

Summary Product Characteristics (SPC)

1. Name of the medicinal product

TELGOOD 80 CT 12.5

2. Qualitative and quantitative composition

Each uncoated tablet contains:

Telmisartan USP 80mg

Chlorthalidone USP 12.5mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

White, round, biconvex, shaped uncoated tablets plain on both sides

4. Clinical particulars

4.1 Therapeutic indications

Treatment of essential hypertension. Telmisartan/Hydrochlorothiazide fixed dose combination (80 mg telmisartan/ 12.5 mg hydrochlorothiazide) is indicated in patients whose blood pressure is not adequately controlled on telmisartan alone.

4.2 Posology and Method of Administration

Posology

Telmisartan/Hydrochlorothiazide should be taken in patients whose blood pressure is not adequately controlled by telmisartan alone. Individual dose titration with each of the two components is recommended before changing to the fixed dose combination. When clinically appropriate, direct change from monotherapy to the fixed combination may be considered.

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

- Telmisartan/Hydrochlorothiazide 80 mg/ 12.5 mg may be administered once daily in patients whose blood pressure is not adequately controlled by Micardis 80 mg

Special populations:

Renal impairment

Periodic monitoring of renal function is advised (see section 4.4).

Hepatic impairment

In patients with mild to moderate hepatic impairment the posology should not exceed Telmisartan/Hydrochlorothiazide 40 mg/ 12.5 mg once daily.

Telmisartan/Hydrochlorothiazide is not indicated in patients with severe hepatic impairment. Thiazides should be used with caution in patients with impaired hepatic function (see section 4.4).

Elderly

No dosage adjustment is necessary.

Paediatric population

The safety and efficacy of Telmisartan/Hydrochlorothiazide in children and adolescents aged below 18 have not been established. No data are available.

Method of administration

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

Precautions to be taken before handling or administering the medicinal product

Telmisartan/Hydrochlorothiazide should be kept in the sealed blister due to the hygroscopic property of the tablets. Tablets should be taken out of the blister shortly before administration (see section 6.6).

4.3 Contraindications

Hypersensitivity to any of the active substances or to any of the excipients listed in section 6.1.

- Hypersensitivity to other sulphonamide-derived substances (since hydrochlorothiazide is a sulphonamide-derived medicinal product).
- Second and third trimesters of pregnancy (see sections 4.4 and 4.6).
- Cholestasis and biliary obstructive disorders.
- Severe hepatic impairment.
- Severe renal impairment (creatinine clearance < 30 ml/min), anuria.
- Refractory hypokalaemia, hypercalcaemia.
- The concomitant use of telmisartan with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m²) (see sections 4.5 and 5.1).

4.4 Special warnings and precautions for use

Pregnancy

Angiotensin II receptor blockers should not be initiated during pregnancy. Unless continued angiotensin II receptor blocker 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 blockers should be stopped immediately, and, if appropriate, alternative therapy should be started (see sections 4.3 and 4.6).

Hepatic impairment

Telmisartan/Hydrochlorothiazide should not be given to patients with cholestasis, biliary obstructive disorders or severe hepatic insufficiency (see section 4.3) 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.

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.

Volume and/or sodium depleted patients

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/Hydrochlorothiazide.

Isolated cases of hyponatraemia accompanied by neurological symptoms (nausea, progressive disorientation, apathy) have been observed with the use of 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 (see sections 4.5 and 5.1).

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 (see section 4.8).

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 (see section 4.8).

- 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 Adrenocorticotrophic hormone (ACTH) (see section 4.5).

- Hyperkalaemia

Conversely, due to the antagonism of the angiotensin II (AT₁) 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 (see section

4.5).

- 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 (see section 4.5).

Ethnic differences

As with all other angiotensin II receptor blockers 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.

Ischaemic heart disease

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.

General

Hypersensitivity reactions to hydrochlorothiazide may occur in patients with or without a history of allergy or bronchial asthma, but are more likely in patients with such a history. Exacerbation or activation of systemic lupus erythematosus has been reported with the use of thiazide diuretics, including hydrochlorothiazide.

Cases of photosensitivity reactions have been reported with thiazide diuretics (see section 4.8). If a photosensitivity reaction occurs during treatment, it is recommended to stop the treatment. If a readministration of the diuretic is deemed necessary, it is recommended to protect exposed areas to the sun or to artificial UVA.

Choroidal effusion, Acute Myopia and Angle-Closure Glaucoma

Hydrochlorothiazide, a sulfonamide, can cause an idiosyncratic reaction, resulting in choroidal effusion with visual field defect, acute transient myopia and acute angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to weeks of drug initiation. Untreated acute angle-closure glaucoma can lead to permanent vision loss. The primary treatment is to discontinue hydrochlorothiazide as rapidly as possible. Prompt medical or surgical treatments may need to be considered if the intraocular pressure remains uncontrolled. Risk factors for developing acute angle- closure glaucoma may

include a history of sulfonamide or penicillin allergy.

Non-melanoma skin cancer

An increased risk of non-melanoma skin cancer (NMSC) [basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)] with increasing cumulative dose of hydrochlorothiazide (HCTZ) exposure has been observed in two epidemiological studies based on the Danish National Cancer Registry. Photosensitizing actions of HCTZ could act as a possible mechanism for NMSC.

Patients taking HCTZ should be informed of the risk of NMSC and advised to regularly check their skin for any new lesions and promptly report any suspicious skin lesions. Possible preventive measures such as limited exposure to sunlight and UV rays and, in case of exposure, adequate protection should be advised to the patients in order to minimize the risk of skin cancer. Suspicious skin lesions should be promptly examined potentially including histological examinations of biopsies. The use of HCTZ may also need to be reconsidered in patients who have experienced previous NMSC (see also section 4.8).

Acute Respiratory Toxicity

Very rare severe cases of acute respiratory toxicity, including acute respiratory distress syndrome (ARDS) have been reported after taking hydrochlorothiazide. Pulmonary oedema typically develops within minutes to hours after hydrochlorothiazide intake. At the onset, symptoms include dyspnoea, fever, pulmonary deterioration and hypotension. If diagnosis of ARDS is suspected, Telmisartan/Hydrochlorothiazide should be withdrawn and appropriate treatment given. Hydrochlorothiazide should not be administered to patients who previously experienced ARDS following hydrochlorothiazide intake.

Intestinal angioedema

Intestinal angioedema has been reported in patients treated with angiotensin II receptor blockers (see section 4.8). These patients presented with abdominal pain, nausea, vomiting and diarrhoea. Symptoms resolved after discontinuation of angiotensin II receptor blockers. If intestinal angioedema is diagnosed, Telmisartan should be discontinued and appropriate monitoring should be initiated until complete resolution of symptoms has occurred.

4.5 Interaction with other medicinal products and other forms of interaction

Lithium

Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors. Rare cases have also been reported with angiotensin II receptor blockers (including Telmisartan/Hydrochlorothiazide). Co-administration of lithium and Telmisartan/Hydrochlorothiazide is not recommended (see section 4.4). If this combination proves essential, careful monitoring of serum lithium level is recommended during concomitant use.

Medicinal products associated with potassium loss and hypokalaemia (e.g. other kaliuretic diuretics, laxatives, corticosteroids, ACTH, amphotericin, carbenoxolone, penicillin G sodium, salicylic acid and derivatives)

If these substances are to be prescribed with the hydrochlorothiazide-telmisartan combination, monitoring of potassium plasma levels is advised. These medicinal products may potentiate the effect of hydrochlorothiazide on serum potassium (see section 4.4).

Iodinated contrast products

In the event of dehydration caused by diuretics, there is an increased risk of acute functional renal failure, particularly during use of high doses of iodinated contrast products. Rehydration before administration of the iodinated product is required.

Medicinal products that may increase potassium levels or induce hyperkalaemia (e.g. ACE inhibitors, potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, cyclosporine or other medicinal products such as heparin sodium)

If these medicinal products are to be prescribed with the hydrochlorothiazide-telmisartan combination, monitoring of potassium plasma levels is advised. Based on the experience with the use of other medicinal products that blunt the reninangiotensin system, concomitant use of the above medicinal products may lead to increases in serum potassium and is, therefore, not recommended (see section 4.4).

Medicinal products affected by serum potassium disturbances

Periodic monitoring of serum potassium and ECG is recommended when Telmisartan/Hydrochlorothiazide is administered with medicinal products affected by serum potassium disturbances (e.g. digitalis glycosides, antiarrhythmics) and the following torsades de pointes inducing medicinal products (which include some antiarrhythmics), hypokalaemia being a predisposing factor to torsades de pointes.

- class Ia antiarrhythmics (e.g. quinidine, hydroquinidine, disopyramide)
- class III antiarrhythmics (e.g. amiodarone, sotalol, dofetilide, ibutilide)
- some antipsychotics (e.g. thioridazine, chlorpromazine, levomepromazine, trifluoperazine, cyamemazine, sulpiride, sultopride, amisulpride, tiapride, pimozide, haloperidol, droperidol)
- others (e.g. bepridil, cisapride, diphemanil, erythromycin IV, halofantrin, mizolastin, pentamidine, sparfloxacin, terfenadine, vincamine IV.)

Digitalis glycosides

Thiazide-induced hypokalaemia or hypomagnesaemia favours the onset of digitalis-induced arrhythmia (see section 4.4).

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.

Other antihypertensive agents

Telmisartan may increase the hypotensive effect of other antihypertensive agents.

Clinical trial data has shown that dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (including acute renal failure) compared to the use of a single RAAS-acting agent (see sections 4.3, 4.4 and 5.1).

Antidiabetic medicinal products (oral agents and insulin)

Dosage adjustment of the antidiabetic medicinal products may be required (see section 4.4).

Metformin

Metformin should be used with precaution: risk of lactic acidosis induced by a possible functional renal failure linked to hydrochlorothiazide.

Cholestyramine and colestipol resins

Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins.

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 diuretic, natriuretic and antihypertensive effects of thiazide diuretics and the antihypertensive effects of angiotensin II receptor blockers.

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 blockers 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 AUC₀₋₂₄ and C_{max} of ramipril and ramiprilat. The clinical relevance of this observation is not known.

Pressor amines (e.g. noradrenaline)

The effect of pressor amines may be decreased.

Nondepolarizing skeletal muscle relaxants (e.g. tubocurarine)

The effect of nondepolarizing skeletal muscle relaxants may be potentiated by hydrochlorothiazide.

Medicinal products used in the treatment for gout (e.g. probenecid, sulfinpyrazone and allopurinol)

Dosage adjustment of uricosuric medications may be necessary as hydrochlorothiazide may raise the level of serum uric acid. Increase in dosage of probenecid or sulfinpyrazone may be necessary. Co-administration of thiazide may increase the incidence of hypersensitivity reactions of allopurinol.

Calcium salts:

Thiazide diuretics may increase serum calcium levels due to the decreased excretion. If calcium supplements or calcium sparing medicinal products (e.g. vitamin D therapy) must be prescribed, serum calcium levels should be monitored and calcium dosage adjusted accordingly.

Beta-blockers and diazoxide

The hyperglycaemic effect of beta-blockers and diazoxide may be enhanced by thiazides.

Anticholinergic agents (e.g. atropine, biperiden) may increase the bioavailability of thiazide- type diuretics by decreasing gastrointestinal motility and stomach emptying rate.

Amantadine

Thiazides may increase the risk of adverse effects caused by amantadine.

Cytotoxic agents (e.g. cyclophosphamide, methotrexate)

Thiazides may reduce the renal excretion of cytotoxic medicinal products and potentiate their myelosuppressive effects.

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.

4.6 Fertility, pregnancy and lactation

Pregnancy

Pregnancy

The use of angiotensin II receptor blockers is not recommended during the first trimester of pregnancy (see section 4.4). The use of angiotensin II receptor blockers is contraindicated during the second and third trimesters of pregnancy (see sections 4.3 and 4.4).

There are no adequate data from the use of

Telmisartan/Hydrochlorothiazide in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3).

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 blockers, similar risks may exist for this class of drugs. Unless continued angiotensin II receptor blocker 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 blockers should be stopped immediately, and, if appropriate, alternative therapy should be started.

Exposure to angiotensin II receptor blocker 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, hyperkalaemia). (See section 5.3). 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 blockers should be closely observed for hypotension (see sections 4.3 and 4.4).

There is limited experience with hydrochlorothiazide during pregnancy, especially during the first trimester. Animal studies are insufficient. Hydrochlorothiazide crosses the placenta. Based on the pharmacological mechanism of action of hydrochlorothiazide its use during the second and third trimester may compromise foeto-placental perfusion and may cause foetal and neonatal effects like icterus, disturbance of electrolyte balance and thrombocytopenia. Hydrochlorothiazide should not be used for gestational oedema, gestational hypertension or preeclampsia due to the risk of decreased plasma volume and placental hypoperfusion, without a beneficial effect on the course of the disease.

Hydrochlorothiazide should not be used for essential hypertension in pregnant women except in rare situations where no other treatment could be used.

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

No studies on fertility in humans with the fixed dose combination or with the individual components have been performed.

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, syncope or vertigo may occasionally occur when taking antihypertensive therapy such as Telmisartan/Hydrochlorothiazide.

If patients experience these adverse events, they should avoid potentially hazardous tasks such as driving or operating machinery.

4.8 Undesirable effects

Summary of the safety profile

The most commonly reported adverse reaction is dizziness. Serious angioedema may occur rarely ($\geq 1/10,000$ to $< 1/1,000$).

The overall incidence of adverse reactions reported with Telmisartan/Hydrochlorothiazide was comparable to those reported with telmisartan alone in randomised controlled trials involving 1471 patients randomised to receive telmisartan plus hydrochlorothiazide (835) or telmisartan alone (636). Dose-relationship of adverse reactions was not established and they showed no correlation with gender, age or race of the patients.

Tabulated list of adverse reactions

Adverse reactions reported in all clinical trials and occurring more frequently ($p \leq 0.05$) with telmisartan plus hydrochlorothiazide than with placebo are shown below according to system organ class. Adverse reactions known to occur with each component given singly but which have not been seen in clinical trials may occur during treatment with Telmisartan/Hydrochlorothiazide.

Adverse reactions have been ranked under headings of frequency using the following convention: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$), not known (cannot be estimated from the available data).

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

Infections and infestations	
Rare:	Bronchitis, pharyngitis, sinusitis
Immune system disorders	
Rare:	Exacerbation or activation of systemic lupus erythematosus ¹
Metabolism and nutrition disorders	
Uncommon: Rare:	Hypokalaemia Hyperuricaemia, hyponatraemia
Psychiatric disorders	
Uncommon: Rare:	Anxiety Depression
Nervous system disorders	

Common:	Dizziness
Uncommon:	Syncope, paraesthesia
Rare:	Insomnia, sleep disorders
Eye disorders	
Rare:	Visual disturbance, vision blurred
Ear and labyrinth disorders	
Uncommon:	Vertigo
Cardiac disorders	
Uncommon:	Tachycardia, arrhythmias
Vascular disorders	
Uncommon:	Hypotension, orthostatic hypotension
Respiratory, thoracic and mediastinal disorders	
Uncommon:	Dyspnoea
Rare:	Respiratory distress (including pneumonitis and pulmonary oedema)
Gastrointestinal disorders	
Uncommon:	Diarrhoea, dry mouth, flatulence
Rare:	Abdominal pain, constipation, dyspepsia, vomiting, gastritis
Hepatobiliary disorders	
Rare:	Abnormal hepatic function/liver disorder ²
Skin and subcutaneous tissue disorders	
Rare:	Angioedema (also with fatal outcome), erythema, pruritus, rash, hyperhidrosis, urticaria
Musculoskeletal, connective tissue and bone disorders	
Uncommon:	Back pain, muscle spasms, myalgia
Rare:	Arthralgia, muscle cramps, pain in limb
Reproductive system and breast disorders	
Uncommon:	Erectile dysfunction
General disorders and administration site conditions	
Uncommon:	Chest pain
Rare:	Influenza-like illness, pain
Investigations	
Uncommon:	Blood uric acid increased
Rare:	Blood creatinine increased, blood creatine phosphokinase increased, hepatic enzyme increased

1: Based on post-marketing experience

2: For further description, please see sub-section “Description of selected adverse reactions”

Additional information on individual components

Adverse reactions previously reported with one of the individual components may be potential adverse reactions with Telmisartan/Hydrochlorothiazide, even if not observed in clinical trials with this product.

Telmisartan:

Adverse reactions occurred with similar frequency in placebo and telmisartan treated patients.

The overall incidence of adverse reactions reported with telmisartan (41.4 %) was usually comparable to placebo (43.9 %) in placebo controlled trials. The following adverse reactions listed below have been accumulated from all clinical trials in patients treated with telmisartan for hypertension or in patients 50 years or older at high risk of cardiovascular events.

Infections and infestations	
Uncommon:	Upper respiratory tract infection, urinary tract infection
Rare:	including cystitis Sepsis including fatal outcome ³
Blood and lymphatic system disorders	

Uncommon: Rare:	Anaemia Eosinophilia, thrombocytopenia
Immune system disorders	
Rare:	Hypersensitivity, anaphylactic reactions
Metabolism and nutrition disorders	
Uncommon: Rare:	Hyperkalaemia Hypoglycaemia (in diabetic patients)
Cardiac disorders	
Uncommon:	Bradycardia
Nervous system disorders	
Rare:	Somnolence
Respiratory, thoracic and mediastinal disorders	
Uncommon: Very rare:	Cough Interstitial lung disease ³
Gastrointestinal disorders	
Rare:	Stomach discomfort
Skin and subcutaneous tissue disorders	
Rare:	Eczema, drug eruption, toxic skin eruption
Musculoskeletal, connective tissue and bone disorders	
Rare:	Arthrosis, tendon pain
Renal and urinary disorders	
Uncommon:	Renal impairment (including acute renal failure)
General disorders and administration site conditions	
Uncommon:	Asthenia
Investigations	
Rare:	Haemoglobin decreased

3: For further description, please see sub-section “*Description of selected adverse reactions*”

Hydrochlorothiazide:

Hydrochlorothiazide may cause or exacerbate hypovolaemia which could lead to electrolyte imbalance (see section 4.4).

Adverse reactions reported with the use of hydrochlorothiazide alone include:

Infections and infestations	
Not known:	Sialadenitis
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Not known:	Non-melanoma skin cancer (Basal cell carcinoma and Squamous cell carcinoma)
Blood and lymphatic system disorders	
Rare: Not known:	Thrombocytopenia (sometimes with purpura) Aplastic anaemia, haemolytic anaemia, bone marrow failure, leukopenia, neutropenia, agranulocytosis,
Immune system disorders	
Not known:	Anaphylactic reactions, hypersensitivity
Endocrine disorders	
Not known:	Diabetes mellitus inadequate control
Metabolism and nutrition disorders	
Common: Rare: Very rare: Not known:	Hypomagnesaemia Hypercalcaemia Hypochloraemic alkalosis Anorexia, appetite decreased, electrolyte imbalance, hypercholesterolaemia, hyperglycaemia, hypovolaemia
Psychiatric disorders	
Not known:	Restlessness
Nervous system disorders	
Rare:	Headache

Not known:	Light-headedness
Eye disorders	
Not known	Xanthopsia, acute myopia, acute angle-closure glaucoma, choroidal effusion
Respiratory, thoracic and mediastinal disorders	
Very rare:	Acute respiratory distress syndrome (ARDS) (see section 4.4)
Vascular disorders	
Not known:	Vasculitis necrotizing
Gastrointestinal disorders	
Common: Not known:	Nausea Pancreatitis, stomach discomfort
Hepatobiliary disorders	
Not known:	Jaundice hepatocellular, jaundice cholestatic
Skin and subcutaneous tissue disorders	
Not known:	Lupus-like syndrome, photosensitivity reactions, skin vasculitis, toxic epidermal necrolysis, erythema multiforme
Musculoskeletal, connective tissue and bone disorders	
Not known:	Weakness
Renal and urinary disorders	
Not known:	Nephritis interstitial, renal dysfunction, glycosuria
General disorders and administration site conditions	
Not known:	Pyrexia
Investigations	
Not known:	Triglycerides increased

Description of selected adverse reactions

Hepatic function abnormal / liver disorder

Most cases of hepatic function abnormal / liver disorder from post-marketing experience with telmisartan occurred in Japanese patients. Japanese patients are more likely to experience these 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 (see section 5.1).

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.

Non-melanoma skin cancer

Based on available data from epidemiological studies, cumulative dose-dependent association between HCTZ and NMSC has been observed (see also sections 4.4 and 5.1).
Intestinal angioedema

Cases of intestinal angioedema have been reported after the use of angiotensin II receptor blockers (see section 4.4).

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicinal product is important as it allows continued monitoring of the benefit–risk balance of the medicinal product. Healthcare professionals are requested to report any suspected adverse reactions to the marketing authorisation holder or, where applicable, via the national reporting system

4.9 Overdose

There is limited information available for telmisartan with regard to overdose in humans. The degree to which hydrochlorothiazide is removed by haemodialysis

has not been established.

Symptoms

The most prominent manifestations of telmisartan overdose were hypotension and tachycardia; bradycardia, dizziness, vomiting, increase in serum creatinine, and acute renal failure have also been reported. Overdose with hydrochlorothiazide is associated with electrolyte depletion (hypokalaemia, hyponatraemia) and hypovolaemia resulting from excessive diuresis. The most common signs and symptoms of overdose are nausea and somnolence. Hypokalaemia may result in muscle spasms and/or accentuate arrhythmia associated with the concomitant use of digitalis glycosides or certain anti-arrhythmic medicinal products.

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 overdose. Serum electrolytes and creatinine should be monitored frequently. If hypotension occurs, the patient should be placed in a supine position, with salt and volume replacements given quickly.

5. Pharmacological properties

5.1 Pharmacodynamic properties

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

Mechanism of action

Telmisartan is an orally active and specific angiotensin II receptor (type AT₁) antagonist. Telmisartan displaces angiotensin II with very high affinity 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 the AT₁ receptor. The binding is long-lasting. Telmisartan does not show affinity for other receptors, including AT₂ 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 events.

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.

Clinical efficacy and safety

Treatment of essential hypertension

After the first dose of telmisartan, the antihypertensive activity gradually becomes evident within 3 hours. The maximum reduction in blood pressure is generally attained 4 to 8 weeks after the start of treatment and is sustained during long-term therapy.

The antihypertensive effect persists constantly over 24 hours after dosing and includes the last 4 hours before the next dose as shown by ambulatory blood pressure measurements. This is confirmed by trough to peak ratios consistently above 80 % seen after doses of 80 and 80 mg of telmisartan in placebo controlled clinical studies. There is an apparent trend to a dose relationship to a time to recovery of baseline systolic blood pressure (SBP). In this respect data concerning diastolic blood pressure (DBP) are inconsistent. In patients with hypertension telmisartan reduces both systolic and diastolic blood pressure without affecting pulse rate. The contribution of the medicinal product's diuretic and natriuretic effect to its hypotensive activity has still to be defined. The antihypertensive efficacy of telmisartan is comparable to that of agents representative of other classes of antihypertensive medicinal products (demonstrated in clinical trials comparing telmisartan to amlodipine, atenolol, enalapril, hydrochlorothiazide, and lisinopril). 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.

The incidence of dry cough was significantly lower in patients treated with telmisartan than in those given angiotensin converting enzyme inhibitors in clinical trials directly comparing the two antihypertensive treatments.

Cardiovascular prevention

ONTARGET (ONGOing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial) compared the effects of telmisartan, ramipril and the combination of telmisartan and ramipril on cardiovascular outcomes in 25620 patients aged 55 years or older with a history of coronary artery disease, stroke, TIA, peripheral arterial disease, or type 2 diabetes mellitus accompanied by evidence of end-organ damage (e.g. retinopathy, left ventricular hypertrophy, macro- or microalbuminuria), which is a population at risk for cardiovascular events.

Patients were randomized to one of the three following treatment groups: telmisartan 80 mg (n = 8542), ramipril 10 mg (n = 8576), or the combination of telmisartan 80 mg plus ramipril 10 mg (n = 8502), and followed for a mean observation time of 4.5 years.

Telmisartan showed a similar effect to ramipril in reducing the primary composite endpoint of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or hospitalization for congestive heart failure. The incidence of the primary endpoint was similar in the telmisartan (16.7 %) and ramipril (16.5 %) groups. The hazard ratio for telmisartan vs. ramipril was 1.01 (97.5 % CI 0.93 - 1.10, p (non-inferiority) = 0.0019 at a margin of 1.13). The all-cause mortality rate was 11.6 % and 11.8 % among telmisartan and ramipril treated patients, respectively.

Telmisartan was found to be similarly effective to ramipril in the pre-specified secondary endpoint of cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke [0.99 (97.5 % CI 0.90 - 1.08), p (non-inferiority) = 0.0004], the primary endpoint in the reference study HOPE (The Heart Outcomes Prevention Evaluation Study), which had investigated the effect of ramipril vs. placebo.

TRANSCEND randomized ACE-I intolerant patients with otherwise similar inclusion criteria as ONTARGET to telmisartan 80 mg (n=2954) or placebo (n=2972), both given on top of standard care.

The mean duration of follow up was 4 years and 8 months. No statistically significant difference in the incidence of the primary composite endpoint (cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or hospitalization for congestive heart failure) was found [15.7 % in the telmisartan and 17.0 % in the placebo groups with a hazard ratio of 0.92 (95 % CI 0.81 - 1.05, p = 0.22)]. There was evidence for a benefit of

telmisartan

compared to placebo in the pre-specified secondary composite endpoint of cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke [0.87 (95 % CI 0.76 - 1.00, $p = 0.048$)]. There was no evidence for benefit on cardiovascular mortality (hazard ratio 1.03, 95 % CI 0.85 - 1.24).

Cough and angioedema were less frequently reported in patients treated with telmisartan than in patients treated with ramipril, whereas hypotension was more frequently reported with telmisartan.

Combining telmisartan with ramipril did not add further benefit over ramipril or telmisartan alone. CV mortality and all cause mortality were numerically higher with the combination. In addition, there was a significantly higher incidence of hyperkalaemia, renal failure, hypotension and syncope in the combination arm. Therefore the use of a combination of telmisartan and ramipril is not recommended in this population.

In the "Prevention Regimen For Effectively avoiding Second Strokes" (PROFESS) trial in patients 50 years and older, who recently experienced stroke, an increased incidence of sepsis was noted for telmisartan compared with placebo, 0.70 % vs. 0.49 % [RR 1.43 (95 % confidence interval 1.00 - 2.06)]; the incidence of fatal sepsis cases was increased for patients taking telmisartan (0.33 %) vs. patients taking placebo (0.16 %) [RR 2.07 (95 % confidence interval 1.14 - 3.76)]. The observed increased occurrence rate of sepsis associated with the use of telmisartan may be either a chance finding or related to a mechanism not currently known.

Two large randomised, controlled trials (ONTARGET (ONgoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial) and VA NEPHRON-D (The Veterans Affairs Nephropathy in Diabetes)) have examined the use of the combination of an ACE-inhibitor with an angiotensin II receptor blocker.

ONTARGET was a study conducted in patients with a history of cardiovascular or cerebrovascular disease, or type 2 diabetes mellitus accompanied by evidence of end-organ damage. For more detailed information see above under the heading "Cardiovascular prevention". VA NEPHRON-D was a study in patients with type 2 diabetes mellitus and diabetic nephropathy.

These studies have shown no significant beneficial effect on renal and/or cardiovascular outcomes and mortality, while an increased risk of hyperkalaemia, acute kidney injury and/or hypotension as compared to monotherapy was observed. Given their similar pharmacodynamic properties, these results are also relevant for other ACE-inhibitors and angiotensin II receptor blockers.

ACE-inhibitors and angiotensin II receptor blockers should therefore not be used concomitantly in patients with diabetic nephropathy.

ALTITUDE (Aliskiren Trial in Type 2 Diabetes Using Cardiovascular and Renal Disease Endpoints) was a study designed to test the benefit of adding aliskiren to a standard therapy of an ACE-inhibitor or an angiotensin II receptor blocker in patients with type 2 diabetes mellitus and chronic kidney disease, cardiovascular disease, or both. The study was terminated early because of an increased risk of adverse outcomes. Cardiovascular death and stroke were both numerically more frequent in the aliskiren group than in the placebo group and adverse events and serious adverse events of interest (hyperkalaemia, hypotension and renal dysfunction) were more frequently reported in the aliskiren group than in the placebo group.

Paediatric population

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

The blood pressure lowering effects of two doses of telmisartan were assessed

in 76 hypertensive, largely overweight patients aged 6 to < 18 years (body weight ≥ 20 kg and ≤ 120 kg, mean 74.6 kg), after taking telmisartan 1 mg/kg (n = 29 treated) or 2 mg/kg (n = 31 treated) over a four-week treatment period. By inclusion the presence of secondary hypertension was not investigated. In some of the investigated patients the doses used were higher than those recommended in the treatment of hypertension in the adult population, reaching a daily dose comparable to 160 mg, which was tested in adults. After adjustment for age group effects mean SBP changes from baseline (primary objective) were -14.5 (1.7) mm Hg in the telmisartan 2 mg/kg group, -9.7 (1.7) mm Hg in the telmisartan 1 mg/kg group, and -6.0 (2.4) in the placebo group. The adjusted DBP changes from baseline were -8.4 (1.5) mm Hg, -4.5 (1.6) mm Hg and -3.5 (2.1) mm Hg respectively. The change was dose dependent. The safety data from this study in patients aged 6 to < 18 years appeared generally similar to that observed in adults. The safety of long term treatment of telmisartan in children and adolescents was not evaluated.

An increase in eosinophils reported in this patient population has not been recorded in adults. Its clinical significance and relevance is unknown.

These clinical data do not allow to make conclusions on the efficacy and safety of telmisartan in hypertensive paediatric population.

Chlorthalidone

Pharmacotherapeutic group: Thiazide-like diuretic

ATC Code: C03BA04

Mechanism of action

Chlorthalidone exerts its therapeutic action by antagonizing sodium-chloride symporter in the distal convoluted tubule of the nephron. It is similar to a thiazide diuretic in its mechanism of action, although it has a mildly altered chemical structure. Both thiazide and thiazide-like diuretics contain a sulfonamide group that also works to inhibit carbonic anhydrase and its antagonistic action at the distal convoluted tubule.

Chlorthalidone inhibits sodium reabsorption at the level of the distal convoluted tubule and thus chloride via inhibition of the Na/Cl symporter. By removing sodium reabsorption at this location, the distal convoluted tubule of the nephron retains a higher sodium content. This lack of reabsorption alters the osmotic gradient and shifts fluid distribution from the outside of the tubule to the inside of the tubule. The increased osmotic load from its increased sodium concentration leads to elevated intratubular volume, thus promoting its diuretic effect. The increased excretion of sodium and extracellular fluid decreases intravascular water and solute concentration. By lowering the intravascular volume and osmotic gradient, the patient has reduced hydrostatic pressure leading to a clinical reduction in blood pressure.

5.2 Pharmacokinetic properties Telmisartan

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-∞}) of telmisartan varies from approximately 6 % (80 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 80 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 l.

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 biexponential decay pharmacokinetics with a terminal elimination half-life of >20 hours. The maximum plasma concentration (C_{max}) 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 (Cl_{tot}) is high (approximately 1,000 ml/min) compared with hepatic blood flow (about 1,500 ml/min).

Special Populations**Paediatric population**

The pharmacokinetics of two doses of telmisartan were assessed as a secondary objective in hypertensive patients (n = 57) aged 6 to < 18 years after taking telmisartan 1 mg/kg or 2 mg/kg over a four-week treatment period. Pharmacokinetic objectives included the determination of the steady-state of telmisartan in children and adolescents, and investigation of age related differences. Although the study was too small for a meaningful assessment of the pharmacokinetics of children under 12 years of age, the results are generally consistent with the findings in adults and confirm the non-linearity of telmisartan, particularly for C_{max}.

Gender

Differences in plasma concentrations were observed, with C_{max} and AUC being approximately 3- and 2-fold higher, respectively, in females compared to males.

Elderly

The pharmacokinetics of telmisartan do 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.

Chlorthalidone

Absorption

Not Available

Volume of distribution

Chlorthalidone has been shown to rapidly concentrate within erythrocytes and subsequently equilibrate via a slow diffusion back into the serum compartment, resulting in a large volume of distribution.

Protein binding

Approximately 75 percent of the drug is bound to plasma proteins, 58 percent of the drug being bound to albumin. This is caused by an increased affinity of the drug to erythrocyte carbonic anhydrase.

Metabolism

Liver

Route of elimination

Approximately 50% of the administered dose is excreted unmetabolized through the kidney, and excretion is characterized by biphasic elimination with a rapid phase followed by a slow secretory phase

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 sodium chloride solution supplementation.

In both 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

Ingredient	Specification
Mannitol DC	BP
Microcrystalline Cellulose	BP
Meglumine	BP
Pvp-K 30	BP
Iso propyl alcohol	BP
Cross Povidone	BP
Aspartame	BP
Magnesium Stearate	BP

6.2 Incompatibilities

None

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store in Cool and Dry Place. Protect from direct sunlight. Store below 30°C.

6.5 Nature and contents of container

10 tablets pack in alu-alu blister such 3 blister pack in 1 mono carton with insert.

6.6 Special precautions for disposal and other handling

As the product contains benzalkonium chloride, soft contact lenses should not be worn during treatment.

7. Marketing Authorisation Holder:

ZAIN PHARMA LTD.

Plot No: 209/13741, Colchester Park,
Go-Down No.1, 2, 3, Off Mombasa
Road, Behind Nice And Lovely
House,
P.O. Box: 100167-00101, Nairobi, Kenya

Manufacturer:

ZAIN PHARMA LTD.

Plot No: 209/13741, Colchester Park,
Go-Down No.1, 2, 3, Off Mombasa
Road, Behind Nice And Lovely
House,
P.O. Box: 100167-00101, Nairobi, Kenya

8. Marketing Authorization Number:

H2025/CTD12003/25334

9. Date of First Registration/ Renewal of The Registration

2025 November 03

10. Date of Revision of the Text:

2025 November 03