Teldis Tablet 80mg

1. NAME OF THE MEDICINAL PRODUCT

Teldis Tablet 80mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 tablet contains 80 mg telmisartan.

Mannitol may have a mild laxative effect.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. PHARMACEUTICAL FORM

Tablet for oral use. The tablet is uncoated.

Description:
It occurs as a white tablet of oval, biconvex shaped; engraved with "879" on one side and "SCP" on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Hypertension
Treatment of essential hypertension.

Cardiovascular risk reduction
TELDIS is indicated for reduction of the risk of myocardial infarction, stroke, or death from cardiovascular causes in patients 55 years of age or older at high risk of developing major cardiovascular events who are unable to take ACE inhibitors.
High risk of cardiovascular events can be evidenced by history of coronary artery disease, peripheral arterial disease, stroke, transient ischemic attack, or high-risk diabetes (insulin-dependent or non-insulin dependent) with evidence of end-organ damage. TELDIS can be used in additional to other needed treatment (such as antihypertensive, antiplatelet or lipid-lowering therapy).
Studies of Telmisartan in this setting do not exclude that it may not preserve a meaningful fraction of the effect of the ACE inhibitor to which it was compared. Consider using the ACE inhibitor first, and, if it is stopped for cough only, consider re-trying the ACE inhibitor after the cough resolves.
Use of telmisartan with an ACE inhibitor is not recommended.

4.2 Posology and method of administration

TELDIS is available at the strength 80 mg only and may not be able to deliver all the dosing recommendations mentioned below. In such cases, other approved strengths of telmisartan should be used.

Dosage
Treatment of essential hypertension
The recommended dose is 40 mg once daily. In cases where the target blood pressure is not achieved, telmisartan dose can be increased to a maximum of 80 mg once daily. 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. Alternatively, telmisartan may be used in combination with thiazide-type diuretics such as hydrochlorothiazide or calcium-channel blockers such as amlodipine,

which have been shown to have an additive blood pressure lowering effect with telmisartan.
In patients with severe hypertension treatment with telmisartan at doses up to 160 mg alone and in combination with hydrochlorothiazide 12.5 - 25 mg daily was well tolerated and effective.

Cardiovascular risk reduction
The recommended dose of TELDIS Tablets is 80 mg once a day and can be administered with or without food. It is not known whether doses lower than 80 mg of telmisartan are effective in reducing the risk of cardiovascular morbidity and mortality.
When initiating TELDIS therapy for cardiovascular risk reduction, monitoring of blood pressure is recommended, and if appropriate adjustment of medications that lower blood pressure may be necessary.

Special Populations
Renal impairment
No posology adjustment is required for patients with renal impairment, including those on haemodialysis. Telmisartan is not removed from blood by hemofiltration and is not dialyzable.

Hepatic impairment
In patients with mild to moderate hepatic impairment TELDIS should be administered with caution. For telmisartan, the posology should not exceed 40 mg once daily (see Contraindications).

Geriatric patients
No dose adjustment is necessary for geriatric patients.

Paediatric patients
The safety and efficacy of TELDIS for use in patients aged below 18 years have not been established.

Method of administration
TELDIS tablets are for once-daily administration and should be swallowed whole with liquid. TELDIS can be taken with or without food.

Handling Instructions
Due to the hygroscopic property of the tablets, they should be taken out of the sealed blister shortly before administration.

4.3 Contraindications
- Hypersensitivity to the active substance or to any of the excipients
- Second and third trimesters of pregnancy
- Lactation
- 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 m^2)

In case of rare hereditary conditions that may be incompatible with an excipient of the product (please refer to “special warnings and precautions”) the use of the product is contraindicated.

4.4 Special warnings and precautions for use

Pregnancy:
Angiotensin II receptor blockers should not be initiated during pregnancy.
Unless continued angiotensin II receptor blocker therapy is considered essential, patients planning pregnancy should be changed to alternative anti-hypertensive treatments which have an established safety profile for use in pregnancy.
When pregnancy is diagnosed, treatment with angiotensin II receptor blocker should be stopped

immediately, and if appropriate, alternative therapy should be started.

Hyperkalaemia:
During treatment with medicinal products that affect the renin-angiotensin-aldosterone system hyperkalaemia may occur, especially in the presence of renal impairment and/or heart failure. Monitoring of serum potassium in patients at risk is recommended.
Based on experience with the use of medicinal products that affect the renin-angiotensin system, concomitant use with potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other medicinal products that may increase the potassium level (heparin, etc.) may lead to an increase in serum potassium and should therefore be co-administered cautiously with telmisartan.

Volume and/or sodium depleted patients:
Symptomatic hypotension, especially after the first dose, may occur in patients who are volume and/or sodium depleted by e.g. vigorous diuretic therapy, dietary salt restriction, diarrhoea or vomiting. Such conditions, especially volume and/or sodium depletion, should be corrected before the administration of telmisartan.

Hepatic impairment:
Telmisartan is mostly eliminated in the bile. Patients with biliary obstructive disorders or hepatic insufficiency can be expected to have reduced clearance. TELDIS should be used with caution in these patients.

Renovascular hypertension:
There is an increased risk of severe hypotension and renal insufficiency when patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney are treated with medicinal products that affect the renin-angiotensin-aldosterone system.

Renal impairment and kidney transplant:
When telmisartan is used in patients with impaired renal function, a periodic monitoring of potassium and creatinine serum levels is recommended. There is no experience regarding the administration of telmisartan in patients with a recent kidney transplant.
Telmisartan is not removed from blood by hemofiltration and is not dialyzable.

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 in susceptible individuals, especially if combining medicinal products that affect this system. Dual blockade of the renin-angiotensin-aldosterone system (e.g. by adding an ACE-inhibitor or the direct renin-inhibitor aliskiren to an angiotensin II receptor blocker) is not recommended and should therefore be limited to individually defined cases with close monitoring of renal function (see Contraindications).

Other conditions with stimulation of the renin-angiotensin-aldosterone system:
In patients whose vascular tone and renal function depend predominantly on the activity of the renin-angiotensin-aldosterone system (e.g. patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis), treatment with medicinal products that affect this system has been associated with acute hypotension, hyperazotaemia, oliguria, or rarely acute renal failure.

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 is not recommended.

Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy:
As with other vasodilators, special caution is indicated in patients suffering from aortic or mitral

stenosis, or obstructive hypertrophic cardiomyopathy.

Diabetes mellitus:
In diabetic patients with an additional cardiovascular risk, i.e. patients with diabetes mellitus and coexistent coronary artery disease (CAD), the risk of fatal myocardial infarction and unexpected cardiovascular death may be increased when treated with blood pressure lowering agents such as ARBs or ACE-inhibitors. In patients with diabetes mellitus CAD may be asymptomatic and therefore undiagnosed. Patients with diabetes mellitus should undergo appropriate diagnostic evaluation, e.g. exercise stress testing, to detect and to treat CAD accordingly before initiating treatment with TELDIS.

Ethnic differences:
As observed for angiotensin converting enzyme inhibitors, angiotensin receptor blockers including telmisartan are apparently less effective in lowering blood pressure in black people than in non-blacks, possibly because of higher prevalence of low-renin states in the black hypertensive population.

Ischaemic heart disease
As with any antihypertensive agent, excessive reduction of blood pressure in patients with ischaemic cardiopathy or ischaemic cardiovascular disease could result in a myocardial infarction or stroke.

4.5 Interaction with other medicinal products and other forms of interaction

Telmisartan may increase the hypotensive effect of other antihypertensive agents.

Co-administration of telmisartan did not result in a clinically significant interaction with digoxin, warfarin, hydrochlorothiazide, glibenclamide, ibuprofen, paracetamol, simvastatin and amlodipine. For digoxin a 20% increase in median plasma digoxin trough concentration has been observed (39% in a single case), monitoring of plasma digoxin levels should be considered.

In one study the co-administration of telmisartan and ramipril led to an increase of up to 2.5-fold in the AUC_{0-24} and C_{max} of ramipril and ramiprilat. The clinical relevance of this observation is not known.

Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors. Cases have also been reported with angiotensin II receptor blocker including telmisartan. Therefore, serum lithium level monitoring is advisable during concomitant use.

Treatment with NSAIDs (i.e. ASA at anti-inflammatory dosage regimens, COX-2 inhibitors and non-selective NSAIDS) is associated with the potential for acute renal insufficiency in patients who are dehydrated. Compounds acting on the Renin-Angiotensin-System like telmisartan may have synergistic effects. Patients receiving NSAIDs and telmisartan should be adequately hydrated and their renal function should be monitored at the beginning of combined treatment.

A reduced effect of antihypertensive drugs like telmisartan by inhibition of vasodilating prostaglandins has been reported during combined treatment with NSAIDs.

4.6 Fertility, pregnancy and lactation

Pregnancy
The use of angiotensin II receptor blockers is not recommended during the first trimester of pregnancy and should not be initiated during pregnancy. When pregnancy is diagnosed, treatment with angiotensin II receptor blocker should be stopped immediately, and, if appropriate, alternative therapy should be started.

Unless continued angiotensin II receptor antagonist therapy is considered essential, patients planning pregnancy should be changed to alternative anti-hypertensive treatments which have an established safety profile for use in pregnancy.

Non-clinical studies with telmisartan do not indicate teratogenic effect, but have shown fetotoxicity.

The use of angiotensin II receptor blockers is contraindicated during the second and third trimester of pregnancy.

Angiotensin II receptor blocker exposure during the second and third trimesters is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalaemia).

Should exposure to angiotensin II receptor blocker have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended.

Infants whose mothers have taken angiotensin II receptor blocker should be closely observed for hypotension.

Lactation
Telmisartan is contraindicated during lactation since it is not known whether it is excreted in human milk. Animal studies have shown excretion of telmisartan in breast milk.

Fertility
No studies on fertility in humans have been performed.
In non-clinical studies, no effects of telmisartan on male and female fertility were observed.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed. However, when driving vehicles or operating machinery it should be taken into account that syncope or vertigo may occasionally occur when taking antihypertensive therapy.

4.8 Undesirable effects

Summary of the safety profile
In patients treated for hypertension, the overall incidence of adverse events reported with telmisartan (41.4%) was usually comparable to those reported with placebo (43.9%) in controlled clinical trials in patients treated for hypertension. The incidence of adverse events was not dose related and showed no correlation with gender, age or race of the patients.

The safety profile of TELDIS in patients treated for cardiovascular risk reduction was consistent with that obtained in hypertensive patients.

Tabulated summary of adverse reactions
The following adverse drug reactions derived from the use of telmisartan as monotherapy in clinical trials in patients treated for hypertension or from post-marketing experience, are shown in the table below classified by MedDRA System organ class and MedDRA Preferred terms. The listing also takes into account serious adverse events and adverse events leading to discontinuation reported in three clinical long-term studies including 21642 patients treated with telmisartan for cardiovascular risk reduction for up to six years.

MedDRA System Organ Class	**Adverse reactions**
Infections and infestations	sepsis (including fatal outcome)
	upper respiratory tract infection
	urinary tract infection
	cystitis
Blood and lymphatic system disorders	thrombocytopenia
	anaemia
	eosinophilia
Immune system disorders	anaphylactic reaction
	hypersensitivity
Metabolism and nutrition disorders	hyperkalaemia
	hypoglycaemia (in diabetic patients)
	hyponatraemia
Psychiatric disorders	depression
	anxiety
	insomnia
Nervous system disorders	syncope (faint)
Eye disorders	visual impairment
Ear and labyrinth disorders	vertigo
Cardiac disorders	bradycardia
	tachycardia
Vascular disorders	hypotension
	orthostatic hypotension
Respiratory, thoracic and mediastinal disorders	dyspnoea
Gastrointestinal disorders	abdominal pain
	diarrhoea
	vomiting
	dyspepsia
	dry mouth
	flatulence
	abdominal discomfort
Hepatobiliary disorders	hepatic function abnormal / liver disorder Most cases of hepatic function abnormal/liver disorder from post-marketing experience with telmisartan occurred in patients in Japan, who are more likely to experience these adverse reactions.
Skin and subcutaneous tissue disorders	angioedema (including fatal outcome)
	drug eruption
	toxic skin eruption
	urticaria
	eczema
	erythema
	rash
	pruritus
	hyperhidrosis
Musculoskeletal and connective tissue disorders	arthralgia
	back pain
	pain in extremity (leg pain)
	tendon pain (tendonitis like symptoms)
	muscle spasms (cramps in legs)
	myalgia

Renal and urinary disorders	renal impairment (including acute kidney injury)
General disorders and administration site conditions	chest pain
	asthenia (weakness)
	influenza like illness
Investigations	hepatic enzyme increased
	blood creatinine increased
	blood creatine phosphokinase increased
	haemoglobin decreased
	blood uric acid increased

4.9 Overdose

Limited information is available with regard to overdose in humans.

Symptoms
The most prominent manifestations of telmisartan overdose were hypotension, tachycardia; bradycardia also occurred.

Therapy
If symptomatic hypotension should occur, supportive treatment should be instituted. Telmisartan is not removed by hemofiltration and is not dialyzable.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Angiotensin II receptor blocker
ATC code: C09CA07

Mode of action
Telmisartan is an orally effective and specific angiotensin II receptor (type AT1) blocker. 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.

In man, 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.

Pharmacodynamics
Treatment of essential hypertension
After the first dose of telmisartan, the antihypertensive activity gradually becomes evident within 3 hours. The maximum reduction in blood pressure is generally attained 4 weeks after the start of treatment and is sustained during long-term therapy.

The antihypertensive effect persists constantly over 24 hours after dosing and includes the last 4 hours before the next dose as shown by ambulatory blood pressure measurements. This is confirmed by trough to peak ratios consistently above 80 % seen after doses of 40 and 80 mg of telmisartan in

placebo controlled clinical studies.

There is an apparent trend to a dose relationship to a time to recovery of baseline SBP. In this respect data concerning DBP are inconsistent.

In patients with hypertension telmisartan reduces both systolic and diastolic blood pressure without affecting pulse rate. The antihypertensive efficacy of telmisartan has been compared to agents representative to other classes of antihypertensive drugs (in clinical trials comparing telmisartan to agents such as amlodipine, atenolol, enalapril, hydrochlorothiazide, losartan, lisinopril, ramipril and valsartan).

Upon abrupt cessation of treatment with telmisartan, blood pressure gradually returns to pre-treatment values over a period of several days without evidence of rebound hypertension.

Telmisartan treatment has been shown in clinical trials to be associated with statistically significant reductions in Left Ventricular Mass and Left Ventricular Mass Index in patients with hypertension and Left Ventricular Hypertrophy.

Telmisartan treatment has been shown in clinical trials (including comparators like losartan, ramipril and valsartan) to be associated with statistically significant reductions in proteinuria (including microalbuminuria and macroalbuminuria) in patients with hypertension and diabetic nephropathy.

The incidence of dry cough was significantly lower in patients treated with telmisartan than in those given angiotensin converting enzyme inhibitors in clinical trials directly comparing the two antihypertensive treatments.

5.2 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) 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. The small reduction in AUC is not expected to cause a reduction in the therapeutic efficacy.

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 (V_{ss}) 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.

After oral (and intravenous) administration telmisartan is nearly exclusively excreted with the faeces, exclusively as unchanged compound. Cumulative urinary excretion is < 2% of dose.

Total plasma clearance (CL_{tot}) is high (approximately 900 ml/min compared with hepatic blood flow (about 1500 ml/min).

Linearity
The maximum plasma concentration (C_{max}) and, to a smaller extent, area under the plasma concentration-time curve (AUC) increase disproportionately with dose. There is no evidence of clinically relevant accumulation of telmisartan.

PK in specific populations
Gender differences
Gender differences in plasma concentrations were observed, C_{max} and AUC being approximately 3- and 2-fold higher, respectively, in females compared to males without relevant influence on efficacy.

Geriatric patients
The pharmacokinetics of telmisartan do not differ between younger and geriatric patients.

Renal impairment
Lower plasma concentrations were observed in patients with renal insufficiency undergoing dialysis. Telmisartan is highly bound to plasma protein in renal-insufficient subjects 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide
Polyvinylpyrrolidone K30
Meglumine
Mannitol EZ
Magnesium Stearate
Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Please refer to the packaging for information on shelf-life.

6.4 Special precautions for storage

Store at or below 30°C

6.5 Nature and contents of container

One blister strip contains 10 tablets. One box contains 3 blister strips.

7. MANUFACTURER

Manufactured by:
STANDARD CHEM. & PHARM. CO., LTD.
No. 6-20, Tuku, Tuku Village, Sinying District, Tainan City 73055, Taiwan

8. DATE OF REVISION OF THE TEXT

08th August 2025