TELSAR 20/40/80
(Telmisartan tablets
20mg/40mg/80mg)

PACKAGE INSERT
TELSAR 20/40/80

1. Product Name
TELSAR 20/40/80 (Telmisartan tablets 20mg/40mg/80mg)

2. Name and Strength of Active Ingredient (s)
Telmisartan tablets 20mg/40mg/80mg

3. Product Description
TELSAR 20 (Telmisartan tablets 20mg)
White to off white, round, flat bevel edged tablets, debossed with 'H' on one side and '162' on other side. The thickness of the tablet is 2.60 ±0.40 mm.

TELSAR 40 (Telmisartan tablets 40mg)
White to off white, oval shaped, biconvex tablets, debossed with 'H' on one side and '163'on other side. The thickness of the tablet is 3.80 ±0.40 mm.

TELSAR 80 (Telmisartan tablets 80mg)
White to off white, oval shaped, biconvex tablets debossed with 'H' on one side and '164'on other side. The thickness of the tablet is 5.00 ±0.40 mm.

4. Pharmacodynamics / Pharmacokinetics
Pharmacodynamics
Telmisartan is an orally effective and specific angiotensin-II receptor (type AT_1) antagonist. It displaces angiotensin II with very high affinity from its binding site at the AT_1 receptor subtype, which is responsible for the unknown actions of angiotensin

II. Telmisartan does not exhibit any partial agonist activity at the AT_1 receptor. Telmisartan selectively binds the AT_1 receptor. The binding long lasting. Telmisartan does not show affinity for other receptors, including AT_2 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 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.

Pharmacokinetics 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 (AUC0-∞) 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 500l.

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 exponential 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 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 does 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.

5. Indication
Hypertension
Treatment of essential hypertension.

Cardiovascular risk reduction
Telmisartan 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. Telmisartan 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.

6. Posology and Mode of administration
Route of Administration : Oral route of administration

Adult
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. Alternatively, Telmisartan may be used in combination with thiazide- type diuretics such as hydrochlorothiazide, which has been shown to have an additive blood pressure lowering effect with telmisartan. 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.
In patients with severe hypertension treatment with Telmisartan at doses up to 160 mg alone and in combination with hydrochlorothiazide 12.5 to 25 mg daily was well tolerated and effective.

Cardiovascular risk reduction
The recommended dose of Telmisartan Tablets is 80mg once a day and can be administered with or without food. It is not known whether doses lower than 80mg of Telmisartan are effective in reducing the risk of cardiovascular morbidity and mortality.

When initiating Telmisaran, therapy for cardiovascular risk reduction, monitoring of blood pressure is recommended, and if appropriate adjustment of medications that lower blood pressure may be necessary.

Telmisartan may be taken with or without food.

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

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

Ederly
No dosing adjustment is necessary.

Children and adolescents
The safety and efficacy of Telmisartan for use in children below 18 years have not been established.

7. Contraindication
Hypersensitivity to telmisartan or any of the excipients of TELSAR, 2nd and 3rd trimester of pregnancy, lactation, biliary obstructive disorders, severe hepatic impairment.

8. Warnings and Precautions
Pregnancy
Angiotensin II receptor antagonists should not be initiated during pregnancy. Unless continued angiotensin II, receptor antagonist therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with angiotensin II receptor antagonists should be stopped immediately, and, if appropriate, alternative therapy should be started.

Hepatic impairment
Telmisartan is not to be given to patients with cholestasis, biliary obstructive disorders or severe hepatic impairment since telmisartan is mostly eliminated with the bile. These patients can be expected to have reduced hepatic clearance for telmisartan. Telmisartan should be used only with caution in patients with mild to moderate hepatic impairment.

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 transplantation
When Telmisartan is used in patients with impaired renal function, periodic monitoring of potassium and creatinine serum levels is recommended. There is no experience regarding the administration of Telmisartan in patients with recent kidney transplantation. When Telmisartan is used in patients with impaired renal function, periodic monitoring of potassium and creatinine serum levels is recommended. There is no experience regarding the administration of Telmisartan in patients with recent kidney transplantation.

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

Dual blockade of the renin-angiotensin-aldosterone system (RAAS)
There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren increases the risk of hypotension, hyperkalaemia and decreased renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is therefore not recommended. If dual blockade therapy is considered absolutely necessary, this should only occur under specialist supervision and subject to frequent close monitoring of renal function, electrolytes and blood pressure.

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 medicinal products that affect this system such as telmisartan 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.

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

Hyperkalaemia
The use of medicinal products that affect the renin-angiotensin-aldosterone system may cause hyperkalaemia.

Size: 180 x 300 mm
Colours: 01, Black

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

Before considering the concomitant use of medicinal products that affect the renin-angiotensin-aldosterone system, the benefit risk ratio should be evaluated.

The main risk factors for hyperkalaemia to be considered are:

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

Close monitoring of serum potassium in at risk patients is recommended.

Ethnic differences
As observed for angiotensin converting enzyme inhibitors, telmisartan and the other angiotensin II receptor antagonists 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.

Other
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.

9. Interactions with other medicaments
Digoxin
When telmisartan was co-administered with digoxin, median increases in digoxin peak plasma concentration and in trough concentration were observed. When initiating, adjusting, and discontinuing telmisartan, monitor digoxin levels in order to maintain levels within the therapeutic range.
As with other medicinal products acting on the renin-angiotensin-aldosterone system, telmisartan may provoke hyperkalaemia. The risk may increase in case of treatment combination with other medicinal products that may also provoke hyperkalaemia (salt substitutes containing potassium, potassium-sparing diuretics, ACE inhibitors, angiotensin II receptor antagonists, non-steroidal anti-inflammatory medicinal products (NSAIDs, including selective COX-2 inhibitors), heparin, immunosuppressive (cyclosporine or tacrolimus), and trimethoprim).

The occurrence of hyperkalaemia depends on associated risk factors. The risk is increased in case of the above-mentioned treatment combinations. The risk is particularly high in combination with potassium sparing-diuretics, and when combined with salt substitutes containing potassium. A combination with ACE inhibitors or NSAIDs, for example, presents a lesser risk provided that precautions for use are strictly followed.
Concomitant use not recommended

Potassium sparing diuretics or potassium supplements
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. If concomitant use is indicated because of documented hypokalaemia, they should be used with caution and with frequent monitoring of serum potassium.

Lithium
Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors, and with angiotensin II receptor antagonists, including telmisartan. If use of the combination proves necessary, careful monitoring of serum lithium levels is recommended.
Concomitant use requiring caution

Non-steroidal anti-inflammatory medicinal products
NSAIDs (i.e. 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 agents 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. Patients should be adequately hydrated and consideration should be given
to monitoring of renal function after initiation of concomitant therapy and periodically thereafter.

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

Other antihypertensive agents
The blood pressure lowering effect of telmisartan can be increased by concomitant use of other antihypertensive medicinal products.
Based on their pharmacological properties it can be expected that the following medicinal products may potentiate the hypotensive effects of all antihypertensive including telmisartan: Baclofen, amifostine. Furthermore, orthostatic hypotension may be aggravated by alcohol, barbiturates, narcotics, or antidepressants.

10.Pregnancy and Lactation
The use angiotensin-II receptor antagonist is not recommended during the 1st trimester and contraindicated during the 2nd and 3rd trimester of pregnancy.

Angiotensin-II receptor antagonists' exposure during the 2nd and 3rd trimester is known to include human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, and hyperkalaemia).

Unless continued, angiotensin II – receptor antagonist therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with angiotensin II- receptor antagonists should be stopped immediately, and appropriate, alternative therapy should be started.

Should exposure to angiotensin-II receptor antagonists have occurred from the 2nd trimester of pregnancy, ultrasound check of renal function and skull is recommended.

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

TELSAR is contraindicated during lactation since it is not known whether it is excreted in human milk

11.Undesirable Effects
The adverse drug reaction listed as follow have been accumulated from patients treated for hypertension.

Infection and infestion: Urinary Tract infections (including cystitis), upper respiratory tract infections, sepsis including fatal outcome.

Blood and Lymphatic System Disorder: Anaemia, eosinophilia, thrombocytopenia. Immune System Disorders: Anaphylactic reaction, hypersensitivity.

Metabolism and Nutrition Disorder: Hyperkalaemia, hypoglycaemia (in diabetic patients).

Psychiatric Disorder: Insomnia, depression, anxiety. Nervous System Disorder: Syncope (faint)

Eye Disorder: Visual Disturbance Ear and Labyrinth Disorder: Vertigo

Cardiac Disorder: Bradycardia, Tachycardia.

Vascular Disorder: Hypotension, orthostatic hypotension. Respiratory Disorder: Dyspnoea.

Gastrointestinal Disorder: Abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting, dry mouth, stomach discomfort.

Hepatobiliary Disorder: Abnormal hepatic function or liver disorder.

Skin and subcutaneous Tissue Disorder: Angioedema (with fatal outcome), eczema, erythema, pruritus, hyperhidrosis, urticarial, drug eruption, toxic skin eruption, toxic skin eruption, rash.

Musculoskeletal, connective Tissue and Bone Disorder: Back pain, Muscle Spasms (cramps in leg), myalgia, arthralgia, pain in extremity (leg pain), tendon pain (tendinitis – like symptoms).

Renal and Urinary Tract Disorder: Renal impairment including acute renal failure.

General Disorder and Administration Site Conditions: Chest pain, influenza-like illness, asthenia (weakness).

12.Overdose
Symptoms
The most prominent manifestations of telmisartan overdose were hypotension and tachycardia; bradycardia dizziness, increase in serum creatinine, and acute renal failure.

Treatment:
Telmisartan is not removed by hemodialysis. 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 overdosage. 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.

13.Storage Condition
Store below 30°C. Store in original package in order to protect from moisture.

14.Dosage Forms and Packaging available
For TELSAR 20, TELSAR 40 & TELSAR 80: 3 blister of 10 tablets (3 x 10's) and 10 blister of 10 tablets (10 x 10's) each are packed in a printed carton along with a package insert.

15.Shelf life: 2 Years

16.Name and address of manufacturer
Hetero Labs Limited,
Unit V, Sy. No 439, 440, 441 & 458,
TSIIC Formulation SEZ, Polepally Village,
Jadcherla Mandal, Mahaboobnagar Dist.
Telangana, India

17.Product registration holder
UNIMED SDN BHD
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18.Date of revision: March 2021