WARNING: when pregnancy is detected Telmisartan should be discontinued as soon as possible as it can cause injury and even death to the developing fetus when used during second and third trimesters of pregnancy.

For the Use of a Registered Medical Practitioner Only

1. Generic Name & Brand Name

Cilnidipine & Telmisartan Tablets

Telpres® LN 80, Telpres® LN 40

2. Qualitative and Quantitative Composition

Telpres® LN 80

Each film coated tablet contains:

Cilnidipine I.P. 10mg

Telmisartan I.P. 80mg

Colour: Red Oxide of Iron and Titanium Dioxide I.P.

Telpres® LN 40

Each film coated tablet contains:

Cilnidipine I.P. 10mg

Telmisartan I.P. 40mg

Colour: Titanium Dioxide I.P.

3. Dosage Form and Strength

Refer section 1 & 2

4. Clinical Particulars

4.1 Therapeutic Indication

The combination is indicated for the treatment of essential hypertension.

4.2 Posology and Method of Administration

Orally take one tablet once daily or as directed by physician.

4.3 Contraindications

Telpres LN is contraindicated

- in patients with known hypersensitivity (e.g., anaphylaxis or angioedema) to telmisartan or cilnidipine or any other component of this product
- Pregnancy
- 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 m2)
- Cardiogenic shock
- Recent history of acute unstable angina or MI

- Severe aortic stenosis
- Heart failure
- Hypotension

4.4 Special Warnings and Precautions for Use

Telmisartan

1. Fetal/Neonatal Morbidity and Mortality

Drugs that act directly on the renin-angiotensin system can cause fetal and neonatal morbidity and death when administered to pregnant women. Discontinue Telmisartan tablets as soon as possible, when pregnancy is detected.

During the second and third trimesters of pregnancy, using drugs which act directly on the renin-angiotensin system has been associated with fetal and neonatal injury, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Oligohydramnios has also been reported, presumably resulting from decreased fetal renal function which have been associated with craniofacial deformation, fetal limb contractures, and hypoplastic lung development.

When patients become pregnant or are considering pregnancy, discontinue the use of Telmisartan as soon as possible.

If no alternative to angiotensin II receptor antagonist is found, mothers should be informed of the potential hazards to their fetuses, and serial ultrasound examinations should be performed to assess the intra-amniotic environment.

If oligohydramnios is observed, telmisartan should be discontinued. Biophysical profiling (BPP), Contraction stress testing (CST), a non-stress test (NST), may be appropriate, depending upon the week of pregnancy. Infants with histories of in utero exposure to an angiotensin II receptor antagonist should be closely monitored for hypotension, oliguria, and hyperkalemia.

2. Hypotension

Symptomatic hypotension may occur after initiation of therapy with Telmisartan, in patients with an activated renin-angiotensin system, such as volume- or salt-depleted patients. This condition should be treated prior to or at start of treatment with Telmisartan, under close medical supervision with a reduced dose.

If hypotension occurs, the patient should be placed in the supine position and, given an intravenous infusion of normal saline, if necessary.

3. Hyperkalemia

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

4. Impaired Hepatic Function

Patients with biliary obstructive disorders or hepatic insufficiency can be expected to have reduced clearance, as the majority of telmisartan is eliminated by biliary excretion. Telmisartan should be initiated at low doses and titrated slowly in these patients.

5. Impaired Renal Function

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.

Long term use of telmisartan in patients with unilateral or bilateral renal artery stenosis has not been established, but an effect similar to that seen with ACE inhibitors can be anticipated.

6. 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. Dual blockade of the renin-angiotensin-aldosterone system (e.g., by adding an ACE-inhibitor to an angiotensin II receptor antagonist) should include close monitoring of renal function.

Patients receiving the combination of Telmisartan and ramipril experienced an increased incidence of renal dysfunction (e.g., acute renal failure), hence concomitant use of these drugs is not recommended.

7. Nursing Mothers

It is unknown whether telmisartan is excreted in human milk. As there is potential for adverse effects on the nursing infant, it should be decided whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

8. Pediatric Use

Safety and effectiveness of Telmisartan in pediatric patients have not been established.

9. Geriatric Use

No overall differences in effectiveness and safety of Telmisartan were observed in elderly patients compared to younger patients.

Cilnidipine

1. Hypotension
2. Poor cardiac reserve
3. heart failure
4. Sudden withdrawal may exacerbate angina
5. Discontinue in patients who experience ischemic pain following administration
6. Pregnancy, lactation.

Use in special population: (Geriatric, Pediatric, Renal Insufficiency, Hepatic Insufficiency): Data not available for the use of this product in Geriatric/Pediatric population and patient with Renal/Hepatic Insufficiency Usual Precaution for calcium channel blockers in these categories of patients and physician's discretion is advised.

Pregnancy: There is no clinical experience with cilnidipine in pregnant women, discretion is advised.

Nursing Mothers/Lactation: Cilnidipine should not be given

4.5 Drugs Interactions

Telmisartan

No.	Drug	Drug Interaction	Remark
1.	Digoxin	Median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) were observed when Telmisartan and Digoxin are administered concomitantly.	Digoxin levels should be monitored when initiating, adjusting, and discontinuing telmisartan
2.	Lithium	Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin II receptor antagonists including telmisartan.	Monitor serum lithium levels during concomitant use.
3.	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 cause deterioration of renal function, including possible acute renal failure. These effects are reversible. The antihypertensive effect of angiotensin II receptor antagonists, including telmisartan may be attenuated by NSAIDs including selective COX-2 inhibitors.	Monitor renal function periodically during concomitant use..
4.	Ramipril and Ramiprilat	Co-administration of telmisartan and ramipril to healthy subjects increases steady-state Cmax and AUC of ramipril and ramiprila tand decreases Cmax and AUC of telmisartan. When co-administering telmisartan and ramipril, the response may be higher due to the possibly additive pharmacodynamic effects of the combined drugs, and also because of the increased exposure to ramipril and ramiprilat	Concomitant use of Telmisartan and ramipril is not recommended.

		in the presence of telmisartan.	
5.	Other Drugs: Acetaminophen, amlodipine, glyburide, simvastatin, hydrochlorothiazide, warfarin, or ibuprofen.	Co-administration of telmisartan did not result in a clinically significant interaction with these drugs	
6.	Drugs that inhibit cytochrome P450 enzymes	Telmisartan is not expected to interact with drugs that inhibit cytochrome P450 enzymes	
7.	drugs metabolized by cytochrome P450 enzymes	Telmisartan does not interact with drugs metabolized by cytochrome P450 enzymes, except for possible inhibition of the metabolism of drugs metabolized by CYP2C19.	

Cilnidipine
Other anti-hypertensives; aldesleukin; antipsychotics that cause hypotension; may modify insulin and glucose responses; quinidine; carbamazepine; phenytoin; rifampicin; cimetidine; erythromycin.

4.6 Use In Special Populations
Pregnancy
Telmisartan has teratogenic effects, Pregnancy Categories C (first trimester) and D (second and third trimesters).
There are no human clinical or animal data concerning the safety of cilnidipine during pregnancy. Until data are available, administration of cilnidipine during pregnancy should be avoided.

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
Safety and effectiveness of telmisartan 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 Telmisartan slowly in patients with biliary obstructive disorders or hepatic insufficiency.

Dosage recommendations have not been established in patients with mild to moderate hepatic impairment; therefore, dose selection of cilnidipine should be cautious and should start at the lower end of the dosing range. Transient and generally clinically insignificant elevations in SGOT, SGPT, alkaline phosphatase, and serum bilirubin have been reported during calcium antagonist therapy in less than 1% of patients.

Impaired Renal Function

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.

Long term use of telmisartan in patients with unilateral or bilateral renal artery stenosis has not been established, but an effect similar to that seen with ACE inhibitors can be anticipated.

4.7 Effects On ability to Drive and Use Machines

Since side effects such as syncope, somnolence, dizziness, or vertigo may occur with use of antihypertensive agents, caution patients about engaging in activities such as driving a vehicle or operating appliances or machinery.

4.8 Undesirable Effects

Telmisartan

Autonomic Nervous System: increased sweating, flushing, impotence,

Body as a Whole: allergy, leg pain, malaise, fever

Cardiovascular: palpitation, angina pectoris, tachycardia, leg edema, abnormal ECG, dependent edema

CNS: insomnia, vertigo, paresthesia, involuntary muscle contractions, somnolence, migraine, hypoesthesia

Gastrointestinal: flatulence, constipation, gastroesophageal reflux, toothache, gastritis, vomiting, dry mouth, hemorrhoids, gastroenteritis, enteritis, nonspecific gastrointestinal disorders

Metabolic: gout, diabetes mellitus, hypercholesterolemia

Musculoskeletal: arthritis, arthralgia, leg cramps

Psychiatric: depression, anxiety, nervousness

Resistance Mechanism: infection, dyspnea, epistaxis, fungal infection, abscess, otitis media

Respiratory: asthma, bronchitis, rhinitis
Skin: dermatitis, eczema, pruritus, rash
Urinary: micturition frequency, cystitis
Vascular: cerebrovascular disorder
Special Senses: conjunctivitis, tinnitus, abnormal vision, earache.

Cilnidipine
Nervous system: Dizziness, headache, depression, cerebral ischemia
General: Flushing, peripheral edema, lethargy, tremors, impotence
Cardiovascular: Hypotension, tachycardia, palpitations **,** myocardial ischemia
Gastrointestinal: Gingival hyperplasia **,** GI disturbances, abnormal liver function
Special senses: Eye pain
Other: Myalgia, Transient blindness, Rashes

4.9 Overdose
Limited data is available with regard to overdosage in humans. The most likely manifestation of overdosage with telmisartan would be dizziness and tachycardia, hypotension; bradycardia could occur from parasympathetic stimulation. Supportive treatment should be instituted, if symptomatic hypotension should occur. Telmisartan is not removed by hemodialysis.

5. Pharmacological Properties
5.1 Mechanism Of Action
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.

Cilnidipine is a third generation dihydropyridine calcium antagonist with a slow onset and long duration of action. Calcium antagonists inhibit influx of extracellular calcium ions into the cells, resulting in decreased vascular smooth muscle tone and vasodilation, leading to a reduction in blood pressure.

5.2 Pharmacodynamic Properties
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, 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) were found.

Cilnidipine is a dihydropyridine calcium-channel blocker. Dihydropyridine derivative selective calcium-channel blockers with mainly vascular effects. Cilnidipine is a N-type

and L-type calcium channel blocker. The effects of cilnidipine on N-type channels give it unique organ-protective properties via the suppression of hyperactivity in the sympathetic nervous system (SNS) and renin-angiotensin-aldosterone system (RAAS). Vasodilatation is caused by Cilnidipine because it inhibits cellular influx of calcium. It has greater selectivity for vascular smooth muscle.

It has little or no action at the SA or AV nodes and negative inotropic activity is rarely seen at therapeutic doses.

5.3 Pharmacokinetic Properties

Parameters	**Telmisartan**
Absorption	Following oral administration, peak concentrations (Cmax) of telmisartan are reached in 0.5 to 1 hour. The pharmacokinetics of orally administered telmisartan are nonlinear Telmisartan shows bi-exponential decay kinetic. 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.
Bioavailability	Food slightly reduces the bioavailability of telmisartan, with a reduction in the AUC of about 6% with the 40 mg tablet and about 20% after a 160 mg dose. Absolute bioavailability of telmisartan is dose dependent. At 40 mg the bioavailability was 42%
Distribution	Plasma protein binding is constant over the concentration range achieved with recommended doses. The volume of distribution is about 500 liters indicating additional tissue binding.
Plasma Protein Binding	Highly bound to plasma proteins (>99.5%) mainly albumin and α1 - acid glycoprotein
Metabolism	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.

Excretion	Most of the administered dose (>97%) is eliminated unchanged in feces via biliary excretion; only minute amounts were found in the urine Total plasma clearance of telmisartan is >800 mL/min.
Half-life	Terminal elimination half-life of approximately 24 hours.

Cilnidipine has been clarified to exert antisympathetic actions in various examinations from cell to human levels, in contrast to classical Ca (2+) channel blockers.
After oral administration of cilnidipine it takes 3 hours to reach the peak concentration. Cilnidipine is rapidly metabolized in human liver microsomes and dehydrogenation of dihydropyridine ring of cilnidipine is crucial for the elimination of cilnidipine. Cytochrome P 4503A (CYP3A) is the major human CYP involved in the dehydrogenation of dihydropyridine ring of cilnidipine.After oral administration, large amount of the drug could be detected in the gallbladder, bladder, liver and kidney. The α-phase half-life is 1.1 hour.

6. Nonclinical Properties

6.1 Animal Toxicology or Pharmacology

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/m^2 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).

Developmental Toxicity

There is no clinical experience with the use of telmisartan tablets in pregnant women. No teratogenic effects were observed when telmisartan was administered to pregnant rats at oral doses of up to 50 mg/kg/day and to pregnant rabbits at oral doses up to 45 mg/kg/day. In rabbits, embryolethality associated with maternal toxicity (reduced body

weight gain and food consumption) was observed at 45 mg/kg/day [about 12 times the maximum recommended human dose (MRHD) of 80 mg on a mg/m^2 basis]. In rats, maternally toxic (reduction in body weight gain and food consumption) telmisartan doses of 15 mg/kg/day (about 1.9 times the MRHD on a mg/m^2 basis), administered during late gestation and lactation, were observed to produce adverse effects in neonates, including reduced viability, low birth weight, delayed maturation, and decreased weight gain. Telmisartan has been shown to be present in rat fetuses during late gestation and in rat milk. The no observed effect doses for developmental toxicity in rats and rabbits, 5 and 15 mg/kg/day, respectively, are about 0.64 and 3.7 times, on a mg/m^2 basis, the maximum recommended human dose of telmisartan (80 mg/day).
No data available on cilnidipine.

7. Description
Telpres LN 80 is supplied for oral administration, as a film coated tablet of Cilnidipine & Telmisartan. Each film coated tablet of Telpres LN 80 contains Cilnidipine 10mg Telmisartan 80mg.

Telpres LN 40 is supplied for oral administration, as a film coated tablet of Cilnidipine & Telmisartan. Each film coated tablet of Telpres LN 40 contains Cilnidipine 10mg Telmisartan 40mg.

8. Pharmaceutical Particulars
8.1 Incompatibilities
Not applicable

8.2 Shelf-Life
Refer pack

8.3 Packaging Information
Refer pack

8.4 Storage and Handing Instructions
Refer pack

9.Patient Counselling Information
Taking Telpres LN tablets during your pregnancy can cause injury and even death to your unborn baby. If you get pregnant, stop taking Telpres LN tablets and call your doctor right away. If you plan to become pregnant, talk to your doctor about other ways to lower your blood pressure.

You should not take Telpres LN tablets if you are allergic (hypersensitive) to the active ingredients (telmisartan/cilnidipine).

Before you take Telpres LN tablets, tell your doctor if you, have liver, kidney, heart or have any other medical conditions or are pregnant or are planning to become pregnant or are breast-feeding or plan to breast-feed.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Take Telpres LN tablets regularly and continuously, as directed by your doctor

Do not interrupt or discontinue Telpres LN tablets without consulting the physician.

You may experience sleepiness, dizziness, lightheadedness, or fainting when taking medicines such as Telpres LN tablets. Use caution when engaging in activities such as driving a car or operating appliances or machinery.

Swallow the whole tablet. Do not crush, chew or break it.

Try to take it at the same day every day.

10. Details of Manufacturer
Refer Pack for manufacturer details.

Marketed By:
Abbott Healthcare Pvt. Ltd.
Angel Space, Bldg. D-4, Gala No. 1 to 6 &
11 to 16 Ground Floor, 101 to 106 &
111 to 116 First Floor, 201 to 206 & 211 to 216
2nd Floor, Pimplas, Dist. Thane, Bhiwandi - 421 302, India.

11. Details of Permission or Licence Number with Date
Refer Pack for Permission/License details

12. Date of Revision
Version: 2.0, dated 14/05/24

For Product Complaints/Adverse events or Queries please write to **webmasterindia@abbott.com**