PROFESSIONAL INFORMATION

TESAR RANGE

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

TESAR 40 mg uncoated tablets

TESAR 80 mg uncoated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TESAR 40 mg: Each tablet contains 40 mg telmisartan.

TESAR 80 mg: Each tablet contains 80 mg telmisartan.

Tesar contains sugar alcohol (mannitol) in the following quantities:

TESAR 40 mg (163,8 mg) and TESAR 80 mg (327,7 mg).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

TESAR 40 mg: White, oblong tablet of 12,0 x 5,9 mm approx. with LC debossed on one side.

TESAR 80 mg: White, oblong tablet of 16,0 x 8,0 mm approx. with LC debossed on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of mild to moderate hypertension, either alone or in combination with hydrochlorothiazide.

Reduction of cardiovascular morbidity and mortality in those patients who are 55 years or older and are at high risk of cardiovascular disease; the benefit of treatment is evident after at least 6

months of continued treatment.

4.2 Posology and method of administration

Adults:

Treatment of mild to moderate hypertension:

The recommended dosage is 40 mg once a day.

The maximum dosage of TESAR is 80 mg once daily.

An additional blood pressure lowering effect can be achieved by combining TESAR and a low dose thiazide diuretic, such as hydrochlorothiazide 12,5 mg, which has been shown to have an additive blood pressure lowering effect with TESAR.

The best antihypertensive result is achieved four to eight weeks after the start of treatment with TESAR.

Reduction of cardiovascular morbidity and mortality:

The recommended dose is 80 mg once daily. Effective reduction in cardiovascular morbidity and mortality with doses lower than 80 mg is unknown.

Monitoring of blood pressure and, if appropriate, adjustment of blood pressure lowering medicines (where necessary) is recommended when initiating TESAR therapy for the reduction of cardiovascular morbidity and mortality.

The benefit of TESAR therapy only becomes evident after 6 months of continued treatment.

Special populations

In patients with renal impairment:

No dosage adjustment is required for patients with mild to moderate renal impairment.

TESAR is not removed from the blood by haemofiltration.

In patients with hepatic impairment:

In patients with mild to moderate hepatic impairment the dosage should not exceed 40 mg once daily.

In the elderly:

No dosage adjustment is necessary.

Paediatric population

Safety and efficacy has not been established in children and adolescents, and it is therefore not recommended that anyone younger than 18 years use TESAR.

Method of administration

Once-daily oral administration.

Missed dose

Doctors should advise patients who forget to take TESAR to take a dose as soon as possible and then continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications

- hypersensitivity to telmisartan or to any of the ingredients of TESAR
- a history of angioedema related to previous therapy with ACE inhibitors or angiotensin receptor blockers (ARBs): These patients must never again be given these medicines
- concomitant use of fluoroquinolones with ARBs, such as TESAR, is contraindicated in patients with moderate to severe renal impairment (creatinine clearance: 30 mL/min) and in elderly patients
- hereditary or idiopathic angioedema

- hypertrophic obstructive cardiomyopathy (HOCM)
- severe renal function impairment (creatinine clearance less than 30 mL/min)
- bilateral renal artery stenosis
- renal artery stenosis in patients with a single kidney
- aortic stenosis
- concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene, amiloride (see section 4.4)
- porphyria
- lithium therapy: Concomitant administration with TESAR may lead to toxic blood concentrations of lithium (see section 4.5)
- pregnancy and lactation (see section 4.6)
- the concomitant use of TESAR with renin inhibitors (aliskiren-containing products) is contraindicated (see section 4.4 and 4.5)
- severe hepatic impairment
- obstructive biliary disorders.

4.4 Special warnings and precautions for use

TESAR should not be initiated during pregnancy.

Should a woman become pregnant while receiving TESAR, the treatment should be stopped promptly and switched to a different class of antihypertensive medicine (see sections 4.3 and 4.6).

Fluoroquinolones:

Concomitant use of fluoroquinolones and angiotensin receptor blockers, such as TESAR, may precipitate acute kidney injury in patients, especially those with moderate to severe renal impairment and elderly patients (see section 4.3).

Renal function should be assessed before initiating treatment and monitored during treatment with fluoroquinolones or ARBs whether used separately or concomitantly.

Dual blockade of the renin-angiotensin-aldosterone system (RAAS):

There is evidence that the concomitant use of ACE inhibitors, angiotensin II receptor blockers (ARBs) and renin inhibitors (aliskiren-containing products) may increase the risk of hypotension, hyperkalaemia and decreases renal function (including acute renal failure).

Dual blockade of RAAS through the combined use of TESAR and renin inhibitors (aliskiren-containing products) is therefore contraindicated (see section 4.3). TESAR should not be used concomitantly with renin inhibitors (aliskiren-containing products) (see section 4.3).

Impaired renal function and kidney transplant:

Periodic monitoring of potassium and creatinine serum levels in such patients is therefore recommended. There is no experience regarding the administration of TESAR in patients with a recent kidney transplant (see section 4.3).

Renal artery stenosis, unilateral, bilateral renal function impairment and renovascular hypertension:

Increases in serum creatinine or blood urea nitrogen concentrations have occurred (see section 4.3). When patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney are treated with medicinal products that effect the renin-angiotensin-aldosterone system such as TESAR, there is an increased risk of severe hypotension and renal insufficiency (see section 4.3).

Hyperkalaemia:

Hyperkalaemia may occur in patients with advanced renal impairment, with heart failure, on renal replacement therapy, on potassium supplements, potassium sparing diuretics, and other

medications that increase potassium levels. Hyperkalaemia, especially in the presence of renal impairment and/or heart failure, may also occur in patients receiving treatment which affects the renin-angiotensin-aldosterone system.

Serum potassium should be monitored in patients at risk. Concomitant use of medication that affects the renin-angiotensin-aldosterone system, such as TESAR, 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 (see section 4.3).

Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy:

TESAR is contraindicated in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy, as is the case with other vasodilators (see section 4.3).

Primary aldosterone:

Use of TESAR in patients with primary aldosteronism is not recommended as they will generally not respond to antihypertensive medicinal products acting through inhibition of the renin-angiotensin system.

Intravascular volume depletion:

Patients who are volume and/or sodium depleted may be prone to symptomatic hypotension, especially after the first dose. This condition should be corrected before taking TESAR. Volume and/or sodium depletion can result from vigorous diuretic therapy, dietary salt restriction, diarrhoea or vomiting.

Impaired hepatic function:

Because of primary elimination of telmisartan via the biliary route, patients with biliary obstructive disorders, or mild to moderate hepatic impairment, can expect to have increased plasma

concentrations due to reduced clearance of telmisartan.

Hypotension:

If a patient is being treated with diuretics, symptomatic hypotension may occur during initiation of therapy.

Congestive heart failure:

May occur in some patients particularly sensitive to changes in the renin-angiotensin-aldosterone system.

Other conditions with stimulation of the renin-angiotensin-aldosterone system:

Treatment with medicines that affect the renin-angiotensin-aldosterone system has been associated with acute hypotension, hyperazotaemia, oliguria, or rarely acute renal failure in patients whose vascular tone and renal function depend predominantly on the activity of the said system (e.g. patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis).

Dehydration:

May occur due to side effects such as excess sweating, diarrhoea, and vomiting.

Diabetes mellitus:

In diabetic patients with an additional cardiovascular risk, i.e. patients with diabetes mellitus and co-existent 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 TESAR.

Other:

ARBs, including TESAR, are apparently less effective in lowering blood pressure in black people than in non-black people, possibly because of higher prevalence of low-renin states in the black hypertensive population.

Excessive reduction in blood pressure in patients with ischaemic cardiopathy or ischaemic cardiovascular disease could result in a myocardial infarction or stroke.

Information on excipients of TESAR:

Contains mannitol and may have a laxative effect.

TESAR contains sugar alcohol (mannitol) in the following quantities; TESAR 40 mg (163,8 mg), TESAR 80 mg (327,7 mg).

4.5 Interaction with other medicines and other forms of interaction

Fluoroquinolones:

Concomitant use of fluoroquinolones and angiotensin receptor blockers, such as TESAR, may precipitate acute injury. The mechanism of the possible interaction between the different classes of medicines, over and above the different mechanisms of kidney damage, is unknown (see section 4.3).

Dual blockade of the RAAS with ARBs, ACE inhibitors, or renin inhibitors:

Clinical data has shown that dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of ACE inhibitors, angiotensin II receptor blockers or renin inhibitors

(aliskiren-containing products) is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (see sections 4.3 and 4.4).

TESAR may increase the hypotensive effect of other antihypertensive medications.

Medicines such as digoxin, warfarin, hydrochlorothiazide, glibenclamide, paracetamol, ibuprofen, simvastatin, and amlodipine did not result in a clinically significant
interaction with TESAR.
For digoxin, a 20 % increase in median plasma digoxin trough concentration has been observed (in a single case a 39 % increase). 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 AUC0-24 and C_{max} of ramipril and ramiprilat. The clinical relevance of this observation is not known.

Lithium:

Increases in serum lithium have been observed (see section 4.3).
Careful monitoring of serum lithium levels is recommended since reversible increases in serum concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors.

NSAIDs:

Renal function monitoring in dehydrated patients is recommended if concomitant treatment with NSAIDs (including aspirin at anti-inflammatory dosage regimes, COX-2 inhibitors and non-selective NSAIDs) is administered. Patients receiving NSAIDs and TESAR should be adequately hydrated and be monitored for renal function at the beginning of combined treatment.

Combined treatment with NSAIDs has also been associated with reduced effect of antihypertensive medicines, such as TESAR, by inhibition of vasodilating prostaglandins.

4.6 Fertility, pregnancy, and lactation

Women of childbearing potential / Contraception in males and females

Women of childbearing age should ensure effective contraception.

Pregnancy

TESAR is contraindicated in pregnancy (see section 4.3 and 4.4).

Safety in pregnancy and lactation has not been established. When pregnancy is planned or confirmed TESAR should be discontinued.

Medicines affecting the renin-angiotensin system, such as TESAR, can cause embryonal toxicity, foetal and neonatal morbidity and mortality when administered to pregnant women. Use of TESAR during second and third trimesters of pregnancy may cause injury or even death to the foetus.

Breastfeeding

TESAR is contraindicated whilst breastfeeding (see section 4.3).

4.7 Effects on ability to drive and use machines

The patient should be cautioned not to use machinery or drive until they know how TESAR affects them.

Dizziness or drowsiness may occasionally occur when taking antihypertensive medication. However, no studies have been performed to ascertain the effect of TESAR on the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

The incidence of adverse events in controlled clinical trials was not dose related and showed no correlation with gender, age or race of the patients.

Tabulated summary of adverse reactions

System Organ Class	**Frequency**	**Side effects**
Infections and Infestations	Less frequent	Urinary tract infections (including cystitis), upper respiratory tract infections
	Frequency unknown	Sepsis including fatal outcome*
Blood and lymphatic system disorders	Less frequent	Thrombocytopenia, anaemia
	Frequency unknown	Eosinophilia*
Immune system disorders	Less frequent	Angioedema (with fatal outcome), hypersensitivity
	Frequency unknown	Anaphylactic reaction*
Metabolism and nutrition disorders	Less frequent	Hyperkalaemia
	Frequency unknown	Hypoglycaemia (in diabetic patients)*
Psychiatric disorders	Less frequent	Nervousness, depression, insomnia
Nervous system disorders	Less frequent	Headache, dizziness, fainting
Eye disorders	Less frequent	Changes in vision
Ear and labyrinth disorders	Less frequent	Vertigo, pounding in the ears

Cardiac disorders	Less frequent	Bradycardia, tachycardia, congestive heart failure, atrial fibrillation, chest pain, myocardial infarction
Vascular disorders	Less frequent	Hypotension, orthostatic hypotension
Respiratory, thoracic, and mediastinal disorders	Less frequent	Dyspnoea, coughing, sinusitis
Gastrointestinal disorders	Less frequent	Dyspepsia, stomach cramps, nausea, vomiting, diarrhoea, dry mouth, flatulence
Hepatobiliary disorders	Frequency unknown	Hepatic function abnormal/liver disorder*
Skin and subcutaneous tissue disorders	Less frequent Frequency unknown	Pruritus, eczema, skin rash, sweating, erythema, drug eruption, toxic skin eruption Urticaria*
Musculoskeletal, connective tissue and bone disorders	Less frequent Frequency unknown	Weakness, myalgia, muscle pain or cramps, back pain, arthralgia, pain in extremity (leg pain) Tendon pain (tendinitis like symptoms)*
Renal and urinary disorders	Less frequent	Renal impairment including acute renal failure
General disorders and administrative site conditions	Less frequent	Influenza-like symptoms, asthenia
Investigations	Less frequent	Blood creatinine increased, haemoglobin decreased, blood uric acid increased, hepatic enzymes increased, blood creatine phosphokinase increased

*Post marketing events.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the online service for adverse drug reaction reporting by following the link: https://www.sahpra.org.za/Publications/Index/8 or http://www.sahpra.org.za/ document/adverse-drug-reactions-and-quality-problem-reporting-form/ An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 Overdose

Signs and symptoms:

Bradycardia, dizziness, hypotension, tachycardia.

Management of overdose:

Overdose must be treated symptomatic and supportive. Haemodialysis cannot be used in treatment of TESAR overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Angiotensin II Antagonists, plain

ATC code: C09CA07

Pharmacological classification: A 7.1.3 Vascular Medicines – other hypotensives.

Mechanism of action

Telmisartan is an angiotensin II receptor antagonist (ARB) and prevents binding of angiotensin II at the AT_1 receptor subtype by displacement. Telmisartan selectively binds with the AT_1 receptor and does not block any ion channels or inhibit human plasma renin.

The binding of telmisartan with AT_1 is long lasting. The inhibitory effect of telmisartan on the AT_1 receptor is 50 % at 24 hours and still measurable at 48 hours.

The onset of anti-hypertensive activity occurs within 3 hours of administration of telmisartan. The maximum effect of telmisartan on blood pressure reduction can be seen within 4 weeks after beginning treatment and will be sustained with long term therapy. Both systolic and diastolic blood pressure is reduced by telmisartan, and it does not affect the heart rate.

There is no evident rebound hypertension with abrupt cessation of telmisartan treatment and blood pressure will return to pre-treatment conditions within days of cessation. There are no known beneficial effects of telmisartan on morbidity or cardiovascular mortality.

Telmisartan treatment has been shown in clinical trials to be associated with statistically significant reductions in proteinuria (including micro-albuminuria and macro-albuminuria) in patients with hypertension and diabetic nephropathy.

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.

5.2 Pharmacokinetic properties

Absorption:

Absorption of telmisartan is rapid, although the amount absorbed

varies.

The absolute bioavailability of telmisartan is dose dependent and is about 42 % for a 40 mg dose, and 58 % for a 160 mg dose. When administered along with food intake, the reduction in area under the plasma concentration-time curve of telmisartan ranges from approximately 6 %, in 40

mg dose, to approximately 19 % in 160 mg dose. This small reduction is thought not to reduce the therapeutic efficacy of telmisartan.

The plasma concentrations in females were found to be higher than those in males, though there was no relevant influence on efficacy.

Distribution:

Telmisartan is highly bound to plasma proteins albumin and alpha-1 acid glycoprotein. The steady-state volume of distribution (V_{dss}) is about 500 L.

Biotransformation:

Metabolisation of telmisartan is through conjugation with the glucuronide.

Elimination:

Terminal elimination half-life of telmisartan is more than 20 hours and is almost exclusively excreted in the faeces mainly as unchanged compound. Less than 2 % of the dose is secreted in the urine.

Plasma clearance is high compared to hepatic blood flow. Approximately 900 mL/min to 1500 mL/min.

Pharmacokinetics in special patient groups

Elderly patients:

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

Patients with renal impairment:

Lower plasma concentrations were seen in patients with renal impairment 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.

Patients with hepatic impairment:

In patients with hepatic impairment, the bioavailability increased to 100 %, and elimination half-life remained unchanged.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Crospovidone

Magnesium stearate

Mannitol (E 421)

Meglumine (for pH-adjustment).

Povidone

Sodium hydroxide (for pH-adjustment).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 30 °C in a dry place.

Keep the tablets in the sealed blister packs due to the hygroscopic property of the tablets.

Tablets should be taken out of the blister shortly before administration.

Keep the blisters in the outer carton until required for use.

6.5 Nature and contents of container

Silver aluminium/aluminium blister strips. Each pack contains 30 tablets per outer carton.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

1st Floor, Grapevine House, Steenberg Office Park

Silverwood Close

Westlake, Cape Town

7945, South Africa

8. REGISTRATION NUMBER(S)

TESAR 40 mg: A45/7.1.3/0978

TESAR 80 mg: A45/7.1.3/0979

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 11 June 2015

10. DATE OF REVISION OF THE TEXT

10 August 2023

NAMIBIA:

TESAR 40 mg: NS2 17/7.1.3/0023

TESAR 80 mg: NS2 17/7.1.3/0024