TECHLOR Tablets (Telmisartan + Chlorthalidone)

### Composition

**TECHLOR 40**

Each bilayer tablet contains:

- Telmisartan..........40 mg
- Chlorthalidone.......12.5 mg

**TECHLOR 80**

Each bilayer tablet contains:

- Telmisartan..........80 mg
- Chlorthalidone.......12.5 mg

### Dosage Form

Tablet

### Description

**TECHLOR** is a fixed-dose combination of telmisartan, an orally active angiotensin receptor blocker (ARB) acting on the angiotensin II type 1 (AT₁) receptor, and chlorthalidone, a thiazide-like diuretic. Thus, the two drugs target two separate mechanisms involved in blood pressure regulation and hence may provide additive blood pressure reduction.

### Pharmacology

#### Pharmacodynamics

The combination of telmisartan and chlorthalidone has been shown to be effective in lowering blood pressure. Both telmisartan and chlorthalidone lower blood pressure by reducing peripheral resistance but through complementary mechanisms.

*Telmisartan*
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. Telmisartan has much greater affinity (more than 3000-fold) for the AT$_1$ receptor than for the angiotensin II type 2 (AT$_2$) receptor.

Telmisartan does not inhibit the angiotensin converting enzyme; hence, it does not affect the response to bradykinin. 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.

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 a 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, high-density and low-density lipoprotein cholesterol, glucose, or uric acid).

**Chlorthalidone**

Chlorthalidone produces diuresis with increased excretion of sodium and chloride. The site of action appears to be the distal convoluted tubule and connecting segment of the nephron (and perhaps the early cortical collecting tubule). The diuretic effects of chlorthalidone lead to decreased extracellular fluid volume, plasma volume, cardiac output, total exchangeable sodium, glomerular filtration rate, and renal plasma flow. Although the mechanism of action of chlorthalidone and related drugs is not wholly clear, sodium and water depletion appear to provide a basis for its antihypertensive effect. Like the thiazide diuretics, chlorthalidone produces dose-related reductions in serum potassium levels, elevations in serum uric acid and blood glucose, and it can lead to decreased sodium and chloride levels.

The diuretic effect of chlorthalidone occurs in approximately 2.6 hours and continues for up to 72 hours.

**Pharmacokinetics**

**Absorption**

**Telmisartan**

Following oral administration, peak concentrations of telmisartan are reached in 0.5-1 hour after dosing. Food slightly reduces the bioavailability of telmisartan, with a reduction in the area under the plasma concentration time curve 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 mg and 160 mg, the bioavailability was 42% and 58%, respectively. The pharmacokinetics of orally administered telmisartan are nonlinear over the dose range of 20-160 mg, with greater than proportional increases of plasma concentrations 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 10-25% of peak plasma concentrations. Telmisartan has an accumulation index in plasma of 1.5-2.0 upon repeated once daily dosing.

**Chlorthalidone**

Following oral administration, peak plasma concentrations of chlorthalidone is reached at 1 hour.

**Distribution**

**Telmisartan**

Telmisartan is highly bound to plasma proteins (more than 99.5%), mainly albumin and alpha1-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.

**Chlorthalidone**

In whole blood, chlorthalidone is predominantly bound to erythrocyte carbonic anhydrase. In the plasma, approximately 75% of chlorthalidone is bound to plasma proteins, 58% of the drug being bound to albumin.

**Metabolism and Elimination**

**Telmisartan**

Following either intravenous or oral administration of 14C-labeled telmisartan, most of the administered dose (more than 97%) was eliminated unchanged in the 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 acylglucuronide; 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 more than 800 mL/min. Terminal half-life and total clearance appear to be independent of dose.

**Chlorthalidone**

The mean plasma half-life of chlorthalidone is about 40 to 60 hours.

The major portion of the drug is excreted unchanged by the kidneys. Non-renal routes of elimination have yet to be clarified. Data are not available regarding percentage of dose as unchanged drug and metabolites, concentration of the drug in body fluids, degree of uptake by a particular organ or in the fetus, or passage across the blood-brain barrier.

**Special Populations**

**Pediatric**

The pharmacokinetics of telmisartan has not been investigated in patients less than 18 years of age.
Geriatric

The pharmacokinetics of telmisartan do not differ between the elderly and those younger than 65 years. The elimination of chlorthalidone in elderly patients is slower than in healthy young adults, although absorption is the same. Therefore, close medical observation is indicated when treating patients of advanced age with chlorthalidone.

Gender

Plasma concentrations of telmisartan are generally 2-3 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.

Renal Impairment

Renal excretion does not contribute to the clearance of telmisartan. Renal dysfunction does not alter the pharmacokinetics of chlorthalidone as well, the rate-limiting factor in the elimination of the drug from blood or plasma being most probably the affinity of the drug to the carbonic anhydrase of erythrocytes. Based on modest experience in patients with mild-to-moderate renal impairment (creatinine clearance of 30-80 mL/min, mean clearance approximately 50 mL/min), no dosage adjustment is necessary for either, telmisartan or chlorthalidone in patients with decreased renal function. Telmisartan is not removed from blood by hemofiltration.

Hepatic Impairment

As the majority of telmisartan is eliminated by biliary excretion, patients with biliary obstructive disorders or hepatic impairment can be expected to have reduced clearance. In patients with hepatic impairment, plasma concentrations of telmisartan are increased, and absolute bioavailability approaches 100%.

Indication

TECHLOR is indicated for the treatment of essential hypertension, to lower blood pressure

- In patients not adequately controlled with monotherapy
- As initial therapy in patients likely to need multiple drugs to help achieve blood pressure goals

Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily stroke and myocardial infarction.

Dosage And Administration

Dosage must be individualized. The usual initial dosage is one tablet of TECHLOR 40 taken orally once daily.

A patient whose blood pressure is not adequately controlled with telmisartan monotherapy 40 mg may be switched to TECHLOR 40. The dose may be increased, if necessary, to two tablets of TECHLOR 40 or one tablet of TECHLOR 80 daily.

A patient whose blood pressure is not adequately controlled with chlorthalidone 25 mg once daily may be
switched to **TECHLOR 40** once/twice daily or **TECHLOR 80** once daily. Patients controlled by 25 mg chlorthalidone but who experience dose-limiting adverse reaction (such as hypokalemia) may be switched to **TECHLOR 40** or **TECHLOR 80** once daily, which will reduce the dose of chlorthalidone without reducing the overall expected antihypertensive response. If blood pressure remains uncontrolled after 2-4 weeks of therapy, other anti-hypertensive agents may be added as required.

Patients titrated to the individual components (telmisartan and chlorthalidone) may instead receive the corresponding dose of **TECHLOR**.

**TECHLOR 40** may be used as initial therapy if a patient is likely to need multiple drugs to achieve blood pressure goals.

The maximum recommended daily dose of telmisartan is 80 mg and chlorthalidone is 50 mg. This means that a maximum number of tablets taken per day should not exceed two tablets of **TECHLOR 40** and one tablet of **TECHLOR 80**.

**TECHLOR 40/80** may be administered with other antihypertensive agents as needed. It may be administered with or without food.

Any volume depletion prior to administration of **TECHLOR** should be corrected, particularly in patients with impaired renal function or those treated with high doses of diuretics.

### Patients with Renal Impairment

The usual regimen of therapy with **TECHLOR** may be followed as long as the patient's creatinine clearance is >30 mL/min, since chlorthalidone, like thiazide diuretics, may lose the diuretic effect after this stage. In patients with severe renal impairment, **TECHLOR** is not recommended.

### Patients with Hepatic Impairment

Due to telmisartan component, **TECHLOR** is not recommended for patients with severe hepatic impairment. In patients with mild to moderate hepatic impairment, the dosage of telmisartan should not exceed 40 mg once daily, i.e. not more than one tablet of **TECHLOR 40** once daily.

### Contraindications

- Hypersensitivity (e.g. anaphylaxis or angioedema) to telmisartan, chlorthalidone or any sulfonamide-derived drugs
- Hypertension during pregnancy
- Biliary obstructive disorders
- Severe hepatic or renal failure (creatinine clearance <30ml/min)
- Patients with anuria
- Refractory hypokalemia, hyponatremia and hypercalcemia
- Symptomatic hyperuricemia (history of gout or uric acid calculi)
- Untreated Addison's disease

Concomitant lithium therapy: The concomitant use of **TECHLOR** with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (Glomerular Filtration Rate < 60 ml/min/1.73 m²)
Warnings And Precautions

Hypotension in Volume- and/or Salt-Depleted Patients

In patients with an activated renin angiotensin system (RAS), 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. This condition should either be corrected prior to administration of TECHLOR, or treatment should be started 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.

Serum Electrolyte Imbalances

**Telmisartan**

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. Periodic determinations of serum electrolytes to detect possible electrolyte imbalances should be considered, particularly in patients at risk.

**Chlorthalidone**

As with all other thiazide-type diuretics, chlorthalidone has been associated with electrolyte disturbances such as hypokalemia, hypomagnesaemia, hyperglycemia and hyponatremia. Since the excretion of electrolytes is increased, a very strict low-salt diet should be avoided.

Like all thiazide diuretics, kaluresis induced by chlorthalidone is dose dependent and varies in extent from one subject to another. Hypokalemia can sensitize the heart or exaggerate its response to the toxic effects of digitalis. Periodic serum electrolyte determinations should be carried out, particularly in patients on digitalis.

Monitoring of serum electrolytes is particularly indicated in the elderly, in patients with ascites due to liver cirrhosis, and in patients with edema due to nephrotic syndrome. There have been isolated reports of hyponatremia with neurological symptoms (e.g. nausea, debility, progressive disorientation and apathy) following thiazide treatment.

For nephrotic syndrome, TECHLOR should be used only under close control in normokalemic patients with no signs of volume depletion.

If hypokalemia is accompanied by clinical signs (e.g. muscular weakness, paresis and electrocardiography alteration), TECHLOR should be discontinued.

Since TECHLOR is a fixed-dose combination of telmisartan and chlorthalidone, chlorthalidone-induced hypokalemia may be attenuated or nullified because of telmisartan-induced hyperkalemia. Hence, combining TECHLOR with a potassium salt or a potassium-sparing diuretic should be avoided.
Telmisartan

Dual blockade of the RAS with ARBs, ACE inhibitors, or aliskiren is associated with increased risks of hypotension, hyperkalemia, and changes in renal function (including acute renal failure) compared to monotherapy.

Clinical trials have shown that 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 patients receiving telmisartan alone or ramipril alone.

In most patients no benefit has been associated with using two RAS inhibitors concomitantly. In general, combined use of RAS inhibitors should be avoided. Close monitoring of blood pressure, renal function, and electrolytes should be done in patients on TECHLOR (due to telmisartan component) and other agents that affect the RAS.

Aliskiren should not be co-administered with TECHLOR in patients with diabetes. Concomitant use of aliskiren with TECHLOR in patients with renal impairment (GFR <60 mL/min/1.73 m²) should be avoided.

Metabolic Effects

Chlorthalidone

Chlorthalidone may raise the serum uric acid level, but attacks of gout are uncommon during chronic treatment.

As with the use of other thiazide diuretics, glucose intolerance may occur; this is manifest as hyperglycemia and glycosuria. Chlorthalidone may very seldom aggravate or precipitate diabetes mellitus; this is usually reversible on stopping therapy.

Small and partly reversible increases in plasma concentrations of total cholesterol, triglycerides, or low-density lipoprotein cholesterol were reported in patients during long-term treatment with thiazides and thiazide-like diuretics. The clinical relevance of these findings is a matter for debate.

Chlorthalidone should not be used as a first-line drug for long-term treatment in patients with overt diabetes mellitus or in subjects receiving therapy for hypercholesterolemia (diet or combined).

As with all antihypertensive agents, a cautious dosage schedule is indicated in patients with severe coronary or cerebral arteriosclerosis.

Drug Interactions

The pharmacokinetics of telmisartan and chlorthalidone are not altered when the drugs are co-administered.

Telmisartan and Chlorthalidone

No drug interaction studies have been conducted with other drugs and TECHLOR, although studies
have been conducted with telmisartan and chlorthalidone, separately.

**Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) 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 ARBs, including telmisartan, may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible. Renal function should be monitored periodically in patients receiving **TECHLOR** tablets and concomitant NSAID therapy.

The antihypertensive effect of ARBs, including telmisartan may be attenuated by NSAIDs including selective COX-2 inhibitors.

Concomitant administration of certain NSAIDs (e.g. indomethacin) may reduce the diuretic and antihypertensive activity of chlorthalidone; there have been isolated reports of a deterioration in renal function in predisposed patients. Therefore, if **TECHLOR** and NSAIDs are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

**Lithium**

Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with ARBs including telmisartan. Thiazide and related diuretics, such as chlorthalidone can also cause a rapid rise in serum lithium levels, as the renal clearance of lithium is reduced by these compounds. Therefore, serum lithium levels should be monitored during concomitant use with **TECHLOR**.

**Digoxin**

When telmisartan was co-administered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) were observed. Monitoring of digoxin levels is recommended when initiating, adjusting, and discontinuing **TECHLOR** for the purpose of keeping the digoxin level within the therapeutic range.

Thiazide-induced hypokalemia or hypomagnesemia may favor the occurrence of digitalis-induced cardiac arrhythmias, hence serum electrolyte levels should also be monitored.

**Telmisartan**

**Aliskiren**

Aliskiren should not be co-administered with **TECHLOR** in patients with diabetes (due to telmisartan component). Use of aliskiren with **TECHLOR** should also be avoided in patients with renal impairment (GFR <60 ml/min).

**Ramipril and Ramiprilat**

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 **TECHLOR** and ramipril is not recommended.

**Others**
Co-administration of telmisartan with acetaminophen, amlodipine, glibenclamide, simvastatin, hydrochlorothiazide, warfarin or ibuprofen did not result in a clinically significant interaction. 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 or are metabolized by cytochrome P450 enzymes, except for possible inhibition of the metabolism of drugs metabolized by CYP2C19.

**Chlorthalidone**

**Anti-diabetic Agents**

It may prove necessary to adjust the dosage of insulin and oral anti-diabetic agents since chlorthalidone, like other thiazide-type diuretics, may affect blood glucose levels.

**Anticholinergic Agents**

The bioavailability of thiazide-type diuretics may be increased by anticholinergic agents (e.g. atropine, biperiden), apparently due to a decrease in gastrointestinal motility and stomach-emptying rate.

**Calcium Salts and Vitamin D**

The pharmacological effects of both calcium salts and vitamin D may be increased to clinically significant levels if given with thiazide diuretics. The resultant hypercalcemia is usually transient but may be persistent and symptomatic (weakness, fatigue, anorexia) in patients with hyperparathyroidism.

**Cyclosporin**

Concomitant treatment with cyclosporin may increase the risk of hyperuricemia and gout-type complications.

**Others**

Diuretics potentiate the action of curare derivatives and antihypertensive drugs (e.g. guanethidine, methyldopa, β-blockers, vasodilators, calcium antagonists and ACE inhibitors).

The hypokalemic effect of diuretics may be potentiated by corticosteroids, adrenocorticotropic hormone, β2 agonists, amphotericin and carbenoxolone.

Absorption of thiazide diuretics is impaired in the presence of anionic exchange resins such as colestyramine. A decrease in the pharmacological effect may be expected.

Concurrent administration of thiazide diuretics may increase the incidence of hypersensitivity reactions to allopurinol, increase the risk of adverse effects caused by amantadine, enhance the hyperglycemic effect of diazoxide, and reduce renal excretion of cytotoxic agents (e.g. cyclophosphamide, methotrexate) and potentiate their myelosuppressive effects.

**Renal Impairment**

As a consequence of inhibiting the RAS, changes in renal function may be anticipated in susceptible individuals. In patients whose renal function may depend on the activity of the RAS (e.g., patients with severe congestive heart failure), treatment with ACE inhibitors and ARBs has been associated
with oliguria and/or progressive azotemia and, rarely, with acute renal failure and/or death. Similar results may be anticipated in patients treated with TECHLOR.

In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen (BUN) were observed. There has been no long-term use of telmisartan in patients with unilateral or bilateral renal artery stenosis, but an effect similar to that seen with ACE inhibitors should be anticipated.

Thiazides, including chlorthalidone, may precipitate azotemia in patients with renal disease, and the effects of repeated administration may be cumulative. TECHLOR should therefore be used with caution in such patients. If progressive renal impairment becomes evident, as indicated by increased blood urea nitrogen, withholding or discontinuing TECHLOR should be considered.

### Hepatic Impairment

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. Chlorthalidone may lead to minor changes in the fluid and electrolyte balance, which may even precipitate hepatic coma in patients with impaired hepatic function or progressive liver disease, especially those with liver cirrhosis. Thus, telmisartan and chlorthalidone should be initiated at low doses and titrated slowly in these patients.

### Pregnancy

**Telmisartan**

**Pregnancy Category D**

Use of drugs that act on the RAS 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, TECHLOR should be 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 RAS 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 RAS for a particular patient, the mother should be apprised of the potential risk to the fetus. Serial ultrasound examinations should be performed to assess the intra-amniotic environment. If oligohydramnios is observed, TECHLOR should be discontinued, unless 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. Infants with histories of in utero exposure to TECHLOR should be closely observed for hypotension, oliguria, and hyperkalemia.

**Chlorthalidone**

Diuretics are best avoided for the management of edema or hypertension in pregnancy as their use
may be associated with hypovolemia, increased blood viscosity and reduced placental perfusion. There have been reports of fetal bone marrow depression, thrombocytopenia, and fetal and neonatal jaundice associated with the use of thiazide diuretics.

### Lactation

It is not known whether telmisartan is excreted in human milk. Chlorthalidone passes into the breast milk. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue TECHLOR, taking into account the importance of the drugs to the mother.

### Pediatric Use

The safety and effectiveness of TECHLOR in pediatric patients have not been established.

**Neonates with a History of In-utero Exposure to Telmisartan**

If oliguria or hypotension occurs, attention should be directed towards 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.

### Geriatric Use

No overall differences in effectiveness and safety of telmisartan and chlorthalidone were observed in elderly patients compared to younger patients. However, greater sensitivity of some older individuals cannot be ruled out. In elderly patients, the elimination of chlorthalidone is slower than in healthy young adults, although absorption is the same. Therefore, a reduction in the recommended adult dosage may be needed. Close medical observation is indicated when treating patients of advanced age with TECHLOR.

### Undesirable Effects

#### Telmisartan

**Clinical Trials Experience**

Because clinical studies are conducted under widely varying conditions, adverse reactions rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

Adverse events experienced with telmisartan have generally been mild and transient in nature and have infrequently required discontinuation of therapy. Adverse events occurring at an incidence of ≥1% in patients treated with telmisartan and at a greater rate than in patients treated with placebo, irrespective of their causal association, are as follows: Upper respiratory tract infection, back pain, sinusitis, diarrhea and pharyngitis.

In addition to these adverse events, 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 patients treated with telmisartan and 6.1% of patients treated with placebo, 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 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:

**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 echocardiography (ECG)

**Central Nervous System:** 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

**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.

**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.

Post-marketing Experience

The most frequent spontaneously reported events during post-approval use of telmisartan 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 (creatine phosphokinase), 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 ARBs, including telmisartan.

Chlorthalidone

The following adverse reactions have been observed with chlorthalidone with the estimated frequency of ≥1%:

Electrolytes and Metabolic Disorders (mainly at higher doses): hypokalemia, hyperuricemia, rise in blood lipids, hyponatremia, hypomagnesemia and hyperglycemia

Skin: urticaria and other forms of skin rash

Cardiovascular System: postural hypotension

Central nervous System: paraesthesia, headache.

Gastro-intestinal Tract: mild nausea and vomiting, gastric pain, constipation and diarrhea

Blood: thrombocytopenia, leucopenia, agranulocytosis and eosinophilia

Other: idiosyncratic pulmonary edema (respiratory disorders), allergic interstitial nephritis.

The following adverse reactions have been observed with chlorthalidone with the estimated frequency of ≥0.01% to <1%:

Electrolytes and Metabolic Disorders: hypercalcaemia, glycosuria, worsening of diabetic metabolic state, gout

Skin: photosensitization
Liver: intrahepatic cholestasis or jaundice

Cardiovascular System: cardiac arrhythmias

Central Nervous System: dizziness

Gastro-intestinal Tract: loss of appetite and minor gastrointestinal distress

Other: impotence

Overdosage

Telmisartan

Limited data are available related to overdosage in humans. The most likely manifestations of overdosage would be hypotension 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.

Chlorothalidone

Symptoms of acute overdosage include nausea, weakness, dizziness and disturbances of electrolyte balance. The oral lethal dose 50 (LD50) of the drug in the mouse and the rat is more than 25,000 mg/kg body weight. The minimum lethal dose (MLD) in humans has not been established. There is no specific antidote but gastric lavage is recommended, followed by supportive treatment. Where necessary, this may include intravenous dextrose-saline with potassium, administered with caution.

Incompatibility

Not applicable.

Shelf-Life

2 years.

Storage And Handling Instructions

Store in a cool, dry place away from light.

Packaging Information

TECHLOR 40: Strip of 10 tablets
TECHLOR 80: Strip of 10 tablets

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TECHLOR Tablets

Source URL: https://ciplamed.com/content/techlor-tablets