Summary of Product Characteristics (SmPC)

1. Name of the Finished Pharmaceutical Product: TEMAZ-40
Generic Name: Telmisartan Tablets USP 40mg

2. Quality and Quantitative Composition

2.1 Qualitative Composition

Composition:

Each uncoated tablet contains:

Telmisartan	USP	40mg
Excipients		q.s

2.2 Quantitative Composition

S.No.	Ingredients	Claim	Specification	Quantity Per tablet (mg or ml)	Quantity Per Tablet (in %)	Function
Active:						
1	Telmisartan*	40mg	USP	40.000mg	20.000	API
Tablet Core:						
2	Mannitol	-------	BP	088.000mg	44.000	Diluent
3	Meglumine	-------	BP	038.000mg	19.000	Diluent
4.	Potassium Hydroxide		BP	010.000mg	05.000	Buffering agennt
5	Colloidal anhydrous silica	-------	BP	008.000mg	04.000	Anti-adherent
6	Sodium Starch Glycolate (Type-A) 1	-------	BP	004.000mg	02.000	Disintegrants
7	Kyron-T 314	-------	IH	005.000mg	02.500	Disintegrants
8	Dichloromethane$		BP	000.030ml	-------	Solvent
9	Purified Talc	-------	BP	003.000mg	01.500	Glidant
10	Magnesium Stearate	-------	BP	004.000mg	02.000	Lubricant
11	Purified Water$	-------	BP	000.030ml	-------	Solvent
			Total	200.000mg	100.00	-------

Average Weight of Tablet: 200mg±3.00%Tablet

* Material calculated on 100% assay basis.

$ Will not remain in the final product.

Abbreviation-USP-United states pharmacopoeia **BP**-British Pharmacopoeia **MG**-Milligram **%**-Percentage **IH**-In-House **ML**-Milliliter **Q.S-quantity sufficient**

3. Pharmaceutical Form

Oral Solid Dosage Form (Uncoated Tablet)

4. Clinical Particulars

4.1 Therapeutic indications

Hypertension

Treatment of essential hypertension in adults.

Cardiovascular prevention

Reduction of cardiovascular morbidity in adults with:

• manifest atherothrombotic cardiovascular disease (history of coronary heart disease, stroke, or peripheral arterial disease) or

• type 2 diabetes mellitus with documented target organ damage

4.2 Posology and method of administration

Posology

Treatment of essential hypertension

The usually effective dose is 40 mg once daily. Some patients may already benefit at a daily dose of 20 mg. In cases where the target blood pressure is not achieved, the dose of telmisartan 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.

Cardiovascular prevention

The recommended dose is 80 mg once daily. It is not known whether doses lower than 80 mg of telmisartan are effective in reducing cardiovascular morbidity.

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

Special populations

Patients with renal impairment

Limited experience is available in patients with severe renal impairment or haemodialysis. A lower starting dose of 20 mg is recommended in these patients.

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

Concomitant use of telmisartan with aliskiren is contraindicated in patients with renal impairment.

Patients with hepatic impairment

Telmisartan is contraindicated in patients with severe hepatic impairment.

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

Elderly patients

No dose adjustment is necessary for elderly patients.

Paediatric population

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

Method of administration

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

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- Second and third trimesters of pregnancy
- Biliary obstructive disorders
- Severe hepatic impairment

The concomitant use of telmisartan with aliskiren is contraindicated in patients with diabetes mellitus or renal impairment.

4.4 Special Warnings and Precautions for Use

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.

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

The use of telmisartan in combination with aliskiren is contraindicated in patients with diabetes mellitus or renal impairment.

As a consequence of inhibiting the renin-angiotensin-aldosterone system, hypotension, syncope, hyperkalaemia, and 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 administering telmisartan with other blockers of the renin-angiotensin-aldosterone system) is therefore not recommended. Close monitoring of renal function is advisable if co-administration is

considered necessary.

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 approptiate 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.

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.

Sorbitol

This medicinal product contains sorbitol (E420). Patients with rare hereditary problems of fructose intolerance should not take Telmisartan.

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.

4.5 Interaction with other medicinal products and other forms of interaction

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

The combination of telmisartan with aliskiren is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m^2) and is not recommended in other patients.

Digoxin

When telmisartan was co-administered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) 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, immunosuppressives (cyclosporin 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. spirinolactone, 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 hypokalemia 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.

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.

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.

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 antihypertensives including telmisartan: Baclofen, amifostine. Furthermore, orthostatic hypotension may be aggravated by alcohol, barbiturates, narcotics or antidepressants.

Corticosteroids (systemic route)

Reduction of the antihypertensive effect.

Monoamine Oxidase Inhibitors (MAOIs)

Due to the risk of serotonin syndrome, duloxetine should not be used in combination with non-selective, irreversible monoamine oxidase inhibitors (MAOIs) or within at least 14 days of discontinuing treatment with an MAOI. Based on the half-life of duloxetine, at least 5 days should be allowed after stopping duloxetine before starting an MAOI.

For selective, reversible MAOIs, like moclobemide, the risk of serotonin syndrome is lower. However, the concomitant use of duloxetine with selective, reversible MAOIs is not recommended.

Inhibitors of CYP1A2

Because CYP1A2 is involved in duloxetine metabolism, concomitant use of duloxetine with potent inhibitors of CYP1A2 is likely to result in higher concentrations of duloxetine. Fluvoxamine (100 mg once daily), a potent inhibitor of CYP1A2, decreased the apparent plasma clearance of duloxetine by about 77% and increased AUC_{o-t} 6-fold. Therefore, duloxetine should not be administered in combination with potent inhibitors of CYP1A2 like fluvoxamine.

CNS Medicinal Products

The risk of using duloxetine in combination with other CNS-active medicinal products has not been systematically evaluated, except in the cases described in this section. Consequently, caution is advised when Cymbalta is taken in combination with other centrally-acting medicinal products or substances, including alcohol and sedative medicinal products (e.g., benzodiazepines, morphinomimetics, antipsychotics, phenobarbital, and sedative antihistamines).

Serotonin Syndrome

In rare cases, serotonin syndrome has been reported in patients using SSRIs (e.g., paroxetine, fluoxetine) concomitantly with serotonergic medicinal products. Caution is advisable if duloxetine is used concomitantly with serotonergic antidepressants like SSRIs, tricyclics like clomipramine or amitriptyline, St John's Wort (Hypericum perforatum), venlafaxine, or triptans, tramadol, pethidine, and tryptophan.

Effect of Duloxetine on Other Medicinal Products

Medicinal products metabolised by CYP1A2: The pharmacokinetics of theophylline, a CYP1A2 substrate, were not significantly affected by co-administration with duloxetine (60 mg twice daily).

Medicinal products metabolised by CYP2D6: Duloxetine is a moderate inhibitor of CYP2D6. When duloxetine was administered at a dose of 60 mg twice daily with a single dose of desipramine, a CYP2D6 substrate, the AUC of desipramine increased 3-fold. The co-administration of duloxetine (40 mg twice daily) increases steady-state AUC of tolterodine (2 mg twice daily) by 71%, but does not affect the pharmacokinetics of its active 5-hydroxyl metabolite and no dosage adjustment is recommended. Caution is advised if Cymbalta is co-administered with medicinal products that are predominantly metabolised by CYP2D6 (risperidone, tricyclic antidepressants, such as nortriptyline, amitriptyline, and imipramine), particularly if they have a narrow therapeutic index (such as flecainide, propafenone, and metoprolol).

Oral contraceptives and other steroidal agents: Results of in vitro studies demonstrate that duloxetine does not induce the catalytic activity of CYP3A. Specific in vivo drug interaction studies have not been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy

The use of angiotensin II receptor antagonists is not recommended during the first trimester of pregnancy. The use of angiotensin II receptor antagonists is contraindicated during the second and third trimesters of pregnancy.

There are no adequate data from the use of Telmisartan in pregnant women. Studies in animals have shown reproductive toxicity.

Epidemiological evidence regarding the risk of teratogenicity following exposure to ACE inhibitors during the first trimester of pregnancy has not been conclusive; however a small increase in risk cannot be excluded. Whilst there is no controlled epidemiological data on the risk with angiotensin II receptor antagonists, similar risks may exist for this class of drugs. 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.

Exposure to angiotensin II receptor antagonist therapy 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, and hyperkalaemia).

Should exposure to angiotensin II receptor antagonists 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 antagonists should be closely observed for hypotension.

Breast-feeding

Because no information is available regarding the use of Telmisartan during breast-feeding, Telmisartan is not recommended and alternative treatments with better established safety profiles during breast-feeding are preferable, especially while nursing a newborn or preterm infant.

Fertility

In preclinical studies, no effects of Telmisartan on male and female fertility were observed.

4.7 Effects on ability to drive and use machines

When driving vehicles or operating machinery it should be taken into account that dizziness or drowsiness may occasionally occur when taking antihypertensive therapy sach as Telmisartan.

4.8 Undesirable effects

Summary of the safety profile

Summary of the safety profile

Serious adverse drug reactions include anaphylactic reaction and angioedema which may occur rarely (≥ 1/10,000 to <1/1,000), and acute renal failure.

The overall incidence of adverse reactions reported with telmisartan was usually comparable to placebo (41.4% vs 43.9 %) in controlled trials in patients treated for hypertension. The incidence of adverse reactions was not dose related and showed no correlation with gender, age or race of the patients. The safety profile of telmisartan in patients treated for the reduction of cardiovascular morbidity was consistent with that obtained in hypertensive patients.

The adverse reactions listed below have been accumulated from controlled clinical trials in patients treated for hypertension and from post-marketing reports. The listing also takes into account serious adverse reactions and adverse reactions leading to discontinuation reported in three clinical long-term studies including 21642 patients treated with telmisartan for the reduction of cardiovascular morbidity for up to six years.

Tabulated summary of adverse reactions

Adverse reactions have been ranked under headings of frequency using the following convention:

very common (≥1/10);

common (≥1/100 to <1/10);
uncommon (≥1/1,000 to <1/100);
rare (≥1/10,000 to <1/1,000);
very rare (<1/10,000).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Infections and infestations
Uncommon: Urinary tract infection including cystitis, upper respiratory tract infection including pharyngitis and sinusitis
Rare: Sepsis including fatal outcome[1]

Blood and the lymphatic system disorders
Uncommon: Anaemia
Rare: Eosinophilia, thrombocytopenia

Immune system disorders
Rare: Anaphylactic reaction, hypersensitivity

Metabolism and nutrition disorders
Uncommon: Hyperkalaemia
Rare: Hypoglycaemia (in diabetic patients)

Psychiatric disorders
Uncommon: Insomnia, depression
Rare: Anxiety

Nervous system disorders
Uncommon: Syncope
Rare: Somnolence

Eye disorders
Rare: Visual disturbance

Ear and labyrinth disorders
Uncommon: Vertigo

Cardiac disorders
Uncommon: Bradycardia
Rare: Tachycardia

Vascular disorders
Uncommon: Hypotension[2], orthostatic hypotension

Respiratory, thoracic and mediastinal disorders
Uncommon: Dyspnoea, cough
Very rare: Interstitial lung disease[4]

Gastrointestinal disorders
Uncommon: Abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting
Rare: Dry mouth, stomach discomfort, dysgeusia

Hepato-biliary disorders
Rare: Hepatic function abnormal/liver disorder[3]

Skin and subcutaneous tissue disorders
Uncommon: Pruritus, hyperhidrosis, rash

Rare:	Angioedema (also with fatal outcome), eczema, erythema, urticaria, drug eruption, toxic skin eruption
Muscoloskeletal and connective tissue disorders	
Uncommon:	Back pain (e.g. sciatica), muscle spasms, myalgia
Rare:	Arthralgia, pain in extremity, tendon pain (tendinitis like symptoms)
Renal and urinary disorders	
Uncommon:	Renal impairment including acute renal failure
General disorders and administration site conditions	
Uncommon:	Chest pain, asthenia (weakness)
Rare:	Influenza-like illness
Investigations	
Uncommon:	Blood creatinine increased
Rare:	Haemoglobin decreased, blood uric acid increased, hepatic enzyme increased, blood creatine phosphokinase increased

Description of selected adverse reactions

Sepsis

In the profess trial, an increased incidence of sepsis was observed with telmisartan compared with placebo. The event may be a chance finding or related to a mechanism currently not known.

Hypotension

This adverse reaction was reported as common in patients with controlled blood pressure who were treated with telmisartan for the reduction of cardiovascular morbidity on top of standard care.

Hepatic function abnormal / liver disorder

Most cases of hepatic function abnormal / liver disorder from post-marketing experience occurred in Japanese patients. Japanese patients are more likely to experience these adverse reactions.

Interstitial lung disease

Cases of interstitial lung disease have been reported from post-marketing experience in temporal association with the intake of telmisartan. However, a causal relationship has not been established.

4.9 Overdose

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

Symptoms: The most prominent manifestations of telmisartan overdose were hypotension and tachycardia; bradycardia, dizziness, increases in serum creatinine, and acute renal failure has also been reported.

Treatment: Telmisartan is not removed by haemodialysis. The patient should be closely monitored, and the treatment should be symptomatic and supportive. Management depends on the time since ingestion and the severity of the symptoms. Suggested measures include induction of emesis and / or gastric lavage. Activated charcoal may be useful in the treatment of

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.

5. Pharmacological Properties

5.1 Pharmacodynamic properties

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

Mechanism of action

Telmisartan is an orally active and specific angiotensin II receptor (type AT_1) antagonist. Telmisartan displaces angiotensin II with very high affinity from its binding site at the AT_1 receptor subtype, which is responsible for the known 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 is long-lasting. Telmisartan does not show affinity for other receptors, including AT_2 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 human, an 80 mg dose of telmisartan almost completely inhibits the angiotensin II evoked blood pressure increase. The inhibitory effect is maintained over 24 hours and still measurable up to 48 hours.

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 ($AUC_{0-\infty}$) of telmisartan varies from approximately 6 % (40 mg dose) to approximately 19 % (160 mg dose). By 3 hours after administration, plasma concentrations are similar whether telmisartan is taken fasting or with food.

Linearity/non-linearity

The small reduction in AUC is not expected to cause a reduction in the therapeutic efficacy. There is no linear relationship between doses and plasma levels. C_{max} 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 (V_{dss}) is approximately 500.

5.3 Preclinical safety data

In preclinical safety studies, doses producing exposure comparable to that in the clinical therapeutic range caused reduced red cell parameters (erythrocytes, haemoglobin, haematocrit),

changes in renal haemodynamics (increased blood urea nitrogen and creatinine), as well as increased serum potassium in normotensive animals. In dogs, renal tubular dilation and atrophy were observed. Gastric mucosal injury (erosion, ulcers or inflammation) also was noted in rats and dogs. These pharmacologically-mediated undesirable effects, known from preclinical studies with both angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists, were prevented by oral saline supplementation.

In species, increased plasma renin activity and hypertrophy/hyperplasia of the renal juxtaglomerular cells were observed. These changes, also a class effect of angiotensin converting enzyme inhibitors and other angiotensin II receptor antagonists, do not appear to have clinical significance.

No clear evidence of a teratogenic effect was observed, however at toxic dose levels of telmisartan an effect on the postnatal development of the offsprings such as lower body weight and delayed eye opening was observed.

There was no evidence of mutagenicity and relevant clastogenic activity in in vitro studies and no evidence of carcinogenicity in rats and mice.

6. Pharmaceutical Particulars

6.1 List of excipients

Mannitol
Meglumine
Potassium Hydroxide
Colloidal anhydrous silica
Sodium Starch Glycolate (Type-A) 1
Kyron-T 314
Dichloromethane
Purified Talc
Magnesium Stearate
Purified Water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C.Protect from light & moisture.

6.5 Nature and contents of container

3 x10 Tablets Packed in printed aluminum foils and base foils.

6.6 Special precautions for disposal

No special requirements.

7. Marketing Authorisation Holder

Marketed by:
Biogenerics Nigeria Limited
13 Hughes Avenue,Alagomeji
Yaba lagos,Lagos Nigeria
www.biogenericsltd.com

Manufactured by:
PSYCHOTROPICS INDIA LIMITED
Plot No. 46 & 49, Sector- 6A,
IIE, SIIDCUL, Haridwar–249403,
(Uttarakhand) INDIA
www.psychoindia.com

8. Marketing Authorisation Numbers

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9. Date Of First Authorisation/Renewal Of The Authorisation

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10. Date Of Revision Of The Text
