PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

TELMISARTAN 20 UNICORN tablets

TELMISARTAN 40 UNICORN tablets

TELMISARTAN 80 UNICORN tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TELMISARTAN 20 UNICORN:

Each tablet contains 20 mg telmisartan.

Contains sugar (mannitol 85 mg/tablet).

TELMISARTAN 40 UNICORN:

Each tablet contains 40 mg telmisartan.

Contains sugar (mannitol 170 mg/tablet).

TELMISARTAN 80 UNICORN:

Each tablet contains 80 mg telmisartan.

Contains sugar (mannitol 339 mg/tablet).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

TELMISARTAN 20 UNICORN:

White to off-white, round, flat face, beveled edge tablets debossed with “B” on one side and plain on the other side.

TELMISARTAN 40 UNICORN:

White to off white, capsule shaped tablets debossed with “H” on one side and plain on other side.

TELMISARTAN 80 UNICORN:

White to off white, oval shaped tablets debossed with “D” on one side and plain on other 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 patients 55 years or older 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

Posology:

Adults:

Treatment of essential hypertension:

The recommended dose is 40 mg once daily.

In cases where the target blood pressure is not achieved, the TELMISARTAN UNICORN dose can be increased to a maximum of 80 mg once daily. Alternatively, TELMISARTAN UNICORN may be used in combination with a low dose thiazide diuretic such as hydrochlorothiazide 12,5 mg, which has been shown to have an additive blood pressure lowering effect with TELMISARTAN UNICORN. 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.

Reduction of cardiovascular morbidity and mortality:

The recommended dose is 80 mg once daily. It is not known whether doses lower than 80 mg of TELMISARTAN UNICORN are effective in preventing cardiovascular morbidity and mortality.

When initiating TELMISARTAN UNICORN therapy for the prevention of cardiovascular morbidity and mortality, monitoring of blood pressure is recommended and, if appropriate, adjustment of medications that lower blood pressure may be necessary. The benefit of treatment is evident only after 6 months of continued treatment.

Renal impairment:

No dosage adjustment is required for patients with renal impairment, including those on haemodialysis. TELMISARTAN UNICORN is not removed from blood by haemofiltration.

Hepatic impairment:

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

Elderly:

No dosing adjustment is necessary.

Children and adolescents up to 18 years:

The safety and efficacy of TELMISARTAN UNICORN for use in children below 18 years have not been established.

Method of administration:

TELMISARTAN UNICORN are for once-daily oral administration and should be taken with liquid, with or without food.

4.3 Contraindications

- Hypersensitivity to telmisartan or to any of the ingredients of TELMISARTAN UNICORN (see section 2 and 6.1).
- A history of angioedema related to previous therapy with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs): These patients must never again be given these medicines.
- Hereditary or idiopathic angioedema.
- Hypertrophic obstructive cardiomyopathy (HOCM).
- Bilateral renal artery stenosis.
- Renal artery stenosis in patients with a single kidney
- Severe renal function impairment (creatinine clearance less than 30 mL/min).
- Aortic stenosis.

- Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene, amiloride (see section 4.4).
- Porphyria.
- Lithium therapy: Concomitant administration with TELMISARTAN UNICORN may lead to toxic blood concentrations of lithium (see section 4.5).
- Pregnancy and lactation (see section 4.4 and 4.6).
- Severe hepatic impairment.
- Obstructive biliary disorders.
- The concomitant use of TELMISARTAN UNICORN with aliskiren-containing products is contraindicated (section 4.4 and 4.5).
- Concomitant use of fluoroquinolones with Angiotensin-converting enzyme (ACE) inhibitors/Angiotensin receptor blockers (ARBs) is contraindicated in patients with moderate to severe renal impairment (Creatinine Clearance ≤ 30 mL/min) and in elderly patients.

4.4 Special warnings and precautions for use

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

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 TELMISARTAN UNICORN (see section 4.3).

Renal impairment and kidney transplant:

When TELMISARTAN UNICORN 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 UNICORN in patients with a recent kidney transplant (see section 4.3).

Intravascular volume depletion:

Symptomatic hypotension, especially after the first dose, may occur in patients who are volume and/or sodium depleted by 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 UNICORN.

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

There is evidence that the concomitant use of angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers or aliskiren may increase the risk of hypotension, hyperkalaemia and decreases renal function (including acute renal failure). Dual blockade of RAAS through the combined use of TELMISARTAN UNICORN and aliskiren is therefore contraindicated (see section 4.3).

TELMISARTAN UNICORN should not be used concomitantly with aliskiren (see section 4.3). ACE-inhibitors and angiotensin II receptor blockers should not be used concomitantly in patients with diabetic nephropathy.

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 medicines that affect this system, such as TELMISARTAN UNICORN, has been associated with acute hypotension, uraemia, oliguria, or acute renal failure.

Concomitant use of fluoroquinolones:

Concomitant use of fluoroquinolones and Angiotensin-converting enzyme (ACE) inhibitors/Angiotensin receptor blockers (ARBs) 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 Angiotensin-converting enzyme (ACE) inhibitors/Angiotensin receptor blockers (ARBs) whether used separately and/or concomitantly.

Primary aldosteronism:

Patients with primary aldosteronism generally will not respond to TELMISARTAN UNICORN. Therefore, the use of TELMISARTAN UNICORN is not recommended.

Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy:

TELMISARTAN UNICORN is contraindicated in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy (see section 4.3).

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

Diabetic patients treated with insulin or antidiabetics:

In these patients hypoglycaemia may occur with TELMISARTAN UNICORN treatment. Therefore, in these patients, appropriate blood glucose monitoring should be considered; a dose adjustment of insulin or antidiabetics may be required, when indicated.

Hyperkalaemia:

During treatment with TELMISARTAN UNICORN, hyperkalaemia may occur, especially in the presence of renal impairment and/or heart failure. Monitoring of serum potassium in patients at risk is recommended.

In the elderly, in patients with renal insufficiency, in diabetic patients, in patients concomitantly treated with other medicines that may increase potassium levels, and/or in patients with intercurrent events, hyperkalaemia may be fatal.

The main risk factors for hyperkalaemia are:

- Diabetes mellitus, renal impairment, age (>70 years)
- Combination with one or more other medicines that affect the renin-angiotensin-aldosterone system and/or potassium supplements. Medicines or therapeutic classes of medicines that may provoke hyperkalaemia are salt substitutes containing potassium, potassium-sparing diuretics, ACE inhibitors, angiotensin II receptor antagonists, non-steroidal anti-inflammatory medicines (NSAIDs, including selective COX-2 inhibitors), heparin, immunosuppressives (ciclosporin or tacrolimus), and trimethoprim.

- Intercurrent events, in particular dehydration, acute cardiac decompensation, metabolic acidosis, worsening of renal function, sudden worsening of the renal condition (e.g. infectious diseases), cellular lysis (e.g. acute limb ischemia, rhabdomyolysis, extend trauma).

Hepatic impairment:

TELMISARTAN UNICORN is mostly eliminated in the bile. Patients with biliary obstructive disorders, cholestasis, or hepatic insufficiency can be expected to have reduced clearance (see section 4.3) and should not take TELMISARTAN UNICORN. TELMISARTAN UNICORN should be used only with caution in patients with mild to moderate hepatic impairment.

Other:

Angiotensin receptor blockers, including TELMISARTAN UNICORN, 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.

4.5 Interaction with other medicines and other forms of interaction

TELMISARTAN UNICORN may increase the hypotensive effect of other antihypertensive medicines.
Co-administration of telmisartan did not result in a clinically significant interaction with warfarin, hydrochlorothiazide, glibenclamide, paracetamol, ibuprofen, simvastatin and amlodipine.

Digoxin:

Co-administration of telmisartan did not result in a clinically significant interaction with digoxin, warfarin, hydrochlorothiazide, glibenclamide, paracetamol, ibuprofen, simvastatin and amlodipine.
When telmisartan was co-administered with digoxin, median increases in digoxin peak plasma concentration (49 %) and in trough concentration (20 %) were observed (in a single case a 39 %). When initiating, adjusting, and discontinuing telmisartan, monitor digoxin levels in order to maintain levels within the therapeutic range.

Potassium sparing diuretics or potassium supplements:

As with other medicines acting on the renin-angiotensin-aldosterone system, telmisartan may provoke hyperkalaemia (see section 4.4). The risk may increase in case of treatment combination with other medicines that may also provoke hyperkalaemia (salt substitutes containing potassium, potassium-sparing diuretics, ACE inhibitors, angiotensin II receptor antagonists, non-steroidal anti-inflammatory medicines [NSAIDs, including selective COX-2 inhibitors], heparin, immunosuppressives [ciclosporin or tacrolimus], and trimethoprim). Angiotensin II receptor antagonists such as telmisartan, attenuate diuretic induced potassium loss. Potassium sparing diuretics e.g. spironolactone, eplerenone, triamterene, or amiloride, potassium supplements, or potassium-containing salt substitutes may lead to a significant increase in serum potassium.

Lithium:

Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors. Increased serum levels have also been reported with telmisartan. Careful monitoring of serum lithium levels is recommended during concomitant use.

Non-steroidal anti-inflammatory Drugs:

Concomitant treatment with NSAIDs (including acetylsalicylic acid at anti- inflammatory dosage regimens, COX-2 inhibitors and non-selective NSAIDs) may reduce the antihypertensive effect of angiotensin II receptor antagonists. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function), the co-administration of angiotensin II receptor antagonists and medicines that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution, especially in the elderly. Compounds acting on the Renin-Angiotensin-System like TELMISARTAN UNICORN may have synergistic effects. Patients receiving NSAIDs and TELMISARTAN UNICORN should be adequately hydrated and be monitored for renal function at the beginning of combined treatment.

A reduced effect of antihypertensive medicines like TELMISARTAN UNICORN by inhibition of vasodilating prostaglandins has been reported during combined treatment with NSAIDs.

Ramipril

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 Cmax of ramipril and ramiprilat. The clinical relevance of this observation is not known.

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

Clinical trial data has shown that dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (see section 4.3 and 4.4).

Based on their pharmacological properties it can be expected that the following medicines may potentiate the hypotensive effects of all antihypertensives including telmisartan: Baclofen, amifostine. Furthermore, orthostatic hypotension may be aggravated by alcohol, barbiturates, narcotics, or antidepressants.

Concomitant use of fluoroquinolones:

Concomitant use of fluoroquinolones and Angiotensin-converting enzyme (ACE) inhibitors/Angiotensin receptor blockers (ARBs) may precipitate acute kidney injury. The mechanism of the possible interaction between the different classes of medicines, over and above different mechanisms of kidney damage, is unknown (see section 4.3).

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 is a risk of hypotension when initiating therapy with telmisartan. To be taken into account with concomitant use.

Corticosteroids (systemic route):

Reduction of the antihypertensive effect.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing age should ensure effective contraception

Pregnancy:

Safety in pregnancy and lactation has not been established (see section 4.3).

When pregnancy is planned or confirmed TELMISARTAN UNICORN should be discontinued.

Medicines affecting the renin-angiotensin system, such as TELMISARTAN UNICORN, can cause embryonal toxicity, foetal and neonatal morbidity and mortality when administered to pregnant women.

Breastfeeding:

TELMISARTAN UNICORN is contraindicated during lactation (see section 4.3).

Fertility:

In preclinical studies, no effects of TELMISARTAN UNICORN 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 dizziness or drowsiness may occasionally occur when taking antihypertensive therapy including TELMISARTAN UNICORN.

4.8 Undesirable effects

Tabulated list of adverse reactions:

System Organ Class	Frequency	Side effect
Infections and infestations	Less frequent	Urinary tract infections (including cystitis), upper respiratory tract infections including pharyngitis and sinusitis
	Frequency unknown	Sepsis including fatal outcome

Blood and the lymphatic system disorders	Less frequent Frequency unknown	Anaemia, thrombocytopenia Eosinophilia
Immune system disorders	Less frequent Frequency unknown	Hypersensitivity, angio-oedema (with fatal outcome) Anaphylactic reaction
Metabolism and nutrition disorders	Less frequent Frequency unknown	Hyperkalaemia Hypoglycaemia (in diabetic patients)
Psychiatric disorders	Less frequent	Depression, insomnia, anxiety
Nervous system disorders	Less frequent	Syncope/fainting, somnolence
Eye disorders	Less frequent	Visual disturbance
Ear and labyrinth disorders	Less frequent	Vertigo
Cardiac disorders	Less frequent	Bradycardia, tachycardia
Vascular disorders	Less frequent	Hypotension, orthostatic hypotension
Respiratory, thoracic and mediastinal disorders	Frequent Less frequent	Cough Dyspnoea, interstitial lung disease
Gastrointestinal disorders	Less frequent	Abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting, dry mouth, stomach discomfort, dysgeusia
Hepato-biliary disorders	Frequency unknown	Hepatic function abnormal/liver disorder

Skin and subcutaneous tissue disorders	Less frequent Frequency unknown	Increased sweating (hyperhidrosis), pruritus, rash, eczema, erythema, drug eruption, toxic skin eruption Urticaria
Musculoskeletal, and connective tissue disorders	Less frequent Frequency unknown	Back pain (e.g. sciatica), muscle spasms (cramps in legs), myalgia, 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 administration site conditions	Less frequent	Chest pain, asthenia (weakness), influenza-like symptoms
Investigations	Less frequent	Blood creatinine increased, haemoglobin decreased, blood uric acid increased, hepatic enzymes increased, blood creatine phosphokinase increased

Reporting of suspected adverse reactions:

Reporting of suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: www.sahpra.org.za.

4.9 Overdose

Symptoms:

Limited information is available with regard to overdose in humans. The most prominent manifestations of telmisartan overdose were hypotension and tachycardia; bradycardia dizziness, increase in serum creatinine, and acute renal failure also occurred.

Management:

If symptomatic hypotension should occur, supportive treatment should be instituted. Telmisartan, as in TELMISARTAN UNICORN is not removed by haemodialysis. Management depends on the time since ingestion and the severity of the symptoms. 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

A 7.1.3 Vascular medicines – other hypotensives

Pharmacotherapeutic group: Angiotensin II Antagonists, plain, ATC Code: C09CA07.

Telmisartan is a specific angiotensin II receptor (type AT1) antagonist. It displaces angiotensin II 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 at the AT1 receptor. The binding is long-lasting. Telmisartan does not inhibit human plasma renin or block ion channels.

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.

After administration of the first dose of telmisartan in hypertensive patients, onset of antihypertensive activity occurs 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 over 24 hours after dosing.

There is an apparent trend to a dose relationship with regard to a time to recovery of baseline systolic blood pressure. In this respect data concerning diastolic blood pressure are inconsistent.

In patients with hypertension, telmisartan reduces both systolic and diastolic blood pressure without affecting pulse rate.

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 proteinuria (including microalbuminuria and macroalbuminuria) 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 of telmisartan is rapid although the amount absorbed varies. The mean absolute bioavailability for telmisartan is about 50 %.

When TELMISARTAN UNICORN is taken with food, the reduction in the area under the plasma concentration-time curve (AUC0-∞) of telmisartan varies from approximately 6 % (40 mg dose) to approximately 19 % (160 mg dose). After 3 hours post 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.

Gender differences in plasma concentrations were observed, Cmax and AUC being approximately 3- and 2-fold higher, respectively, in females compared to males without relevant influence on efficacy.

Telmisartan is highly 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.

Telmisartan is metabolised by conjugation to the glucuronide. No pharmacological activity has been shown for the conjugate. 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, area under the plasma concentration-time curve (AUC) increase disproportionately with dose. There is no evidence of clinically relevant accumulation of telmisartan.

Plasma concentrations were higher in females than in males, without relevant influence on efficacy.

After oral administration telmisartan is nearly exclusively excreted with the faeces, mainly as unchanged compound. Cumulative urinary excretion is < 2 % of dose. Total plasma clearance (CL_{tot}) is high (approximately 900 mL/min) when compared with hepatic blood flow (about 1 500 mL/min).

Special Populations

Elderly patients:

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

Patients with 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.

Patients with 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

Meglumine

Sodium Hydroxide

Povidone

Mannitol

Magnesium Stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store at or below 25 °C.

Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

OPA/Al/PVC - Al blister strips containing 7 or 10 tablets each, packed in an outer carton.

Pack size: 28 or 30 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION

Unicorn Pharmaceuticals (Pty) Ltd

Cnr. Searle & Pontac Streets

Cape Town, 8001

South Africa

8. REGISTRATION NUMBERS

Telmisartan 20 Unicorn: 48/7.1.3/0725

Telmisartan 40 Unicorn: 48/7.1.3/0726

Telmisartan 80 Unicorn: 48/7.1.3/0727

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of registration: 01 February 2022.

10. DATE OF REVISION OF THE TEXT

Not applicable