:
4'-[[4-Methyl-6-(1-methyl-1*H*-benzimidazol-2-yl)-2-propyl-1*H*-benzimidazol-1-yl] methyl] bi phenyl-2-carboxylic acid

Molecular weight: 514.6 g/mol

pKa: 4.45

Telmisartan is a specific non-peptide angiotensin II receptor (type AT1) antagonist. Telmisartan is a white or slightly yellowish crystalline powder. It is practically insoluble in water, slightly soluble in methanol and sparingly soluble in methylene chloride.

TELEXA® 80 is available as tablets for oral administration. Tablets containing 80 mg of Telmisartan are available.

PHARMACOLOGIC PROPERTIES:

PHARMACODYNAMICS

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.

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.

There is also an AT2 receptor found in many tissues, but AT2 is not known to be associated with cardiovascular homeostasis. Telmisartan has much greater affinity (>3,000 fold) for the AT1 receptor than for the AT2 receptor.

Blockade of the renin-angiotensin system with ACE inhibitors, which inhibit the biosynthesis of angiotensin II from angiotensin I, is widely used in the treatment of hypertension. ACE inhibitors also inhibit the degradation of bradykinin, a reaction also catalyzed by ACE. Telmisartan does not inhibit ACE (kininase II), it does not affect the response to bradykinin. Whether this difference has clinical relevance is not yet known. Telmisartan does not bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation.

Blockade of the angiotensin II receptor inhibits the negative regulatory feedback of angiotensin II on renin secretion, but the resulting increased plasma renin activity and angiotensin II circulating levels do not overcome the effect of telmisartan on blood pressure

In addition to blocking the RAS, telmisartan acts as a selective modulator of peroxisome proliferator-activated receptor gamma (PPAR-γ), a central regulator of insulin and glucose metabolism. It is believed that telmisartan's dual mode of action may provide protective benefits against the vascular and renal damage caused by diabetes and cardiovasculr disease (CVD).

Telmisartan has a PPARγ agonist activity. Its activity at the peroxisome proliferator-activated receptor delta (PPAR-δ) receptor has prompted speculation around its potential. Telmisartan activates PPAR-δ receptors in several tissues.

In humans, an 80 mg dose of telmisartan almost completely inhibits the angiotensin II evoked increase in blood pressure. The inhibitory effect is maintained over 24 hours and still measurable up to 48 hours.

After administration of the first dose of telmisartan, onset of antihypertensive activity occurs gradually within 3 hours. The maximal reduction in blood pressure is generally attained 4-8 weeks after the start of treatment. With ambulatory blood pressure monitoring and conventional blood pressure measurements, the 24 hour trough to peak ratio for 40-80 mg doses of telmisartan was >70% for both systolic and diastolic blood pressure.

In patients with hypertension, telmisartan reduces both systolic and diastolic blood

pressure without affecting pulse rate. The antihypertensive efficacy of telmisartan is independent of gender or age, and has been compared to antihypertensive drugs including amlodipine, atenolol, enalapril, ramipril, hydrochlorothiazide, lisinopril and valsartan. Telmisartan (40-120 mg once daily) is at least as effective as amlodipine (5-10 mg) and atenolol (50-100 mg once daily). Telmisartan (20-80 mg once daily) is equivalent to enalapril (5-20 mg once daily), and telmisartan (40-160 mg once daily) is comparable to lisinopril (10-40 mg once daily).

Upon abrupt cessation of treatment, blood pressure gradually returns to pre-treatment values over a period of several days without evidence of rebound hypertension

PHARMACOKINETICS

Absorption

Following oral administration of telmisartan, absorption is rapid (t_{max} ranges from 0.5 to 2 hours) although the amount absorbed varies. Peak concentrations (C_{max}) of telmisartan are reached in 0.5-1 hour after dosing. Telmisartan is quickly but to varying degrees absorbed from the gut. The average bioavailability is about 50% (42–100%). Food slightly reduces the bioavailability of telmisartan, with a reduction in the area under the plasma concentration-time curve (AUC) of about 6% with the 40 mg tablet and about 20% after a 160 mg dose.

The absolute bioavailability of telmisartan is dose dependent. The mean absolute bioavailability of 40 mg telmisartan was 40%, whereas the mean absolute bioavailability of the 160 mg dose amounted to about 60%. The pharmacokinetics of orally administered telmisartan are nonlinear over the dose range 20-160 mg, with greater than proportional increases of plasma concentrations (C_{max} and AUC) with increasing doses.

Telmisartan shows bi-exponential decay kinetics with a terminal elimination half life of approximately 24 hours. Trough plasma concentrations of telmisartan with once daily dosing are about 10-25% of peak plasma concentrations. Telmisartan has an accumulation index in plasma of 1.5 to 2.0 upon repeated once daily dosing.

There is no evidence of clinically relevant accumulation of telmisartan taken at the recommended dose. When telmisartan is taken with food, the reduction in the area under the plasma concentration-time curve ($AUC_{0-\infty}$) of telmisartan varies from approximately 6% (40 mg dose) to approximately 19% (160 mg dose). The small reduction in AUC should not cause a reduction in the therapeutic efficacy. Therefore, telmisartan may be taken with or without food.

Distribution

Telmisartan is highly bound to plasma protein (>99.5%), mainly albumin and alpha-1-acid glycoprotein. The mean steady state apparent volume of distribution (Vdss) is approximately 6.6 L/kg.

Metabolism

Telmisartan undergoes substantial first-pass metabolism by conjugation to the acylglucuronide. No pharmacological activity has been shown for the conjugate. Telmisartan is not metabolized by the cytochrome P450 system.

Excretion

Telmisartan is characterized by bi-exponential decay pharmacokinetics with a terminal elimination half-life of 18.3-23.0 hours. It has the longest half-life of any ARB (24 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 1000 mL/min) when compared with hepatic blood flow (about 1500 mL/min).

SPECIAL POPULATIONS

Elderly patients: The pharmacokinetics of telmisartan does not differ between younger and elderly patients (i.e., patients older than 65 years of age).

Patients with renal impairment: Lower plasma concentrations were observed in patients with renal insufficiency (creatinine clearance 30-80 mL/min) undergoing dialysis, however, this has proved not to be of clinical significance. Telmisartan is highly bound to plasma proteins in renal-insufficient subjects and cannot be removed by dialysis.

Patients with hepatic impairment: Pharmacokinetic studies in patients with hepatic impairment showed an increase in absolute bioavailability up to nearly 100%.

Gender: Plasma concentrations are generally 2-3 times higher in females than in males. In clinical trials, however, no clinically significant increases in blood pressure response or incidences of orthostatic hypotension were found in females. No dosage adjustment is necessary.

Children: There are limited data on the pharmacokinetics of telmisartan in patients less than 18 years of age.

TELMISARTAN STUDIES:

ONTARGET (**ON**going **T**elmisartan **A**lone and in Combination with **R**amipril **G**lobal **E**ndpoint **T**rial) study evaluated prevention of cardiovascular morbidity and mortality in patients with known high risk for its occurrence either due to history of coronary artery disease, stroke, transient ischemic attack, peripheral vascular disease, or diabetes mellitus accompanied by evidence of end-organ damage (e.g. retinopathy, left ventricular hypertrophy, macro- or microalbuminuria), which represents a broad cross-section of patients at high risk of cardiovascular events.

The **TRANSCEND** (**T**elmisartan **R**andomised **A**ssessme**N**t **S**tudy in a**CE** i**N**tolerant subjects with cardiovascular **D**isease) and **PROFESS** (**PR**event**io**n Regimen **F**or **E**ffectively avoiding **S**econd **S**trokes studies included different populations, ACE-I intolerant patients and those with a recent stroke (< 120 days), respectively; and evaluated prevention of cardiovascular morbidity and mortality and secondary stroke prevention, respectively as the primary endpoint.

In addition, there was a significantly higher incidence of hyperkalaemia, renal failure, hypotension and syncope in the combination group. Therefore the use of a combination of telmisartan and ramipril is not recommended in this population.

INDICATIONS

TELEXA® 80 tablets are indicated for:

- Treatment of hypertension (High blood pressure), Heart failure and Diabetic kidney disease
- Prevention of cardiovascular morbidity and mortality in patients 55 years or older with coronary artery disease, peripheral artery disease, previous stroke, transient ischemic attack or high risk diabetes with evidence of end organ damage.

CONTRAINDICATIONS

Telmisartan is contraindicated if,

- Hypersensitivity to any of the components of the product
- Pregnancy
- Lactation
- Biliary obstructive disorders OR Bilateral renal artery stenosis in which it can cause kidney failure
- Severe hepatic impairment
- Some drugs affecting the Renin–angiotensin system (RAS), telmisartan can cause birth defects, stillbirths, and neonatal deaths.
- The concomitant use of telmisartan with aliskirenis contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60ml/min/1.73 m^2)

In case of rare hereditary conditions that may be incompatible with an excipient of the product, the use of the product is contraindicated (see PRECAUTIONS).

PRECAUTIONS

Renal artery stenosis and kidney transplant

There are no data available on the use of telmisartan in patients who have had a kidney transplant. There is an increased risk of severe hypotension and renal insufficiency when patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney are treated with medicinal products that affect the renin-angiotensin-aldosterone system.

Increases in serum creatinine have been observed in studies with ACE-inhibitors in patients with single or bilateral renal artery stenosis. An effect similar to that observed with ACE inhibitors should be anticipated with telmisartan.

Impaired renal function

When telmisartan is used in patients with impaired renal function, periodic monitoring of potassium and creatinine serum levels is recommended.

As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. 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 angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists has been associated with acute hypotension,

oliguria and/or progressive uraemia and rarely with acute renal failure and/or death.

Dual blockade of the renin-angiotensin-aldosterone system

As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function (including acute renal failure) have been reported in susceptible individuals, especially if combining medicinal products that affect this system. Dual blockade of the renin-angiotensin-aldosterone system (e.g. by adding an ACE-inhibitor or the direct renin-inhibitor aliskiren to an angiotensin II receptor antagonist) should therefore be limited to individually defined cases with close monitoring of renal function (see CONTRAINDICATIONS).

In the ONTARGET trial, patients receiving the combination of telmisartan and ramipril did not obtain any additional benefit compared to monotherapy, but experienced an increased incidence of hyperkalaemia, renal failure, hypotension and syncope compared with groups receiving telmisartan alone or ramipril alone. Concomitant use of telmisartan and ramipril is therefore not recommended in patients with already controlled blood pressure.

Combination use of ACE inhibitors or angiotensin receptor antagonists, anti-inflammatory drugs and thiazide diuretics

The use of an ACE-inhibitor or angiotensin receptor antagonist, an anti-inflammatory drug (NSAID or COX-2 inhibitor) and a thiazide diuretic at the same time increases the risk of renal impairment. This includes use in fixed-combination products containing more than one class of drug. Combined use of these medications should be accompanied by increased monitoring of serum creatinine, particularly at the institution of the combination. The combination of drugs from these three classes should be used with caution particularly in elderly patients or those with pre-existing renal impairment.

Primary aldosteronism

Patients with primary aldosteronism generally will not respond to antihypertensive medicinal products acting through inhibition of the renin-angiotensin system. Therefore, the use of telmisartan is not recommended.

Diabetes Mellitus

Exploratory post-hoc analyses of two placebo-controlled telmisartan trials suggested an increased risk of fatal myocardial infarction and unexpected cardiovascular death (death occurring within 24 hours of the onset of symptoms without confirmation of cardiovascular cause, and without clinical or post mortem evidence of other etiology) in patients with diabetes mellitus who have no documented medical history of either coronary heart disease or myocardial infarction. In patients with diabetes mellitus, coronary heart disease may be asymptomatic and can therefore remain undiagnosed. Treatment with the blood pressure lowering agent telmisartan may further reduce coronary perfusion in these patients. For this reason, patients with diabetes mellitus should undergo specific diagnostics and be treated accordingly before initiating therapy with telmisartan.

Aortic and mitral valve stenosis, and obstructive hypertrophic cardiomyopathy

As with other vasodilators, special caution is indicated in patients suffering from aortic or mitral valve stenosis, or obstructive hypertrophic cardiomyopathy.

Hyperkalaemia

During treatment with medicinal products that affect the renin-angiotensin-aldosterone system, hyperkalaemia may occur, especially in the presence of renal impairment and/or heart failure. Monitoring of serum potassium levels in patients at risk is recommended.

Based on experience with the use of medicinal products that affect the renin-angiotensin system, concomitant use with potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, or other medicinal products that may increase the potassium level (e.g., heparin, etc.) may lead to an increase in serum potassium and should, therefore, be co-administered cautiously with telmisartan.

Hepatic impairment

The majority of telmisartan is eliminated in the bile. Patients with biliary obstructive disorders or severe hepatic insufficiency can be expected to have reduced clearance.

Telmisartan is, therefore, contraindicated for use in these patients.

Telmisartan should only be used with caution in patients with mild to moderate hepatic impairment (see DOSAGE AND ADMINISTRATION).

Sorbitol

TELEXA® 80 contains sorbitol, Patients with rare hereditary condition of fructose intolerance should not take this product.

Sodium- and/or volume-depleted patients

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, and diarrhoea or vomiting. Such conditions, especially volume and/or sodium depletion, should be corrected before the administration of telmisartan.

Use in cardiac failure

Telmisartan may be used in patients with congestive heart failure. However patients should be carefully observed for hypotension when initiating therapy.

Other

As observed for angiotensin converting enzyme inhibitors, angiotensin receptor antagonists including telmisartan 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. As with any antihypertensive agent, excessive reduction of blood pressure in patients with ischemic cardiopathy or ischemic cardiovascular disease could result in a myocardial infarction or stroke.

Effects on Fertility

No studies on fertility in humans have been performed. Fertility of male and female rats was unaffected at oral telmisartan doses up to 100 mg/kg/day.

Use in Pregnancy: Category D

Angiotensin II receptor antagonists should not be initiated during pregnancy. The use of angiotensin II receptor antagonists is not recommended during the first trimester of pregnancy. When pregnancy is diagnosed, treatment with angiotensin II receptor antagonists should be stopped immediately, and, if appropriate, alternative therapy should be started. The use of angiotensin II receptor antagonists is contraindicated during the second and third trimester of pregnancy.

Although there is no clinical experience with telmisartan in pregnant women, *in utero* exposure to drugs that act directly on the renin-angiotensin system can cause foetal and neonatal morbidity and even death. Several dozen cases have been reported in the world literature in patients who were taking angiotensin converting enzyme inhibitors. Therefore, when pregnancy is detected, telmisartan should be discontinued as soon as possible.

Preclinical studies with telmisartan do not indicate teratogenic effect, but have shown fetotoxicity.

Angiotensin II receptor antagonists exposure during the second and third trimesters is known to induce human foetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalaemia). Oligohydramnios reported in this setting, presumably resulting from decreased foetal renal function, has been associated with foetal limb contractures, craniofacial deformation, and hypoplastic lung development. Prematurity, intrauterine growth retardation, and patent ductus arteriosus have also been reported, although it is not clear whether these occurrences were due to exposure to the drug.

These adverse effects do not appear to occur when drug exposure has been limited to the first trimester. Mothers whose embryos and foetuses are exposed to an angiotensin II receptor antagonist only during the first trimester should be so informed. Women of child-bearing age should be warned of the potential hazards to their foetus should they become pregnant.

Unless continued angiotensin II receptor antagonist therapy is considered essential, patients planning pregnancy should be changed to alternative anti-hypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with angiotensin II receptor antagonists should be stopped immediately, and, if appropriate, alternative therapy should be started.

Should exposure to angiotensin II receptor antagonists have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended. Infants whose mothers have taken angiotensin II receptor antagonists should be closely observed for hypotension, oliguria and hyperkalaemia.

Telmisartan has been shown to cross the placenta in rats. There were no teratogenic effects when telmisartan was administered orally to rats and rabbits during the period of organogenesis at doses up to 50 and 45 mg/kg/day, respectively. However, foetal resorptions were observed at the highest dose level in rabbits. Administration of 50 mg/kg/day telmisartan to rats during pregnancy and lactation caused a decrease in birth weight and suppression of postnatal growth and development of the offspring.

The no-effect dose level in rabbits was 15 mg/kg/day, and corresponded to a plasma AUC value that was about 9 times higher than that anticipated in women at the highest recommended dose. Plasma drug levels were not measured at the high dose level in rats,

but data from other studies suggest that they would have been similar to those in women at the maximum recommended dose.

Use in Lactation

Telmisartan is contraindicated during lactation since it is not known whether it is excreted in human milk. Animal studies have shown excretion of telmisartan in breast milk. No clinical trials have been carried out in lactating women. Therefore, lactating women should either not be prescribed telmisartan or should discontinue breastfeeding, if telmisartan is administered. Telmisartan is excreted in the milk of lactating rats. When administered orally to lactating rats at 50 mg/kg/day, telmisartan suppressed postnatal growth and development of the offspring.

Use in Children

The safety and efficacy of telmisartan for use in children below 18 years have not been established.

Effects on ability to drive and use machines

There are no data to suggest that telmisartan affects the ability to drive and use machines. However, when driving or operating machinery it should be taken into account that with antihypertensive therapy, occasionally dizziness or drowsiness may occur.

Carcinogenicity

In studies on mice and rats did not show any increases in tumor incidences when telmisartan was administered in the diet at doses up to 1000 and 100 mg/kg/day, respectively. Plasma AUC values at the highest dose levels were approximately 60 and 15 times greater, respectively, than those anticipated in humans at the maximum recommended dose.

Genotoxicity

Telmisartan was not genotoxic in a battery of tests for gene mutations and clastogenicity.

INTERACTIONS WITH OTHER MEDICINES

Telmisartan may increase the hypotensive effect of other antihypertensive agents.
Other interactions of clinical significance have not been identified. Co-administration of telmisartan did not result in a clinically significant interaction with digoxin, warfarin, hydrochlorothiazide, glibenclamide, ibuprofen, paracetamol, simvastatin and amlodipine.

Telmisartan increases blood potassium levels. Combination with potassium preparations or potassium-sparing diuretics could cause hyperkalaemia (excessive potassium levels).

When telmisartan was co-administered with digoxin, an increase in digoxin AUC (22%), Cmax (50%), and Cmin (13%) values was observed. It is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing telmisartan to avoid possible over- or under- digitalization.

In one study, the co-administration of telmisartan 80 mg once daily and ramipril 10 mg once daily to healthy subjects increases steady-state C_{max} and AUC of ramipril 2.3- and 2.1 fold, respectively, and C_{max} and AUC of ramiprilat 2.4- and 1.5-fold, respectively. In contrast, C_{max} and AUC of telmisartan decrease by 31% and 16% respectively. The clinical relevance of this observation is not fully known. When co-administering telmisartan and ramipril, the response may be greater because of the possibly additive pharmacodynamics effects of the combined drugs and also because of the increased exposure to ramipril and ramiprilat in the presence of telmisartan. Combining telmisartan with ramipril in the ONTARGET trial resulted in a significantly higher incidence of hyperkalaemia, renal failure, hypotension and syncope compared to telmisartan alone or ramipril alone. Concomitant use of telmisartan and ramipril is therefore not recommended in patients with already controlled blood pressure and should be limited to individually defined cases with close monitoring of renal function (see also PRECAUTIONS).

Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors. Cases have also been reported with angiotensin II receptor antagonists including telmisartan. Careful monitoring of serum lithium levels is recommended during concomitant use.

Treatment with NSAIDs (i.e. aspirin at anti-inflammatory dosage regimens, COX-2 inhibitors and non-selective NSAIDs) is associated with the potential for acute renal insufficiency in patients who are dehydrated. Combination with NSAIDs, especially in patients with impaired kidney function, has a risk of causing (usually reversible) kidney failure. Compounds acting on the renin-angiotensin system like telmisartan may have synergistic effects. Patients receiving NSAIDs and telmisartan should be adequately hydrated and be monitored for renal function at the beginning of combined treatment. A reduced effect of antihypertensive drugs like telmisartan by inhibition of vasodilating prostaglandins has been reported during combined treatment with NSAIDs.

Telmisartan is not metabolized by the cytochrome P450 system and had no effects *in vitro* on cytochrome P450 enzymes, except for some inhibition of CYP2C19. Telmisartan is not expected to interact with drugs that inhibit, or are metabolized by, cytochrome P450 enzymes.

ADVERSE EFFECTS

Adverse reactions have usually been mild and transient in nature and have only infrequently required discontinuation of therapy. The incidence of adverse reactions was not dose related and showed no correlation with gender, age or race of the patients.
After the first dose of telmisartan, the incidence of symptomatic orthostatic hypotension with symptoms severe enough to be reported as an adverse event

It cannot be determined whether these events were causally related to telmisartan tablets:

Infections and infestations: upper respiratory tract infections (including rhinitis), bronchitis, urinary tract infections (including cystitis), infection, fungal infection, abscess, otitis media

Immune system disorders: allergy
Metabolism and nutrition disorders: gout, hypercholesterolaemia, diabetes mellitus
Psychiatric disorders: anxiety, insomnia, depression, nervousness
Nervous system disorders: somnolence, migraine, paraesthesia, hypoaesthesia
Eye disorders: visual disturbance, conjunctivitis
Ear and labyrinth disorders: vertigo, tinnitus, earache
Cardiac disorders: tachycardia, bradycardia, palpitation, angina pectoris
Vascular disorders: hypotension, flushing, cerebrovascular disorder
Respiratory disorders*:* dyspnoea, asthma, epistaxis
Gastrointestinal disorders: dry mouth, flatulence, stomach discomfort, vomiting, constipation, gastritis, haemorrhoids, gastroenteritis, enteritis, gastroesophageal reflux, toothache
Skin and subcutaneous tissue disorders*:* eczema, pruritus, hyperhidrosis, rash, dermatitis
Musculoskeletal, connective tissue and bone disorders: arthralgia, involuntary muscle contractions or muscle spasms (cramps in legs) or pain in extremity (leg pain), arthritis
Renal and urinary tract disorders: micturition frequency
Reproductive system and breast disorders: impotence
General disorders and administration site conditions: malaise, fever, leg oedema, dependent oedema
Investigations: abnormal

ECG LABORATORY FINDINGS

No significant differences in changes in laboratory test parameters were observed in clinical studies with telmisartan.

Hemoglobin decreased**:** A greater than 2 g/dL decrease in hemoglobin was observed in 0.8% telmisartan patients compared with 0.3% placebo patients. No patients discontinued therapy due to anaemia.

Blood creatinine increased**:** A 0.5 mg/dL rise or greater in creatinine was observed in 0.4% telmisartan patients compared with 0.3% placebo patients. One telmisartan-treated patient discontinued therapy due to increases in creatinine and blood urea nitrogen.

Hepatic enzymes increased**:** Occasional elevations of liver chemistries occurred in patients treated with telmisartan; all marked elevations occurred at a higher frequency with placebo. No telmisartan-treated patients discontinued therapy due to abnormal hepatic function.

Prevention of cardiovascular morbidity and mortality:

Because common adverse reactions were well characterized in studies of telmisartan in hypertension, only adverse events leading to discontinuation and serious adverse events were recorded in subsequent studies of telmisartan in the prevention of cardiovascular morbidity and mortality.

The safety profile of telmisartan in patients treated for the prevention of cardiovascular morbidity and mortality was consistent with that obtained in hypertensive patients.

In clinical studies with patients at high risk of developing major cardiovascular events, cases of sepsis, including some with fatal outcomes, have been reported.

Post-Marketing Experience

In addition, the following have also been reported since the introduction of telmisartan in the market:

Blood and lymphatic system disorders:

Uncommon: anaemia
Rare: eosinophilia, thrombocytopenia

Immune system disorders:

Rare: anaphylactic reaction, hypersensitivity

Metabolism and nutrition disorders:

Uncommon: hyperkalaemia
Rare: hypoglycemia (in diabetic patients)

Nervous system disorders:

Uncommon: syncope (faint)

Cardiac disorders:

Uncommon: bradycardia

Vascular disorders:

Uncommon: hypotension, orthostatic hypotension

Hepatobiliary disorders:

Rare: hepatic function abnormal / liver disorder*

* Most cases of hepatic function abnormal / liver disorder from post-marketing experience with telmisartan occurred in patients in Japan, who are more likely to experience these adverse reactions.

Skin and subcutaneous tissue disorders:

Rare: angioedema (with fatal outcome), erythema, urticaria, drug eruption, toxic skin eruption

Musculoskeletal, connective tissue and bone disorders:

Rare: tendon pain (tendinitis like symptoms)

Renal and urinary tract disorders:

Uncommon: renal impairment including acute renal failure (see PRECAUTIONS)

General disorders and administration site conditions:

Uncommon: asthenia (weakness)

Investigations:

Uncommon: blood uric acid increased, blood creatine phosphokinase (CPK) increased

DOSAGE AND ADMINISTRATION

Treatment of Hypertension:

***Adults*:** The recommended dose is 40-80 mg once daily. In cases where the target blood pressure is not achieved, telmisartan dose can be increased to 80 mg once daily. 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, while reduction in blood pressure is achieved after the first dose, the maximum antihypertensive effect is generally attained four to eight weeks after the start of treatment.

Prevention of cardiovascular morbidity and mortality

The recommended dose is 80 mg once daily. It is not known whether doses lower than 80 mg of telmisartan are effective in preventing cardiovascular morbidity and mortality.

When initiating telmisartan therapy for the prevention of cardiovascular morbidity and mortality, monitoring of blood pressure is recommended, and if appropriate, adjustment of medications that lower blood pressure may be necessary.

TELEXA® 80 may be administered with or without food.

***Elderly*:** No dosing adjustment is necessary.

***Renal impairment*:** No dose adjustment is required for patients with renal impairment, including those on haemodialysis. Telmisartan is not removed from blood by haemofiltration.

***Hepatic impairment*:** In patients with mild to moderate hepatic impairment, the dosage should not exceed 40 mg once daily (see PRECAUTIONS).

OVERDOSAGE

Limited information is available with regard to overdose in humans. The most prominent manifestations of telmisartan overdose were hypotension and tachycardia; bradycardia also occurred. If symptomatic hypotension should occur, supportive treatment should be instituted. Telmisartan is not removed by haemodialysis.

STORAGE CONDITION: Store below 25°C in dry place. Keep out of reach of children.

PRESENTATION: Telmisartan 80mg Tablets

PACKING: 1*10 TAB

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