# Summary of Product Characteristics (SmPC)

1. **Name of the Finished Pharmaceutical Product: TELDURET 40/12.5mg**
   **Generic Name:** Telmisartan & Hydrochlorothiazide Tablets USP

2. **Quality and Quantitative Composition**

**2.1 Qualitative Composition**

**Composition:**

Each uncoated bilayered tablet contains:
Telmisartan USP 40mg
Hydrochlorothiazide USP 12.5mg
Colour: Sunset Yellow Lake
(In Hydrochlorothiazide Layer)

**2.2 Quantitative Composition**

| S.No. | Ingredients | Claim | Specification | Quantity Per tablet (mg or ml) | Quantity Per Tablet (in %) | Function |
|---|---|---|---|---|---|---|
| **LAYER-1 (WHITE PART)** | | | | | | |
| **Active:** | | | | | | |
| 1 | Telmisartan* | 40mg | USP | 040.00mg | 017.780 | API |
| **Tablet Core:** | | | | | | |
| 2 | Mannitol | ------- | BP | 124.500mg | 055.333 | Diluent |
| 3 | Meglumine | ------- | BP | 027.000mg | 012.000 | Diluent |
| 4 | Potassium Hydroxide | ------- | BP | 010.000mg | 004.444 | Buffering agennt |
| 5 | Dichloromethane** | ------- | BP | 000.030ml | ------ | Solvent |
| 6 | Purified Water** | ------- | BP | 000.020ml | ------ | Solvent |
| 7 | Purified Talc | ------- | BP | 003.000mg | 001.333 | Glidant |
| 8 | Magnesium Stearate | ------- | BP | 004.000mg | 001.780 | Lubricant |
| 9 | Sodium Starch Glycolate (Type-A) 1 | ------- | BP | 005.000mg | 002.222 | Disintegrant |
| 10 | Colloidal anhydrous silica | ------- | BP | 004.000mg | 001.780 | Anti-adherent |
| 11 | Kyron-T 314 | ------- | IH | 007.500mg | 003.333 | Disintegrant |
| | | | **Total** | **225.00mg** | **100.00** | ------- |
| **LAYER-2 (COLOUR PART)** | | | | | | |
| **Active:** | | | | | | |
| 1. | Hydrochlorothiazide* | 12.5mg | USP | 012.500mg | 009.620 | API |
| **Tablet Core:** | | | | | | |
| 2. | Lactose monohydrate | -------- | BP | 046.000mg | 035.384 | Diluent |
| 3. | Maize Starch | -------- | BP | 033.000mg | 025.384 | Diluent |
| 4. | Microcrystalline Cellulose | -------- | BP | 021.400mg | 016.461 | Diluent |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5. | Col. Sunset Yellow Lake | -------- | IH | 000.300mg | 000.230 | Colourant |
| 6. | Povidone (K-30) | -------- | BP | 002.500mg | 001.923 | Binder |
| 7. | Isopropyl Alcohol** | -------- | BP | 000.060ml | ------- | Solvent |
| 8. | Purified Talc | -------- | BP | 002.500mg | 001.923 | Glidant |
| 9. | Magnesium Stearate | -------- | BP | 002.000mg | 001.538 | Lubricant |
| 10. | Croscarmellose Sodium | -------- | BP | 004.000mg | 003.076 | Disintegrant |
| 11. | Colloidal anhydrous silica | -------- | BP | 000.600mg | 000.461 | Anti-adherent |
| 12. | Microcrystalline Cellulose-102 | -------- | BP | 005.200mg | 004.000 | Diluent |
| | | | **Total** | **130.00mg** | **100.00** | ------- |

**Average Weight of Tablet: 355.00mg±3.00%/Tablet(White 225.00mg + Colour 130.00mg)**
* 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**, Qty.:**Quantity, **Tab.:** Tablet, **Spec.:** Specification, **API:** Active Pharmaceutical Ingredient.

## 3. Pharmaceutical Form

Oral Solid Dosage Form (Uncoated Tablet)

## 4. Clinical Particulars

### 4.1 Therapeutic indications

**Hypertension**

Telmisartan/hydrochlorothiazide is indicated for the treatment of hypertension.

### 4.2 Posology and method of administration

Telmisartan and Hydrochlorothiazide 40 mg/12.5 mg may be administered once daily in patients whose blood pressure is not adequately controlled by Telmisartan 40mg.

**Patients with renal impairment:** Periodic monitoring of renal function is advised

**Patients with hepatic impairment:** In patients with mild to moderate hepatic impairment the posology should not exceed Telmisartan and hydrochlorothiazide 40 mg/12.5 mg once daily. Tablet is not indicated in patients with severe hepatic impairment. Hydrochlorothiazide should be used with caution.

**Elderly patients**

No dose adjustment is necessary.

**Paediatric population**

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

**Method of administration**

Oral use.

Telmisartan & Hydrochlorothiazide Tablets can be taken with or without food.

## 4.3 Contraindications

-Hypersensitivity to the active substances or to any of the excipients.
-Hypersensitivity to other sulphonamide-derived substances (since hydrochlorothiazide is a sulphonamidederived
medicinal product)
-Second and third trimesters of pregnancy
-Cholestasis and biliary obstructive disorders
-Severe hepatic impairment
-Severe renal impairment (creatinine clearance <30 ml/min)
-Refractory hypokalaemia, hypercalcaemia
The concomitant use of telmisartan & hydrochlorothiazide with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (GFR <
60 ml/min/1.73 m).

## 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/Hydrochlorothiazide should not be given to patients with cholestasis, biliary obstructive disorders or severe hepatic insufficiency since telmisartan is mostly eliminated with the bile. These patients can be expected to have reduced hepatic clearance for telmisartan. In addition, Telmisartan/Hydrochlorothiazide should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma. There is no clinical experience with Telmisartan/Hydrochlorothiazide in patients with 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 (RAAS).

Renal impairment and kidney transplantation

Telmisartan/Hydrochlorothiazide should not be used in patients with severe renal impairment (creatinine clearance <30 ml/min) (see section 4.3). There is no experience regarding the administration of Telmisartan/Hydrochlorothiazide in patients with recent kidney transplantation. Experience with Telmisartan/Hydrochlorothiazide is modest in the patients with mild to moderate renal impairment, therefore periodic monitoring of potassium, creatinine and uric acid serum levels is recommended. Thiazide diuretic associated azotaemia may occur in patients with impaired renal function.

Intravascular hypovolaemia

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 should be corrected before the administration of Telmisartan/Hydrochlorothiazide.

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 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/Hydrochlorothiazide 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.

Metabolic and endocrine effects

Thiazide therapy may impair glucose tolerance, whereas hypoglycaemia may occur in diabetic patients under insulin or antidiabetic therapy and telmisartan treatment. Therefore, in these patients blood glucose monitoring should be considered; a dose adjustment of insulin or antidiabetics may be required, when indicated. Latent diabetes mellitus may become manifest during thiazide therapy.

An increase in cholesterol and triglyceride levels has been associated with thiazide diuretic therapy; however, at the 12.5 mg dose contained in Telmisartan/Hydrochlorothiazide, minimal or no effects were reported. Hyperuricaemia may occur or frank gout may be precipitated in some patients receiving thiazide therapy.

Electrolyte imbalance

As for any patient receiving diuretic therapy, periodic determination of serum electrolytes should be performed at appropriate intervals. Thiazides, including hydrochlorothiazide, can cause fluid or electrolyte imbalance (including hypokalaemia, hyponatraemia and hypochloraemic alkalosis). Warning signs of fluid or electrolyte imbalance are dryness of

mouth, thirst, asthenia, lethargy, drowsiness, restlessness, muscle pain or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea or vomiting.

Hypokalaemia

Although hypokalaemia may develop with the use of thiazide diuretics, concurrent therapy with telmisartan may reduce diuretic-induced hypokalaemia. The risk of hypokalaemia is greater in patients with cirrhosis of liver, in patients experiencing brisk diuresis, in patients who are receiving inadequate oral intake of electrolytes and in patients receiving concomitant therapy with corticosteroids or Adrenocorticotropic hormone (ACTH).

- Hyperkalaemia

Conversely, due to the antagonism of the angiotensin II ($AT_1$) receptors by the telmisartan component of Telmisartan/Hydrochlorothiazide, hyperkalaemia might occur. Although clinically significant hyperkalaemia has not been documented with Telmisartan/Hydrochlorothiazide, risk factors for the development of hyperkalaemia include renal insufficiency and/or heart failure, and diabetes mellitus. Potassium-sparing diuretics, potassium supplements or potassium-containing salt substitutes should be co-administered cautiously with Telmisartan/Hydrochlorothiazide.

- Hyponatraemia and hypochloraemic alkalosis

There is no evidence that Telmisartan/Hydrochlorothiazide would reduce or prevent diuretic-induced hyponatraemia. Chloride deficit is generally mild and usually does not require treatment.

- Hypercalcaemia

Thiazides may decrease urinary calcium excretion and cause an intermittent and slight elevation of serum calcium in the absence of known disorders of calcium metabolism. Marked hypercalcaemia may be evidence of hidden hyperparathyroidism. Thiazides should be discontinued before carrying out tests for parathyroid function.

- Hypomagnesaemia

Thiazides have been shown to increase the urinary excretion of magnesium, which may result in hypomagnesaemia.

Lactose Monohydrate

This medicinal product contains lactose monohydrate. Patients with rare hereditary problems of fructose intolerance and/or with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Ethnic differences

As with all other angiotensin II receptor antagonists, telmisartan is apparently less effective in lowering blood pressure in black patients than in non blacks, possibly because of higher prevalence of low renin states in the black hypertensive population.

## 4.5 Interaction with other medicinal products and other forms of interaction

**Telmisartan**

**Digoxin:** When telmisartan was coadministered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) were observed. It is, therefore, recommended that digoxin levels be monitored when initiating, adjusting, and

discontinuing telmisartan to avoid possible over- or under-digitalization.

**Warfarin:** Telmisartan administered for 10 days slightly decreased the mean warfarin trough plasma

Concentration; this decrease did not result in a change in International Normalized Ratio (INR).

**Other Drugs:** Coadministration of telmisartan did not result in a clinically significant interaction with acetaminophen, amlodipine, glibenclamide, simvastatin, hydrochlorothiazide or ibuprofen. Telmisartan is not metabolized by the cytochrome P450 system and had no effects in vitro on cytochrome P450 enzymes, except for some inhibition of CYP2C19. Telmisartan is not expected to interact with drugs that inhibit cytochrome P450 enzymes; it is also not expected to interact with drugs metabolized by cytochrome P450 enzymes, except for possible inhibition of the metabolism of drugs metabolized by CYP2C19.

**Hydrochlorothiazide**

When administered concurrently, the following drugs may interact with thiazide diuretics:

**Alcohol, barbiturates, or narcotics:** Potentiation of orthostatic hypotension may occur.

**Antidiabetic drugs (oral agents and insulin):** Dosage adjustment of the antidiabetic drug may be required.

**Other antihypertensive drugs:** Additive effect or potentiation.

**Cholestyramine and colestipol resins:** Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins. Single doses of either cholestyramine or colestipol resins bind the hydrochlorothiazide and reduce its absorption from the gastrointestinal tract by up to 85% and 43%, respectively.

**Corticosteroids, ACTH:** Intensified electrolyte depletion, particularly hypokalemia.

**Pressor amines (e.g., norepinephrine):** Possible decreased response to pressor amines but not sufficient to preclude their use.

**Skeletal muscle relaxants, nondepolarizing (e.g., tubocurarine):** Possible increased responsiveness to the muscle relaxant.

**Lithium:** Should not generally be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Refer to the package insert for lithium preparations before use of such preparations with telmisartan/hydrochlorothiazide.

**Non-steroidal anti-inflammatory drugs:** In some patients, the administration of a non-steroidal antiinflammatory agent can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassiumsparing and thiazide diuretics. Therefore, when telmisartan/hydrochlorothiazide and non-steroidal anti-inflammatory agents are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

## 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/Hydrochlorothiazide in pregnant

women. Studies in animals have shown reproductive toxicity

Breast-feeding

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

Hydrochlorothiazide is excreted in human milk in small amounts. Thiazides in high doses causing intense diuresis can inhibit the milk production. The use of Telmisartan/Hydrochlorothiazide during breast feeding is not recommended. If Telmisartan/Hydrochlorothiazide is used during breast feeding, doses should be kept as low as possible.

Fertility

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

## 4.7 Effects on ability to drive and use machines

Telmisartan/Hydrochlorothiazide can have influence on the ability to drive and use machines. Dizziness or drowsiness may occasionally occur when taking Telmisartan/Hydrochlorothiazide.

## 4.8 Undesirable effects

### 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.

### 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 |

## 4.9 Overdose

**Telmisartan**

Limited data are available with regard to overdosage in humans. The most likely manifestation of overdosage with telmisartan would be hypotension, dizziness and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted. Telmisartan is not removed by hemodialysis.

**Hydrochlorothiazide**

The most common signs and symptoms observed in patients are those caused by electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration resulting from excessive diuresis. If digitalis has also been administered, hypokalemia may accentuate cardiac arrhythmias. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established.

# 5. Pharmacological Properties

## 5.1 Pharmacodynamic properties

**Pharmacotherapeutic group:** Telmisartan/hydrochlorothiazide is a combination of telmisartan, an orally active angiotensin II antagonist acting on the $AT_1$ receptor subtype, and hydrochlorothiazide, a diuretic.

**Mechanism of action**

Angiotensin II is formed from angiotensin I in a reaction catalyzed by angiotensin-converting enzyme (ACE, kininase II). Angiotensin II is the principal pressor agent of the renin-angiotensin system, with effects that include vasoconstriction, stimulation of synthesis and release of aldosterone, cardiac stimulation, and renal reabsorption of sodium.

Telmisartan blocks the vasoconstrictor and aldosterone secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the $AT_1$ receptor in many tissues, such as vascular smooth muscle and the adrenal gland. Its action is therefore independent of the pathways for angiotensin II synthesis.

Blockade of the angiotensin II receptor inhibits the negative regulatory feedback of angiotensin II on rennin secretion, but the resulting increased plasma renin activity and angiotensin II circulating levels do not overcome the effect of telmisartan on blood pressure.

Hydrochlorothiazide is a thiazide diuretic. Thiazides affect the renal tubular mechanisms of electrolyte reabsorption, directly increasing excretion of sodium salt and chloride in approximately equivalent amounts. Indirectly, the diuretic action of hydrochlorothiazide reduces plasma volume, with consequent increases in plasma renin activity, increases in aldosterone secretion, increases in urinary potassium loss, and decreases in serum potassium.

The mechanism of the antihypertensive effect of thiazides is not fully understood.

## 5.2 Pharmacokinetic properties

### Absorption

**Telmisartan:** Following oral administration peak concentrations of telmisartan are reached in 0.5 – 1.5 h after dosing. The absolute bioavailability of telmisartan at 40 mg and 160 mg was 42 % and 58 %, respectively. Food slightly reduces the bioavailability of telmisartan with a reduction in the area under the plasma concentration time curve (AUC) of about 6 % with the 40 mg tablet and about 19 % after a 160 mg dose. By 3 hours after administration plasma concentrations are similar whether telmisartan is taken fasting or with food. The small reduction in AUC is not expected to cause a reduction in the therapeutic efficacy. The pharmacokinetics of orally administered telmisartan are non-linear over doses from 20 – 160 mg with greater than proportional increases of plasma concentrations ($C_{max}$ and AUC) with increasing doses. Telmisartan does not accumulate significantly in plasma on repeated administration.

**Hydrochlorothiazide:** Following oral administration of Telmisartan peak concentrations of hydrochlorothiazide are reached in approximately 1.0 – 3.0 hours after dosing. Based on cumulative renal excretion of hydrochlorothiazide the absolute bioavailability was about 60 %.

### Distribution

Telmisartan is highly bound to plasma proteins (>99.5 %) mainly albumin and alpha l- acid glycoprotein. The apparent volume of distribution for telmisartan is approximately 500 litres indicating additional tissue binding.

Hydrochlorothiazide is 68 % protein bound in the plasma and its apparent volume of distribution is 0.83 – 1.14 l/kg.

## 5.3 Preclinical safety data

In preclinical safety studies performed with co-administration of telmisartan and hydrochlorothiazide in normotensive rats and dogs, doses producing exposure comparable to that in the clinical therapeutic range caused no additional findings not already observed with administration of either substance alone. The toxicological findings observed appear to have no relevance to human therapeutic use.

Toxicological findings also well known from preclinical studies with angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists were: a reduction of red cell parameters (erythrocytes, haemoglobin, haematocrit), changes of renal haemodynamics (increased blood urea nitrogen and creatinine), increased plasma renin activity, hypertrophy/hyperplasia of the juxtaglomerular cells and gastric mucosal injury. Gastric lesions could be prevented/ameliorated by oral saline supplementation and group housing of animals. In dogs renal tubular dilation and atrophy were observed. These findings are considered to be due to the pharmacological activity of telmisartan.

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.

Telmisartan showed no evidence of mutagenicity and relevant clastogenic activity in *in vitro* studies and no evidence of carcinogenicity in rats and mice. Studies with hydrochlorothiazide

have shown equivocal evidence for a genotoxic or carcinogenic effect in some experimental models. However, the extensive human experience with hydrochlorothiazide has failed to show an association between its use and an increase in neoplasms.

## 6. Pharmaceutical Particulars

### 6.1 List of excipients

Mannitol
Meglumine
Potassium Hydroxide
Dichloromethane
Purified Water
Purified Talc
Magnesium Stearate
Sodium Starch Glycolate
(Type-A) 1
Colloidal anhydrous silica
Kyron-T 314
Lactose monohydrate
Maize Starch
Microcrystalline Cellulose
Col. Sunset Yellow Lake
Povidone (K-30)
Isopropyl Alcohol
Croscarmellose Sodium
Microcrystalline Cellulose-102

### 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**

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