For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

TORCILIN–T

(Telmisartan 40 mg and Cilnidipine 10 mg Tablets)

COMPOSITION:

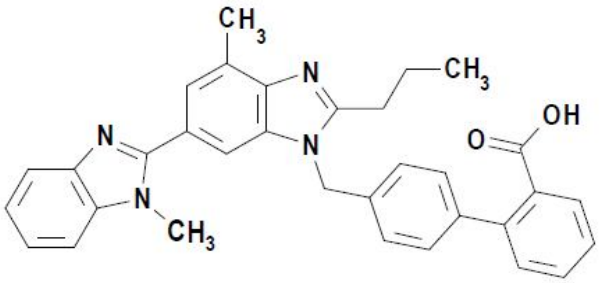
Each film coated tablet contains:
Telmisartan I.P. 40 mg
Cilnidipine 10 mg
Excipients q.s.
Colours: Red Oxide of Iron & Titanium Dioxide I.P

WARNING: FETAL TOXICITY
When pregnancy is detected, discontinue the product as soon as possible.
Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus

DESCRIPTION

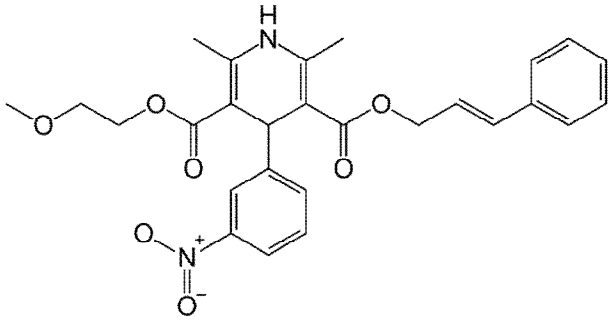
Telmisartan

Telmisartan is a non-peptide angiotensin II receptor (type AT1) antagonist. Telmisartan, a nonpeptide molecule, is chemically described as 4'-[[4-Methyl- 6-(1-methyl-1*H*-benzimidazol-2-yl)-2-propyl-1*H*-benzimidazol-1-yl]-methyl]-biphenyl-2-carboxylic acid. It has empirical formula $C_{33}H_{30}N_4O_2$ and molecular weight is 514.6. The chemical structure of Telmisartan is:



Cilnidipine

Cilnidipine is the novel calcium antagonist accompanied with L-type and N-type calcium channel blocking function and belonging to the chemical class O3-(2-methoxyethyl) O5-[(E)-3-phenylprop-2-enyl] 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine- 3,5-dicarboxylate. Clinidipine is crystalline powder of pale yellow which has not taste and smell. Its molecular formula is $C_{27}H_{28}N_2O_7$ and its molecular weight is 492.52. The structural formula is:



CLINICAL PHARMACOLOGY

Telmisartan

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 AT_1 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 AT_2 receptor found in many tissues, but AT_2 is not known to be associated with cardiovascular homeostasis. Telmisartan has much greater affinity (>3,000 fold) for the AT_1 receptor than for the AT_2 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. Because 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.

Cilnidipine

Unlike other calcium channel antagonists, cilnidipine blocks the influx of Ca^{2+} ions into both vascular smooth muscle at the level of L-type Ca^{2+} channels and neuronal cells at the level of N-type Ca2+ channels. The L-type Ca^{2+} channel blockade by cilnidipine affects predominantly vascular smooth muscle, thereby producing vasodilation of peripheral resistance vessels and coronary arteries. The blockade of N-type Ca^{2+} channels affects predominantly peripheral nerve endings of sympathetic neurons, thereby dilating blood vessels by lowering plasma catecholamine levels. Cilnidipine produced greater reductions in blood pressure in patients with hypertension than in healthy volunteers. Although increases in heart rate were noted in studies with conventional L-type selective DHPs, the changes in heart rate with cilnidipine were

negligible, even in patients with rapid blood pressure reduction. Thus, it appears that the hypotension-induced baroreflex sympathetic stimulation is attenuated by this inhibitory action on N-type Ca^{2+} channels and that even greater blood pressure-lowering effects are achieved with cilnidipine. Furthermore, cilnidipine antagonized the increase in blood pressure in response to acute cold stress, which is not usually depressed by L-type Ca^{2+} channel antagonists. Direct negative inotropic effects were not, however, detected in hypertensive patients who received cilnidipine.

Cilnidipine is a dihydropyridine calcium-channel blocker. It inhibits cellular influx of calcium, thus causing vasodilatation. It has greater selectivity for vascular smooth muscle. It has little or no action at the SA or AV nodes and -ve inotropic activity is rarely seen at therapeutic doses.

Telmisartan
Pharmacodynamics
In normal volunteers, a dose of telmisartan 80 mg inhibited the pressor response to an intravenous infusion of angiotensin II by about 90% at peak plasma concentrations with approximately 40% inhibition persisting for 24 hours.

Plasma concentration of angiotensin II and plasma renin activity (PRA) increased in a dose-dependent manner after single administration of telmisartan to healthy subjects and repeated administration to hypertensive patients. The once-daily administration of up to 80 mg telmisartan to healthy subjects did not influence plasma aldosterone concentrations. In multiple dose studies with hypertensive patients, there were no clinically significant changes in electrolytes (serum potassium or sodium), or in metabolic function (including serum levels of cholesterol, triglycerides, HDL, LDL, glucose, or uric acid).

In 30 hypertensive patients with normal renal function treated for 8 weeks with telmisartan 80 mg or telmisartan 80 mg in combination with hydrochlorothiazide 12.5 mg, there were no clinically significant changes from baseline in renal blood flow, glomerular filtration rate, filtration fraction, renovascular resistance, or creatinine clearance.

Telmisartan
Pharmacokinetics
Following oral administration, peak concentrations (Cmax) of telmisartan are reached in 0.5 to 1 hour after dosing. 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. At 40 and 160 mg the bioavailability was 42% and 58%, respectively. The pharmacokinetics of orally administered telmisartan are nonlinear over the dose range 20 to 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% to 25% of peak plasma concentrations. Telmisartan has an accumulation index in plasma of 1.5 to 2.0 upon repeated once daily dosing.

Distribution
Telmisartan is highly bound to plasma proteins (>99.5%), mainly albumin and α1 - acid glycoprotein. Plasma protein binding is constant over the concentration range achieved with recommended doses. The volume of distribution for telmisartan is approximately 500 liters indicating additional tissue binding.

Metabolism and Elimination
Following either intravenous or oral administration of ^{14}C-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).

Telmisartan is metabolized by conjugation to form a pharmacologically inactive acyl glucuronide; the glucuronide of the parent compound is the only metabolite that has been identified in human plasma and urine. After a single dose, the glucuronide represents approximately 11% of the measured radioactivity in plasma. The cytochrome P450 isoenzymes are not involved in the metabolism of telmisartan.

Total plasma clearance of telmisartan is >800 mL/min. Terminal half-life and total clearance appear to be independent of dose.

Cilnidipine
Pharmacokinetics
After oral administration, large amount of the drug could be detected in the gallbladder, bladder, liver and kidney. Approximately 18 %-29 % and 80 % of the dose was excreted in urine and feces, respectively within 72 h in dogs. The purpose of this experiment was to investigate the metabolism of cilnidipine in human liver microsomes *in vitro* and the effects of selective CYP450 inhibitors on the metabolism of cilnidipine in human liver microsomes and the major CYP450 isoform involved in the metabolism of cilnidipine.

Telmisartan
Specific Populations
Renal Insufficiency
No dosage adjustment is necessary in patients with decreased renal function. Telmisartan is not removed from blood by hemofiltration

Hepatic Insufficiency
In patients with hepatic insufficiency, plasma concentrations of telmisartan are increased, and absolute bioavailability approaches 100%.

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

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

Pediatric Patients
Telmisartan pharmacokinetics have not been investigated in patients <18 years of age.

INDICATIONS
Torcilin-T is indicated for the treatment of hypertension

DOSAGE AND ADMINISTRATION

Dosage must be individualized. Starting dose is one tablet once a day or as directed by physician. Torcilin-T may be administered with or without food. Torcilin-T is usually recommended after breakfast.

CONTRAINDICATION
Contraindicated in patients with known hypersensitivity (e.g., anaphylaxis or angioedema) to telmisartan or cilinidipine or any other component of this product.

Cilnidipine should not be administered in pregnant women and women suspected of being pregnant.

Cardiogenic shock, recent MI or acute unstable angina and severe aortic stenosis.

Cilnidipine should carefully administration in following patients: There is a possibility that the blood concentration raises patients with severe hepatic dysfunction and patients with a history of adverse reactions suffered from calcium antagonist.

Special attention required when administered to patients with serious liver dysfunction because this agent is metabolized in the liver.

WARNINGS AND PRECAUTIONS
Telmisartan
Pregnancy Category D
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. When pregnancy is detected, discontinue Telmisartan as soon as possible.

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. Either correct this condition prior to administration of Telmisartan, or start treatment under close medical supervision with a reduced dose.

If hypotension does occur, the patient should be placed in the supine position and, if necessary, given an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further treatment, which usually can be continued without difficulty once the blood pressure has stabilized.

Hyperkalemia
Hyperkalemia may occur in patients on ARBs, particularly in patients with advanced renal impairment, heart failure, on renal replacement therapy, or on potassium supplements, potassium-sparing diuretics, potassium-containing salt substitutes or other drugs that increase potassium levels. Consider periodic determinations of serum electrolytes to detect possible electrolyte imbalances, particularly in patients at risk.

Impaired Hepatic Function
As the majority of telmisartan is eliminated by biliary excretion, patients with biliary obstructive disorders or hepatic insufficiency can be expected to have reduced clearance. Initiate telmisartan at low doses and titrate slowly in these patients.

Impaired Renal Function
As a consequence of inhibiting the renin-angiotensin-aldosterone system, anticipate changes in renal function 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.

In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen were observed. There has been no long term use of Telmisartan in patients with unilateral or bilateral renal artery stenosis, but anticipate an effect similar to that seen with ACE inhibitors.

Dual Blockade of the Renin-Angiotensin-Aldosterone System
Dual blockade of the RAS with angiotensin-receptor blockers, ACE inhibitors, or aliskiren is associated with increased risks of hypotension, hyperkalemia, and changes in renal function (including acute renal failure) compared to monotherapy.

The reported ONTARGET trial enrolled 25,620 patients ≥55 years old with atherosclerotic disease or diabetes with end-organ damage, randomizing them to telmisartan only, ramipril only, or the combination, and followed them for a median of 56 months. Patients receiving the combination of telmisartan and ramipril did not obtain any additional benefit compared to monotherapy, but experienced an increased incidence of renal dysfunction (e.g., acute renal failure) compared with groups receiving telmisartan alone or ramipril alone.

In most patients no benefit has been associated with using two RAS inhibitors concomitantly. In general, avoid combined use of RAS inhibitors. Closely monitor blood pressure, renal function, and electrolytes in patients on telmisartan and other agents that affect the RAS.

Do not co-administer aliskiren with telmisartan in patients with diabetes. Avoid concomitant use of aliskiren with telmisartan in patients with renal impairment (GFR <60 mL/min/1.73 m^2).

Cilnidipine
Sudden withdrawal may exacerbate angina. Discontinue in patients who experience ischemic pain, hypotension, poor cardiac reserve and heart failure following administration. Patient may feel dizziness due to decrease the pressure. So, do not work at height, drive a car or operate heavy machinery while taking this medicine. An ingredient in grapefruit juice may intensify the medicine's effect so avoid drinking grape fruit juice as much as possible.

Administrations of calcium antagonists suddenly stop, the patients develop the symptoms have been reported. Hence, it was reduced gradually and requiring withdrawal of the agent is performed carefully monitored.

Telmisartan
Carcinogenesis, Mutagenesis, Impairment of Fertility
There was no evidence of carcinogenicity when telmisartan was administered in the diet to mice and rats for up to 2 years. The highest doses administered to mice (1000 mg/kg/day) and rats (100 mg/kg/day) are, on a mg/m^2 basis, about 59 and 13 times, respectively, the maximum recommended human dose (MRHD) of telmisartan. These same doses have been shown to provide average systemic exposures to telmisartan >100 times and >25 times, respectively, the systemic exposure in humans receiving the MRHD (80 mg/day).

Genotoxicity assays did not reveal any telmisartan-related effects at either the gene or chromosome level. These assays included bacterial mutagenicity tests with Salmonella and E. coli (Ames), a gene mutation test with Chinese hamster V79 cells, a cytogenetic test with human lymphocytes, and a mouse micronucleus test.

No drug-related effects on the reproductive performance of male and female rats were noted at 100 mg/kg/day (the highest dose administered), about 13 times, on a mg/m2 basis, the MRHD of telmisartan. This dose in the rat resulted in an average systemic exposure (telmisartan AUC as

determined on day 6 of pregnancy) at least 50 times the average systemic exposure in humans at the MRHD (80 mg/day).

USE IN SPECIFIC POPULATIONS
Telmisartan
Pregnancy
Pregnancy Category D
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. When pregnancy is detected, discontinue Telmisartan as soon as possible. These adverse outcomes are usually associated with use of these drugs in the second and third trimester of pregnancy. Most epidemiologic studies examining fetal abnormalities after exposure to antihypertensive use in the first trimester have not distinguished drugs affecting the renin-angiotensin system from other antihypertensive agents. Appropriate management of maternal hypertension during pregnancy is important to optimize outcomes for both mother and fetus.

In the unusual case that there is no appropriate alternative to therapy with drugs affecting the renin-angiotensin system for a particular patient, apprise the mother 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. Fetal testing may be appropriate, based on the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury. Closely observe infants with histories of in utero exposure to Telmisartan for hypotension, oliguria, and hyperkalemia.

Nursing Mothers
It is not known whether telmisartan is excreted in human milk, but telmisartan was shown to be present in the milk of lactating rats. Because of the potential for adverse effects on the nursing infant, decide whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use
Neonates with a history of in utero exposure to Telmisartan:
If oliguria or hypotension occurs, direct attention toward support of blood pressure and renal perfusion. Exchange transfusions or dialysis may be required as a means of reversing hypotension and/or substituting for disordered renal function. Safety and effectiveness in pediatric patients have not been established.

Geriatric Use
Of the total number of patients receiving Telmisartan in hypertension clinical studies, 551 (19%) were 65 to 74 years of age and 130 (4%) were 75 years or older. No overall differences in effectiveness and safety were observed in these patients compared to younger patients and other

reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Of the total number of patients receiving Telmisartan in the cardiovascular risk reduction study (ONTARGET), the percentage of patients ≥65 to <75 years of age was 42%; 15% of patients were ≥75 years old. No overall differences in effectiveness and safety were observed in these patients compared to younger patients and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Hepatic Insufficiency
Monitor carefully and uptitrate slowly in patients with biliary obstructive disorders or hepatic insufficiency.

DRUG INTERACTION
Telmisartan
Aliskiren:
Do not co-administer aliskiren with Telmisartan in patients with diabetes. Avoid use of aliskiren with Telmisartan in patients with renal impairment (GFR <60 mL/min).

Digoxin:
When Telmisartan was co-administered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) were observed. Therefore, monitor digoxin levels 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 II receptor antagonists including Telmisartan. Therefore, monitor serum lithium levels during concomitant use.

Non-Steroidal Anti-Inflammatory Agents including Selective Cyclooxygenase-2 Inhibitors (COX-2 Inhibitors):
In patients who are elderly, volume-depleted (including those 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 attenuated by NSAIDs including selective COX-2 inhibitors.

Ramipril and Ramiprilat:

Co-administration of telmisartan 80 mg once daily and ramipril 10 mg once daily to healthy subjects increases steady-state Cmax and AUC of ramipril 2.3- and 2.1-fold, respectively, and Cmax and AUC of ramiprilat 2.4- and 1.5-fold, respectively. In contrast, Cmax and AUC of telmisartan decrease by 31% and 16%, respectively. When co-administering telmisartan and ramipril, the response may be greater because of the possibly additive pharmacodynamic effects of the combined drugs, and also because of the increased exposure to ramipril and ramiprilat in the presence of telmisartan. Concomitant use of Telmisartan and ramipril is not recommended.

Other Drugs:
Co-administration of telmisartan did not result in a clinically significant interaction with acetaminophen, amlodipine, glyburide, simvastatin, hydrochlorothiazide, warfarin, or ibuprofen. 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 cytochrome P450 enzymes; it is also not expected to interact with drugs metabolized by cytochrome P450 enzymes, except for possible inhibition of the metabolism of drugs metabolized by CYP2C19.

Cilnidipine
Other antihypertensives and antipsychotics that cause hypotension may modify insulin and glucose responses. Quinidine, carbamazepine, phenytoin, rifampicin, cimetidine and erythromycin are also interacted with the Cilnidipine.

ADVERSE REACTIONS

Telmisartan
Telmisartan has been evaluated for safety in more than 3700 patients, including 1900 treated for over six months and more than 1300 for over one year.

Adverse experiences have generally been mild and transient in nature and have only infrequently required discontinuation of therapy. In placebo-controlled trials involving 1041 patients treated with various doses of Telmisartan (20-160mg) monotherapy for up to 12 weeks, an overall incidence of adverse events similar to that of placebo was observed.

Adverse events occurring at an incidence of 1% or more in patients treated with Telmisartan and at a greater rate than in patients treated with placebo, irrespective of their causal association, are presented in the following table.

	Telmisartan N =1455 %	**Placebo N = 380 %**
Upper Respiratory tract Infection	7	6
Back Pain	3	1
Sinusitis	3	2
Diarrhea	3	2
Pharyngitis	1	0

In addition to the adverse events in the table, the following events occurred at a rate of ≥1% but were at least as frequent in the placebo group: influenza-like symptoms, dyspepsia, myalgia, urinary tract infection, abdominal pain, headache, dizziness, pain, fatigue, coughing,

hypertension, chest pain, nausea, and peripheral edema. Discontinuation of therapy because of adverse events was required in 2.8% of 1455 patients treated with Telmisartan tablets and 6.1% of 380 placebo patients in placebo-controlled clinical trials.

The incidence of adverse events was not dose-related and did not correlate with gender, age, or race of patients.

The incidence of cough occurring with telmisartan in 6 placebo-controlled trials was identical to that noted for placebo-treated patients (1.6%).

In addition to those listed above, adverse events that occurred in more than 0.3% of 3500 patients treated with Telmisartan monotherapy in controlled or open trials are listed below. It cannot be determined whether these events were causally related to Telmisartan tablets:

Autonomic Nervous System: impotence, increased sweating, flushing; Body as a Whole: allergy, fever, leg pain, malaise; Cardiovascular: palpitation, dependent edema, angina pectoris, tachycardia, leg edema, abnormal ECG; CNS: insomnia, somnolence, migraine, vertigo, paresthesia, involuntary muscle contractions, hypoesthesia; Gastrointestinal: flatulence, constipation, gastritis, vomiting, dry mouth, hemorrhoids, gastroenteritis, enteritis, gastroesophageal reflux, toothache, nonspecific gastrointestinal disorders; Metabolic: gout, hypercholesterolemia, diabetes mellitus; Musculoskeletal: arthritis, arthralgia, leg cramps; Psychiatric: anxiety, depression, nervousness; Resistance Mechanism: infection, fungal infection, abscess, otitis media; Respiratory: asthma, bronchitis, rhinitis, dyspnea, epistaxis; Skin: dermatitis, rash, eczema, pruritus; Urinary: micturition frequency, cystitis; Vascular: cerebrovascular disorder; and Special Senses: abnormal vision, conjunctivitis, tinnitus, earache.

During initial clinical studies, a single case of angioedema was reported (among a total of 3781 patients treated).

Clinical Laboratory Findings
In placebo-controlled clinical trials, clinically relevant changes in standard laboratory test parameters were rarely associated with administration of Telmisartan tablets.

Hemoglobin: 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 because of anemia.

Creatinine: 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 because of increases in creatinine and blood urea nitrogen.

Liver Enzymes: 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 because of abnormal hepatic function.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Telmisartan. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate reliably their frequency or establish a causal relationship to drug exposure. Decisions to include these reactions in labeling are typically based on one or more of the following factors: (1) seriousness of the reaction, (2) frequency of reporting, or (3) strength of causal connection to Telmisartan.

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, diarrhea, 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, including Telmisartan.

Cilnidipine

Skin, skin appendages failure: Desquamation, Quincke's edema, Hair loss, Hives, Pruritus**,** Erythema multiforme**,** Papule**,** Rash, Cutaneous dryness and Drying periocular.

Central-peripheral nervous system disorders: Stiff neck, Stiffness of muscle, Dizziness**,** Cool feeling, Disorientation, Headache, Sluggishness, Musculus gastrocnemius spasticity, Difficulty walking, Vertigo, Lightheadedness and Sense to hand vibration.

Impaired vision: Eye abnormalities and Hyperemia, irritation of eyes.

Special sensory impairment of other: Reduced sense of taste and Dysgeusia (bitter).

Mental disorder: Vaguely, Somnolence, Forget things and Insomnia.

Digestive tract disorders: Gastritis, Gastric ulcer, Gastrointestinal hemorrhage, Nausea and vomiting, Diarrhea, Stomatitis, Dry mouth, Gingival hypertrophy**,** Hemorrhagic gastritis**,** Brash, Anorexia, Stomach discomfort, Epigastric pain, Constipation, Sense of fullness in the abdomen and Periodontitis.

Liver and bile duct disorders: Liver dysfunction, Hepatocyte damage, Rise of AST, Elevation of ALT and Increase in serum bilirubin.

Metabolism and nutrition disorders: LDH rise, Serum inorganic phosphorus rise, Serum inorganic phosphorus reduction**,** CPK raise, CPK decline, Serum potassium rise, Decrease in

serum potassium**,** Serum calcium rise, Fasting blood glucose level rise, Blood sugar levels**,** Serum cholesterol rise, Hyperlipidemia, Blood uric acid increased, Hyponatremia, Serum total protein rise, Urine sugar positive and Triglyceride rise.

Cardiovascular disorders (general): Heart failure, Reduction in blood pressure, ST depression, abnormal electrocardiogram, ST segment elevation, CRP rise, cardiothoracic ratio increase, Myocardial infarction, Heart rate, heart rhythm disorder, Atrioventricular block, Atrial tachycardia, Palpitation, Ventricular tachycardia, Atrial fibrillation, Tachycardia, T-wave inversion, Blood vessels (cardiac) failure, Facial redness, Generalized redness and Transient ischemic stroke.

Respiratory Disorder: Respiratory failure, Pharynx different feeling, Sore throat, Throat burning sensation, Dyspnea, Cough and Epistaxis.

Blood disorder: Red blood cell disorder, Hemoglobin increase**,** Polycythemia, Anemia Erythropenia, Decreased hemoglobin, Hematocrit value decrease, Hematocrit increase, White blood cell-reticuloendothelial disorder, Variation of eosinophils, Eosinophilia, Leukopenia, Leukocytosis, Changes in neutrophil, Change (rod) neutrophil, Change (segmental) neutrophil, Changes in lymphocyte, Platelet-bleeding coagulopathy, Thrombocytopenia.

Urological disorder: Blood creatinine increased, renal function deterioration, renal failure, Uric protein rise, Urea nitrogen rise, Decrease in urinary volume, frequent urination, Urinary sediment (red blood cells) and Urine sediment (white blood cell).

General: Facial edema, Facial puffiness, Chest pain, Chest distress sense, Tightness of the chest, Bad mood**,** General malaise (feeling), Edema, glow of the face, Hot flushes, Face heat sensation, Weakness, Lower leg edema, Worsening heart failure, Feeling of warmth. Dizziness, flushing, headache, hypotension, peripheral oedema, tachycardia, palpitations, GI disturbances, increased micturition frequency, lethargy, eye pain, depression, ischaemic chest pain, cerebral or myocardial ischaemia, transient blindness, rashes, fever, abnormal liver function, gingival hyperplasia, myalgia, tremor and impotence.

OVERDOSAGE

Limited data are available with regard to overdosage in humans. The most likely manifestation of over dosage with Telmisartan would be hypotension, dizziness and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted. Telmisartan is not removed by hemodialysis.

EXPIRY DATE

Do not use later than date of expiry.

STORAGE

Store in a Cool Place. Protect from Light & Moisture. Keep out of reach of children.

PRESENTATION
Torcilin–T tablets are available in blister strip of 10 tablets.

MARKETED BY


TORRENT PHARMACEUTICALS LTD.
Torrent House, Off Ashram Road,
Ahmedabad-380 009, INDIA

IN/TORCILIN-T/40,10mg/Feb-15/01/PI