

1. NAME OF THE MEDICINAL PRODUCT: TELMISARTAN TABLETS BP 80 MG

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:
Each uncoated tablet contains:
Telmisartan BP 80 mg
Excipients…… QS
Approved colour used.

Excipients with known effect: Lake sunset yellow

3. PHARMACEUTICAL FORM: Uncoated Tablets

Description: Orange coloured, capsule shaped, biconvex, uncoated tablet breakline on one side and plain on other side.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
TELMISARTAN TABLETS BP 80 MG are indicated for the treatment of essential hypertension in adults. It is also indicated for the reduction of cardiovascular morbidity in adults with manifest atherothrombotic cardiovascular disease (history of coronary heart disease, stroke, or peripheral arterial disease) or type 2 diabetes mellitus with documented target organ damage.

4.2 Posology and method of administration

Posology

Treatment of essential hypertension

The usually effective dose is 40 mg once daily. Some patients may already benefit at a daily dose of 20 mg. 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 prevention

The recommended dose is 80 mg once daily. It is not known whether doses lower than 80 mg of telmisartan are effective in reducing cardiovascular morbidity. When initiating telmisartan therapy for the reduction of cardiovascular morbidity, close monitoring of blood pressure is recommended, and if appropriate adjustment of medications that lower blood pressure may be necessary.

Renal impairment

Limited experience is available in patients with severe renal impairment or haemodialysis. A lower starting dose of 20 mg is recommended in these patients. No posology adjustment is required for patients with mild to moderate renal impairment.

Elderly

No dose adjustment is necessary for elderly patients

Method of Administration

For oral use.

4.3 Contraindications

TELMISARTAN TABLETS BP 80 MG are contraindicated in patients:

- Hypersensitivity to the active substances or to any of the excipients used in the formulation
- Second and third trimester of pregnancy.
- Biliary obstructive disorders.
- severe hepatic impairment

4.4 Special warnings and precautions for use

TELMISARTAN TABLETS BP 80 MG should not be used in patients with,

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 TABLETS BP 80 MG is not to be given to patients with cholestasis, biliary obstructive disorders or severe hepatic impairment. since telmisartan is mostly eliminated with the bile. These patients can be expected to have reduced hepatic clearance for telmisartan. **TELMISARTAN TABLETS BP 80 MG** should be used only with caution in patients with mild to moderate hepatic impairment.

Renal impairment and kidney transplantation

When **TELMISARTAN TABLETS BP 80 MG** 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 TABLETS BP 80 MG** in patients with recent kidney transplantation.

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 TABLETS BP 80 MG** is not recommended.

4.5 Interaction with other medicinal products and other forms of interaction

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 therapy), or with compromised renal function, coadministration 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 , 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, warfarin, simvastatin, hydrochlorothiazide 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.

Concomitant use not recommended.
Potassium sparing diuretics or potassium supplements
Angiotensin II receptor antagonists such as telmisartan, attenuate diuretic induced potassium loss. Potassium sparing diuretics e.g. spirinolactone, eplerenone, triamterene, or amiloride, potassium supplements, or potassium-containing salt substitutes may lead to a significant increase in serum potassium. If concomitant use is indicated because of documented hypokalaemia, they should be used with caution and with frequent monitoring of serum potassium.

Concomitant use requiring caution.
Diuretics (thiazide or loop diuretics)
Prior treatment with high dose diuretics such as furosemide (loop diuretic) and hydrochlorothiazide (thiazide diuretic) may result in volume depletion, and in a risk of hypotension when initiating therapy with telmisartan.

To be taken into account with concomitant use.
Other antihypertensive agents
The blood pressure lowering effect of telmisartan can be increased by concomitant use of other antihypertensive medicinal products.

Corticosteroids (systemic route)
Reduction of the antihypertensive effect

4.6 Pregnancy and Lactation
Pregnancy
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.

Lactation
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.

Fertility
There is no strong clinical evidence that telmisartan impairs male or female fertility at therapeutic doses.

4.7 Effects on ability to drive and use machines
When driving vehicles or operating machinery it should be taken into account that dizziness or drowsiness may occasionally occur when taking antihypertensive therapy such as Telmisartan.

4.8 Undesirable effects
Adverse reactions have been ranked under headings of frequency using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000).
Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Infections and infestations
Uncommon: Urinary tract infection including cystitis, upper respiratory tract infection including pharyngitis and sinusitis
Rare: Sepsis including fatal outcome

Blood and the lymphatic system disorders
Uncommon: Anaemia
Rare: Eosinophilia, thrombocytopenia

Immune system disorders
Rare: Anaphylactic reaction, hypersensitivity

Metabolism and nutrition disorders
Uncommon: Hyperkalaemia
Rare: Hypoglycaemia (in diabetic patients)

Psychiatric disorders
Uncommon: Insomnia, depression
Rare: Anxiety

Nervous system disorders
Uncommon: Syncope
Rare: Somnolence

Eye disorders
Rare: Visual disturbance
Ear and labyrinth disorders
Uncommon: Vertigo

Cardiac disorders
Uncommon: Bradycardia
Rare: Tachycardia

Vascular disorders
Uncommon: Hypotension , orthostatic hypotension

Respiratory, thoracic and mediastinal disorders
Uncommon: Dyspnoea, cough
Very rare: Interstitial lung disease

Gastrointestinal disorders
Uncommon: Abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting
Rare: Dry mouth, stomach discomfort, dysgeusia

Skin and subcutaneous tissue disorders
Uncommon: Pruritus, hyperhidrosis, rash
Rare: Angioedema (also with fatal outcome), eczema, erythema, urticaria, drug eruption, toxic skin eruption

Muscoloskeletal and connective tissue disorders
Uncommon: Back pain (e.g. sciatica), muscle spasms, myalgia
Rare: Arthralgia, pain in extremity, tendon pain (tendinitis like symptoms)

Renal and urinary disorders
Uncommon: Renal impairment including acute renal failure

General disorders and administration site conditions
Uncommon: Chest pain, asthenia (weakness)
Rare: Influenza-like illness

Investigations
Uncommon: Blood creatinine increased
Rare: Haemoglobin decreased, blood uric acid increased, hepatic enzyme increased, blood creatine phosphokinase increased

4.9 Overdose
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.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Angiotensin II Antagonists
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 characterised 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

5.2 Pharmacokinetic properties
Absorption and Bioavailability
Absorption of telmisartan is rapid although the amount absorbed varies. The mean absolute bioavailability for telmisartan is about 50 %. When telmisartan is taken with food, the reduction in the area under the plasma concentration-time curve ($AUC_{0-\infty}$) of telmisartan varies from approximately 6 % (40 mg dose) to approximately 19 % (160 mg dose). By 3 hours after administration, plasma concentrations are similar whether telmisartan is taken fasting or with food

Distribution
Telmisartan is largely bound to plasma protein (>99.5 %), mainly albumin and alpha-1 acid glycoprotein. The mean steady state apparent volume of distribution (Vdss) is approximately 500 l.

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

Elimination
Telmisartan is characterised by biexponential decay pharmacokinetics with a terminal elimination half-life of >20 hours. The maximum plasma concentration (C_{max}) and, to a smaller extent, the area under the plasma concentration-time curve (AUC), increase disproportionately with dose. There is no evidence of clinically relevant accumulation of telmisartan taken at the recommended dose. Plasma concentrations were higher in females than in males, without relevant influence on efficacy. After oral (and intravenous) administration, telmisartan is nearly exclusively excreted with the faeces, mainly as unchanged compound. Cumulative urinary excretion is <1 % of dose. Total plasma clearance (Cl_{tot}) is high (approximately 1,000 ml/min) compared with hepatic blood flow (about 1,500 ml/min).

Special populations
Gender
Differences in plasma concentrations were observed, with Cmax and AUC being approximately 3- and 2-fold higher, respectively, in females compared to males.

Renal Impairment
In patients with mild to moderate and severe renal impairment, doubling of plasma concentrations was observed. However, lower plasma concentrations were observed in patients with renal insufficiency undergoing dialysis. 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

Hepatic impairment
Pharmacokinetic studies in patients with hepatic impairment showed an increase in absolute bioavailability up to nearly 100 %. The elimination half-life is not changed in patients with hepatic impairment.

5.3 Preclinical safety data
In preclinical safety studies, doses producing exposure comparable to that in the clinical therapeutic range caused reduced red cell parameters (erythrocytes, haemoglobin, haematocrit), changes in renal haemodynamics (increased blood urea nitrogen and creatinine), as well as increased serum potassium in normotensive animals. In dogs, renal tubular dilation and atrophy were observed. Gastric mucosal injury (erosion, ulcers or inflammation) also was noted in rats and dogs. These pharmacologically-mediated undesirable effects, known from preclinical studies with both angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists, were prevented by oral saline supplementation. In both species, increased plasma renin activity and hypertrophy/hyperplasia of the renal juxtaglomerular cells were observed. These changes, also a class effect of angiotensin converting enzyme inhibitors and other angiotensin II receptor antagonists, do not appear to have clinical significance. No clear evidence of a teratogenic effect was observed, however at toxic dose levels of telmisartan an effect on the postnatal development of the offsprings such as lower body weight and delayed eye opening was observed.There was no evidence of mutagenicity and relevant clastogenic activity in in vitro studies and no evidence of carcinogenicity in rats and mice

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Microcrystalline cellulose, Crospovidone, Lake sunset yellow, Meglumine, Sodium hydroxide, Polysorbate 80, Polacrilin Potassium (Kyron T314), Magnesium stearate

6.2 Incompatibilities
Not applicable

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store below 30°C in a dry and dark place.
Keep all medicines out of reach of children.

6.5 Nature and contents of container
Packing
Primary packing: 10 Tablets in an ALU-ALU blister.
Secondary packing: 3 Blisters are packed in a carton along with leaflet.
Tertiary packing: Such 10 cartons are packed in a shrink. Such 40 Shrinks are packed in a 5 Ply shipper sealed with BOPP tape & strap with strapping roll.

6.6 Special precautions for disposal and other handling
No special requirements.

7. APPLICANT / MANUFACTURER
Applicant

Name and address	**M/s. ELIORA CHEMICALS & PHARMACEUTICALS LIMITED** 38, Adaranijo Street, Pedro Road, Somolu, Lagos state
Tel	-
Fax	-
Email	-

Manufacturer

Name and address	**M/s. IMPULSE PHARMA PVT. LTD.** J-201, J-202/1, MIDC Tarapur, Boisar, Dist. Palghar - 401506, Maharashtra State, India.
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