WARNING
FETAL TOXICITY

- **When pregnancy is detected, discontinue Telmisartan as soon as possible**
- **Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus**

For the Use of a Registered Medical Practitioner Only

1. Generic Name & Brand Name

Telmisartan Tablets I.P. 20/40/80 mg

Telpres® 20, Telpres® 40, Telpres® 80

2. Qualitative and Quantitative Composition

Telpres® 20

Each uncoated tablet contains:

Telmisartan I.P.	20 mg
Excipients	q.s

Telpres® 40

Each uncoated tablet contains:

Telmisartan I.P.	40 mg
Excipients	q.s

Telpres® 80

Each uncoated tablet contains:

Telmisartan I.P.	80 mg
Excipients	q.s

3. Dosage Form and Strength

Kindly refer section 1 & 2

4. Clinical Particulars

4.1 Therapeutic Indication

For the management of essential hypertension

For the prevention of cardiovascular morbidity and mortality in patients 55 years older at high risk of cardiovascular disease

4.2 Posology and Method of Administration

Dosage must be individualized for each patient. The initial dose of Telmisartan is 40 mg once daily with or without food. The response of blood pressure is dose-related over the range of 20 to 80 mg.

The antihypertensive effect is apparent within 2 weeks and maximal reduction in BP is attained generally after 4 weeks. When additional blood pressure reduction is required, a diuretic may be given concomitantly.

Initial dosage adjustment is not necessary for elderly patients or patients with renal impairment, including those on hemodialysis.

Telmisartan tablets may be administered with other antihypertensive agents.

4.3 Contraindications
Contraindicated in patients with known hypersensitivity to Telmisartan or any other component of this product.

4.4 Special Warnings and Precautions for Use
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.

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.

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.

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.

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.

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.

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. No drug-related effects on the reproductive performance of male and female rats were noted.

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.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

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

4.5 Drugs Interactions

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 result in deterioration of renal function, including possible acute renal failure. These effects are usually 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 in patients receiving Telmisartan and NSAID therapy concomitantly.
4.	Ramipril and Ramiprilat	Co-administration of Telmisartan and ramipril to healthy subjects increases steady-state Cmax and AUC of ramiprilandramiprilatand decreases Cmax and AUC of Telmisartan. 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.
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.	

4.6 Use in Special Populations
Pregnancy Teratogenic Effects, Pregnancy Categories C (first trimester) and D (second and third trimesters). 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 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 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.

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 such as TELMISARTAN tablets, caution patients about engaging in activities such as driving a vehicle or operating appliances or machinery.

4.8 Undesirable Effects
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.

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

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. 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.

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.

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 over the dose range 20 to 160 mg, with greater than proportional increases of plasma concentrations (Cmax and AUC) with increasing doses. 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 and 160 mg the bioavailability was 42% and 58%, respectively.

Distribution	Plasma protein binding is constant over the concentration range achieved with recommended doses. The volume of distribution is approximately 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.

6. Nonclinical Properties

6.1 Animal Toxicology or Pharmacology

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/m2 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). 13.3 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/m2 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/m2 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/m2 basis, the maximum recommended human dose of telmisartan (80 mg/day).

7. Description

Telpres 20 - is supplied for oral administration, as an uncoated tablet of Telmisartan. Each uncoated tablet of Telpres 20 contains Telmisartan 20mg.

Telpres 40 - is supplied for oral administration, as an uncoated tablet of Telmisartan. Each uncoated tablet of Telpres 40 contains Telmisartan 40mg.

Telpres 80 - is supplied for oral administration, as an uncoated tablet of Telmisartan. Each uncoated tablet of Telpres 80 contains Telmisartan 80mg.

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

Pregnancy Inform female patients of childbearing age about the consequences of exposure to drugs that act on the renin-angiotensin system. Advise these patients to report pregnancies to their physicians as soon as possible. Potential Interference with Mental Alertness and Motor Performance Since side effects such as syncope, somnolence, dizziness, or vertigo may occur with use of antihypertensive agents such as TELMISARTAN tablets, caution patients about engaging in activities such as driving a vehicle or operating appliances or machinery.

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

Refer Pack for Permission/License details

12. Date of Revision

Version: 4.0, dated 15/05/2024

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