Proposed Prescribing Information
For the use of a Registered Medical Practitioner or a Hospital or a Laboratory

TELDAY TABLETS 40/80 MG
TELMISARTAN TABLETS 40/80 mg

BRAND OR PRODUCT NAME
TELDAY TABLETS 40/80 MG

NAME AND STRENGTH OF ACTIVE SUBSTANCE(S)
TELDAY TABLETS 40 MG
Each uncoated tablet contains: Telmisartan Ph. Eur…… 40 mg

TELDAY TABLETS 80 MG
Each uncoated tablet contains: Telmisartan Ph. Eur…… 80 mg

PRODUCT DESCRIPTION
TELDAY TABLETS 40 MG
White or off-white to yellowish oblong biconvex uncoated tablets with break line on one side and plain on the other side.

TELDAY TABLETS 80 MG
White or off-white to yellowish oval biconvex uncoated tablets with break line on one side and plain on other side.

DOSAGE FORM
Uncoated tablet

PHARMACODYNAMICS / PHARMACOKINETICS
Pharmacodynamics
Pharmacotherapeutic group: Angiotensin II Antagonists, plain, ATC Code: C09CA07.

Mechanism of action
Telmisartan is an orally active and specific angiotensin II receptor (type AT1) antagonist. 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. The functional role of these receptors is not known, nor is the effect of their possible overstimulation by angiotensin II, whose levels are increased by telmisartan. Plasma aldosterone levels are decreased by telmisartan. Telmisartan does not inhibit human plasma renin or block ion channels. 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.

In human, an 80 mg dose of telmisartan 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.

Pharmacokinetics

Absorption

Absorption of Telmisartan is rapid although the amount absorbed varies. The mean absolute bioavailability for Telmisartan is about 50 %.

Linearity/non-linearity

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.

Biotransformation

Telmisartan is metabolised by conjugation to the glucuronide of the parent compound. No pharmacological activity has been reported for the conjugate.

Elimination

Telmisartan is characterised by biexponential decay pharmacokinetics with a terminal elimination half-life of >20 hours.

Special Populations

Elderly patients:

The pharmacokinetics of telmisartan do not differ between the elderly and those younger than 65 years.

Patients with renal impairment:

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.

Patients with hepatic impairment:

Patients with hepatic impairment reported an increase in absolute bioavailability up to nearly 100 %. The elimination half-life is not changed in patients with hepatic impairment.

INDICATION

Hypertension:

Treatment of essential hypertension.

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 of cardiovascular events can be evidenced by 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 can be used in additional to other needed treatment (such as antihypertensive, antiplatelet or lipid lowering therapy).

Use of telmisartan with ACE inhibitor is not recommended.

RECOMMENDED DOSAGE AND MODE OF ADMINISTRATION

Adults

Treatment of essential hypertension

The usually effective dose is 40 mg once daily. 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. 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 risk reduction

The recommended dose of telmisartan tablet is 80 mg once a day and can be administered with or without food. It is not known whether doses lower than 80 mg of Telmisartan are effective in reducing the risk of cardiovascular morbidity and mortality. When initiating Telmisartan therapy for the reduction of cardiovascular risk reduction, monitoring of blood pressure is recommended, and if appropriate adjustment of medications that lower blood pressure may be necessary.

Renal impairment

No posology adjustment is required for patients with renal impairment, including those on haemodialysis. Telmisartan is not removed from blood by hemofiltration.

Hepatic impairment

In patients with mild to moderate hepatic impairment, the Posology should not exceed 40 mg once daily.

Elderly

No dosing adjustment is necessary.

Children and adolescents

The safety and efficacy of telmisartan for use in children below 18 years have not been established. Telmisartan may be taken with or without food.

Mode of Administration

Telmisartan tablets are for once-daily oral administration and should be taken with liquid, with or without food.

Precautions to be taken before handling or administering the medicinal product.

Telmisartan should be kept in the sealed blister due to the hygroscopic property of the tablets. Tablets should be taken out of the blister shortly before administration

CONTRAINDICATIONS

- Hypersensitivity to the active substance or to any of the excipients
- Second and third trimesters of pregnancy
- Lactation
- Biliary obstructive disorders
- Severe hepatic impairment
- The concomitant use of Telmisartan with aliskiren is contraindicated in patients with diabetes

mellitus or renal impairment (GFR < 60 ml/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.

WARNINGS AND PRECAUTIONS

Pregnancy:

Angiotensin II receptor antagonists should not be initiated during pregnancy. Unless continued angiotensin II receptor antagonist 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 diagnosed, treatment with angiotensin II receptor antagonists should be stopped immediately, and, if appropriate, alternative therapy should be started.

Hepatic impairment:

Telmisartan is mostly eliminated with the bile. Patients with biliary obstructive disorders or hepatic insufficiency can be expected to have reduced clearance. Telmisartan should be used with caution in these patients.

Renovascular hypertension:

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.

Renal impairment and kidney transplantation:

When Telmisartan is used in patients with impaired renal function, periodic monitoring of potassium and creatinine serum levels is recommended. There is no experience regarding the administration of Telmisartan in patients with recent kidney transplantation.

Intravascular hypovolaemia:

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

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 rennin-inhibitor to an angiotensin II receptor antagonist) is therefore be limited to individually defined cases with close monitoring of renal function.

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 has been associated with acute hypotension, hyperazotaemia, oliguria, or rarely acute renal failure.

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.

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

Diabetic patients treated with insulin or antidiabetics
In these patients hypoglycaemia may occur under Telmisartan treatment. Therefore, in these patients an appropriate blood glucose monitoring should be considered; a dose adjustment of insulin or antidiabetics may be required, when indicated.

Hyperkalaemia:
During treatment with medicinal products that affect the rennin-angiotensin-aldosterone system hyperkalaemia may occur, especially in presence of renal impairment and/or heart failure. Monitoring of serum potassium in patients at risk is recommended. Based on experience with the use of medicinal products that affect the rennin-angiotensin system, concomitant use with potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other medicinal products that may increase the potassium level (heparin, etc.) may lead to an increase in serum potassium and should therefore be co-administered cautiously with telmisartan.

Diabetes mellitus:
In diabetic patients with an additional cardiovascular risk, i.e. patients with diabetes mellitus and coexistent coronary artery disease (CAD), the risk of fatal myocardial infarction and unexpected cardiovascular death may be increased when treated with blood pressure lowering agents such as ARBs or ACE-inhibitors. In patients with diabetes mellitus CAD may be asymptomatic and therefore undiagnosed. Patients with diabetes mellitus should undergo appropriate diagnostic evaluation, e.g. exercise stress testing, to detect and to treat CAD accordingly before initiating treatment with telmisartan.

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.

Others:
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.

Effects on ability to drive and use machines
No studies on the effect on the ability to drive and use machines have been performed. However, when driving vehicles or operating machinery it should be taken into account that dizziness or drowsiness may occasionally occur when taking antihypertensive therapy.

INTERACTIONS WITH OTHER MEDICAMENTS

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.

For digoxin a 20% increase in median plasma digoxin trough concentration has been observed (39% in a single case) monitoring of plasma digoxin levels should be considered.

Co-administration of telmisartan and ramipril may lead to increase of up to 2.5 fold in the AUC0-24 and Cmax of ramipril and ramiprilat. The clinical relevance of this observation is not known.

Reversible increases in serum lithium concentration and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors. Cases have been also reported with angiotensin II receptor antagonists including Telmisartan. Therefore, serum lithium level monitoring is advisable during concomitant use.

Treatment with NSAIDs (i.e. ASA 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. 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.

STATEMENT ON USAGE DURING PREGNANCY AND LACTATION

The use of angiotensin II receptor antagonists is not recommended during the first trimester of pregnancy. The use of angiotensin II receptor antagonists is contraindicated during the second and third trimesters of pregnancy.

Angiotensin II receptor antagonists exposure during the second and third trimesters is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalaemia).

Unless continued angiotensin II receptor antagonist 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 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.

Telmisartan is contraindicated during lactation since it is not known whether it is excreted in human milk.

ADVERSE EFFECTS / UNDESIRABLE EFFECTS

Infections and Infestations: Sepsis including fatal outcome, urinary tract infections (including cystitis), upper respiratory tract infections including pharyngitis and sinusitis.

Blood and Lymphatic System Disorders: Anaemia, eosinophilia, thrombocytopenia.

Immune System Disorders: Anaphylactic reaction, hypersensitivity.

Metabolism and Nutrition Disorders: Hyperkalaemia, Hypoglycaemia (in diabetic patients).

Psychiatric Disorders: Anxiety, insomnia, depression.

Nervous System Disorders: Syncope (faint), Somnolence.

Eye Disorders: Visual disturbance.

Ear and Labyrinth Disorders: Vertigo.

Cardiac Disorders: Bradycardia, tachycardia.

Vascular Disorders: Hypotension, orthostatic hypotension.

Respiratory Disorders: Dyspnoea, cough, Interstitial lung disease.

Gastrointestinal Disorders: Abdominal pain, diarrhoea, dry mouth, dyspepsia, flatulence, stomach discomfort, vomiting.

Hepatobiliary Disorders: Abnormal hepatic function or liver disorder.

Skin and Subcutaneous Tissue Disorders: Angioedema (also with fatal outcome), eczema, erythema, pruritus, hyperhidrosis, urticaria, drug eruption, toxic skin eruption, rash.

Musculoskeletal, Connective Tissue and Bone Disorders: Arthralgia, back pain (e.g. sciatica), muscle spasms, pain in extremity, myalgia, tendon pain (tendinitis-like symptoms).

Renal and Urinary Tract Disorders: Renal impairment including acute renal failure.

General Disorders and Administration Site Conditions: Chest pain, influenza-like illness, asthenia (weakness).

Investigations: Decreased haemoglobin; increased blood uric acid, blood creatinine, hepatic enzymes and blood creatine phosphokinase (CPK).

OVERDOSE AND TREATMENT
There is limited information available with regard to overdose in humans.

Symptoms: The most prominent manifestations of telmisartan overdose were hypotension and tachycardia; bradycardia dizziness, increase in serum creatinine, and acute renal failure have also been reported.

Treatment: 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 overdosage. 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.

STORAGE CONDITIONS
Store below 30°C. Protect from moisture.

PACKAGING AVAILABLE
Telmisartan tablets are packed in Alu-Alu blister of 7 tablets. Such blister strips containing 7 tablets are packed in boxes of 28's along with product information leaflet.

DATE OF REVISION OF PACKAGE INSERT
19 April, 2018

NAME AND ADDRESS OF MANUFACTURER

TORRENT PHARMACEUTICALS LTD.
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INDIA.