# Telmilok®

## Telmisartan Ph. Eur.

**PRESENTATION**
**Telmilok®** 40: Each tablet contains Telmisartan Ph. Eur. 40 mg.
**Telmilok®** 80: Each tablet contains Telmisartan Ph. Eur. 80 mg.

**PHARMACOLOGY**
*Pharmacodynamic Properties*
Pharmacotherapeutic group: Angiotensin II Antagonists, plain, 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 characterized 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 events.
In human, an 80 mg dose of telmisartan almost completely inhibits the angiotensin II evoked blood pressure increase. The inhibitory effect is maintained over 24 hours and still measurable up to 48 hours.

*Pharmacokinetic Properties*
Absorption
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. Linearity/non-linearity The small reduction in AUC is not expected to cause a reduction in the therapeutic efficacy. There is no linear relationship between doses and plasma levels. Cmax and to a lesser extent AUC increase disproportionately at doses above 40 mg.

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.
Biotransformation
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 (Cmax) 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 (Cltot) is high (approximately 1,000 ml/min) compared with hepatic blood flow (about 1,500 ml/min).

Special Populations
Paediatric population
The pharmacokinetics of two doses of telmisartan were assessed as a secondary objective in hypertensive patients (n = 57) aged 6 to < 18 years after taking telmisartan 1 mg/kg or 2 mg/kg over a four-week treatment period. Pharmacokinetic objectives included the determination of the steady-state of telmisartan in children and adolescents, and investigation of age related differences. Although the study was too small for a meaningful assessment of the pharmacokinetics of children under 12 years of age, the results are generally consistent with the findings in adults and confirm the non-linearity of telmisartan, particularly for Cmax.
Gender
Differences in plasma concentrations were observed, with Cmax and AUC being approximately 3- and 2-fold higher, respectively, in females compared to males.
Elderly
The pharmacokinetics of telmisartan do not differ between the elderly and those younger than 65 years.
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.

**INDICATION**
• Treatment of Hypertension, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions.
• Cardiovascular (CV) Risk reduction in patients unable to take ACE inhibitors.

**DOSAGE & ADMINISTRATION**
For Hypertension the dose is 40 mg Once daily and maximum dose is 80 mg once daily. For Cardiovascular (CV) Risk reduction dose is 80 mg Once daily.

**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.

**OVERDOSE**
There is limited information available with regard to overdose in humans.
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 overdose. 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.

**SIDE EFFECTS**
Upper respiratory tract infection, Back pain, Sinusitis, Diarrhea, Pharyngitis, influenza-like symptoms, dyspepsia, myalgia, urinary tract infection, abdominal pain, headache, dizziness, fatigue, coughing, nausea, peripheral edema, increased sweating, flushing, allergy, fever, leg pain, malaise, palpitation, angina pectoris, tachycardia, abnormal ECG, insomnia, migraine, vertigo, paresthesia, hypoesthesia, flatulence.

**PRECAUTIONS**
Hypotension
In some patients symptomatic hypotension may occur after initiation of therapy with Telmisartan.
Hyperkalemia
Hyperkalemia may also occur in some 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.
Impaired Hepatic Function
In patients with biliary obstructive disorders or hepatic insufficiency can be expected to have reduced clearance. Initiate Telmisartan at low doses and titrate slowly in these patients.

**DRUG INTERACTION**
Digoxin: When co-administered with digoxin, median increases in digoxin peak plasma concentration were observed. Non-Steroidal Anti-Inflammatory Agents including Selective COX-2 Inhibitors: In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, co-administration of NSAIDs, including selective COX-2 inhibitors, with angiotensin II receptor antagonists, including Telmisartan, may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible. Monitor renal function periodically in patients receiving Telmisartan and NSAID therapy. The antihypertensive effect of angiotensin II receptor antagonists, including Telmisartan may be attenuated by NSAIDs including selective COX-2 inhibitors.

**CONTRAINDICATION**
Aliskiren and ACE Inhibitors.

**USE IN PREGNANCY AND LACTATION**
Pregnancy- Telmisartan can cause fetal harm when administered to a pregnant woman.
Lactation- There is no information regarding the presence of Telmisartan in human milk. Nursing woman would not to breastfeed during treatment with Telmisartan.

**STORAGE**
Store below 30°C, in a dry place.
Keep all medicines out of reach of children.

**HOW SUPPLIED**
**Telmilok®** 40: Each box contains 10 / 20 / 30 / 50 / 100 Tablets in blister pack.
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**SQUARE**