SUMMARY OF PRODUCT CHARACTERISTICS

1.NAME OF THE MEDICINAL PRODUCT

Velmi-H Plus Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:

Telmisartan USP……... 80 mg

Hydrochlorothiazide USP…… 12.5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM.

White coloured round shaped, uncoated tablet with breakline on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of essential hypertension.
The fixed-dose combination of telmisartan 80 mg/hydrochlorothiazide 12.5 mg is indicated in adults whose blood pressure is not adequately controlled with telmisartan alone.
The fixed-dose combination may be used in patients who have been appropriately stabilised on the individual components given separately.
The combination should not be used for initial treatment of hypertension unless the individual components have been titrated to the appropriate doses.

4.2 Posology and method of administration

Posology

Adults, including the elderly.
The recommended dose is one tablet once daily. Telmisartan/hydrochlorothiazide 80 mg/12.5 mg may be administered once daily in patients whose blood pressure is not adequately controlled with telmisartan 80 mg once daily.

Individual dose titration with each component is recommended before changing to the fixed-dose combination. When clinically appropriate, direct change from telmisartan monotherapy to the fixed-dose combination may be considered.
The maximum antihypertensive effect is generally achieved within 4–8 weeks after initiation or dose adjustment.

Paediatric population

The safety and efficacy of telmisartan/hydrochlorothiazide in children and adolescents below 18 years have not been established. No data are available. Therefore, it should not be used in children.

Patients with renal impairment

Periodic monitoring of renal function is recommended. Telmisartan/hydrochlorothiazide is not recommended in patients with severe renal impairment (creatinine clearance <30 mL/min). Loop diuretics are preferred over thiazides in patients with severe renal impairment.

Patients with hepatic impairment

In patients with mild to moderate hepatic impairment, the dosage should generally not exceed telmisartan/hydrochlorothiazide 40 mg/12.5 mg once daily. Telmisartan/hydrochlorothiazide is contraindicated in patients with severe hepatic impairment. Hydrochlorothiazide should be used with caution in patients with impaired hepatic function.

Method of administration

Telmisartan/hydrochlorothiazide tablets should be taken orally and should be swallowed whole with liquids. It can be taken once daily with or without food. Because of the hygroscopic nature of the tablets, they should be removed from the blister immediately before administration.

4.3 Contraindications

Telmisartan/hydrochlorothiazide is contraindicated in patients with:

- Hypersensitivity to telmisartan, hydrochlorothiazide, other sulfonamide-derived medicinal products, or any of the excipients listed in section 6.1;
- Second and third trimesters of pregnancy;
- Cholestasis and biliary obstructive disorders;
- Severe hepatic impairment;
- Severe renal impairment (creatinine clearance <30 mL/min);

- Anuria;
- Refractory hypokalaemia;
- Hypercalcaemia;
- Concomitant use with aliskiren-containing products in patients with diabetes mellitus or renal impairment (GFR <60 mL/min/1.73 m²).

4.4 Special warnings and precautions for use

Other causes of frequent urination (heart failure or renal disease) should be assessed before treatment. If a urinary tract infection is present, an appropriate antibacterial therapy should be started. (PPB safety template clause matched).

Telmisartan/hydrochlorothiazide tablets should be used with caution in patients with:

- Pregnancy: Angiotensin II receptor blockers (ARBs) should not be initiated during pregnancy. When pregnancy is diagnosed, treatment with telmisartan should be stopped immediately and alternative antihypertensive therapy should be initiated.
- Hepatic impairment: Telmisartan is predominantly eliminated in the bile. Patients with cholestasis, obstructive biliary disorders or severe hepatic impairment should not receive telmisartan/hydrochlorothiazide. Patients with mild to moderate hepatic impairment should be treated cautiously.
- Renovascular hypertension: There is an increased risk of severe hypotension and renal impairment when patients with bilateral renal artery stenosis or stenosis of the artery to a solitary functioning kidney are treated.
- Renal impairment and renal transplantation: Periodic monitoring of renal function is recommended during treatment. There is limited experience with telmisartan/hydrochlorothiazide in patients with recent renal transplantation.
- Hypovolaemia and hypotension: Symptomatic hypotension, particularly after the first dose, may occur in patients who are volume- and/or sodium-depleted. Such conditions should be corrected before initiation of treatment.
- Dual blockade of the RAAS: Concomitant use of telmisartan with aliskiren is contraindicated in patients with diabetes mellitus or renal impairment. Combined blockade through the use of an ARB and an ACE inhibitor or aliskiren is generally not recommended.
- Electrolyte disturbances (Hyperkalaemia, Hypokalaemia, Hyponatraemia, Hypercalcaemia, Hypomagnesaemia): Thiazides and ARBs can disrupt standard systemic

mineral metrics. Periodic monitoring of serum potassium, sodium, calcium, and magnesium is highly recommended.

- Metabolic and endocrine effects: Hydrochlorothiazide may impair glucose tolerance. Dose adjustment of antidiabetic treatment may be required. Latent diabetes mellitus may become manifest during thiazide therapy.
- Acute myopia and secondary angle-closure glaucoma: Hydrochlorothiazide has been associated with an idiosyncratic reaction resulting in acute transient myopia and acute angle-closure glaucoma. Discontinue treatment as rapidly as clinically possible.
- Photosensitivity and Non-melanoma skin cancer: Photosensitivity reactions and increased risk of non-melanoma skin cancer have been reported with cumulative exposure to hydrochlorothiazide. Patients should protect exposed areas from excessive sunlight.
- Systemic lupus erythematosus: Thiazide diuretics have been reported to exacerbate or activate systemic lupus erythematosus.

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacological interactions

Concomitant medication with other medicinal products with antihypertensive properties may result in more pronounced therapeutic effects and undesirable effects.

Pharmacokinetic interactions

- Digoxin: Co-administration observed increases in median peak plasma concentration and trough concentration of digoxin. Monitoring of digoxin concentrations is appropriate.
- Lithium: Reversible increases in serum lithium concentrations and toxicity have been reported. Concomitant use is not recommended.
- Potassium-sparing diuretics and potassium supplements: Concomitant use may increase serum potassium concentrations. Such combinations should be used cautiously.
- Non-steroidal anti-inflammatory drugs (NSAIDs): NSAIDs may reduce the antihypertensive effect of telmisartan and increase the risk of deterioration of renal function, including possible acute renal failure.
- Diuretics: Prior treatment with high-dose diuretics may result in volume depletion and increase the risk of hypotension when telmisartan treatment is initiated.
- Antidiabetic medicines and Metformin: Hydrochlorothiazide may impair glucose tolerance. Dose adjustment of insulin or oral antidiabetic medicines may be required.

Dehydration related to hydrochlorothiazide increases the risk of lactic acidosis with metformin.

- Cholestyramine and colestipol: Absorption of hydrochlorothiazide is reduced by anion-exchange resins.
- Corticosteroids, ACTH, and Cardiac glycosides: Concomitant use may increase electrolyte depletion, particularly hypokalaemia, and increase the risk of cardiac glycoside toxicity.
- Anticholinergic medicines: May increase the bioavailability of hydrochlorothiazide by decreasing gastrointestinal motility.

4.6 Fertility, pregnancy and lactation

Pregnancy

The use of telmisartan/hydrochlorothiazide is contraindicated during the second and third trimesters of pregnancy. Use during the first trimester is not recommended. When pregnancy is diagnosed, treatment should be discontinued immediately and alternative antihypertensive therapy considered.

Breast-feeding

Telmisartan/hydrochlorothiazide is not recommended during breast-feeding. Alternative antihypertensive treatment with an established safety profile during lactation is preferred, particularly while nursing a newborn or preterm infant. Hydrochlorothiazide is excreted into breast milk and high doses may inhibit lactation.

4.7 Effects on ability to drive and use machines

Since telmisartan/hydrochlorothiazide may cause dizziness or drowsiness, the ability to drive and use machines may be negatively affected, particularly when initiating treatment or changing the dose.

4.8 Undesirable effects

Due to the pharmacological effects, telmisartan/hydrochlorothiazide tablets may cause undesirable effects of mild or moderate severity. The most commonly reported adverse reactions include dizziness and gastrointestinal disturbances.

Reporting of suspected adverse reactions

If you experience any side effects, talk to your doctor or pharmacist. By reporting side effects, you can help provide more information on the safety of this product. Healthcare professionals are

requested to report any suspected adverse reactions via Pharmacy and Poisons Board, Pharmacovigilance Electronic Reporting System (PvERS): https://pv.pharmacyboardkenya.org.

4.9 Overdose

Symptoms

The most prominent manifestation of telmisartan overdose is likely to be hypotension and tachycardia; bradycardia may also occur. Overdose with hydrochlorothiazide is associated with excessive diuresis and may result in dehydration and electrolyte depletion, including hypokalaemia and hyponatraemia. Other manifestations include dizziness, weakness, nausea, vomiting, and cardiac arrhythmias.

Treatment

Treatment should be symptomatic and supportive. The patient should be closely monitored. If significant hypotension occurs, the patient should be placed supine and appropriate fluid and electrolyte replacement should be administered. Serum electrolytes, creatinine, and renal function should be monitored. Activated charcoal and gastric lavage may be considered following a recent substantial ingestion where clinically appropriate. Telmisartan is not removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

- Pharmacotherapeutic group: Angiotensin II receptor antagonists and diuretics
- ATC code: C09DA07

Mechanism of action

Telmisartan/hydrochlorothiazide combines two antihypertensive agents with complementary mechanisms. Telmisartan is an orally active and specific angiotensin II receptor subtype 1 (AT1) antagonist. It displaces angiotensin II from its binding site at the AT1 receptor without partial agonist activity. Hydrochlorothiazide is a thiazide diuretic. Its principal action is inhibition of sodium and chloride reabsorption in the renal tubules, increasing the urinary excretion of sodium, chloride, and water.

Pharmacodynamic effects

Concomitant administration of telmisartan and hydrochlorothiazide produces an additive antihypertensive effect. Telmisartan tends to reduce the potassium loss associated with

hydrochlorothiazide treatment through inhibition of the renin-angiotensin-aldosterone system. The antihypertensive effect develops gradually and is maintained over 24 hours.

5.2 Pharmacokinetic properties

Absorption

Following oral administration, peak plasma concentrations of telmisartan are reached approximately 0.5–1 hour after administration. Absolute bioavailability is dose-dependent. Hydrochlorothiazide is rapidly absorbed following oral administration.

Distribution

Telmisartan is highly bound to plasma proteins, principally albumin and a1-acid glycoprotein. Its apparent volume of distribution is approximately 500 litres. Hydrochlorothiazide is approximately 68% protein bound and distributes into red blood cells.

Biotransformation

Telmisartan is metabolised by conjugation to a pharmacologically inactive glucuronide. Cytochrome P450 enzymes do not contribute significantly to telmisartan metabolism. Hydrochlorothiazide is not significantly metabolised.

Elimination

Telmisartan is eliminated almost exclusively in the faeces, mainly as unchanged drug. It has a terminal elimination half-life of approximately 24 hours. Hydrochlorothiazide is eliminated predominantly unchanged in the urine, with a half-life of approximately 6–15 hours.

5.3 Preclinical safety data

Non-clinical studies with telmisartan and hydrochlorothiazide revealed no special hazard for humans based on conventional studies of safety pharmacology, repeated-dose toxicity, genotoxicity, and carcinogenicity. Preclinical effects observed with telmisartan were consistent with exaggerated pharmacological activity resulting from blockade of the renin-angiotensin system.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core Tablet

- Lactose monohydrate

- Microcrystalline cellulose
- Povidone
- Meglumine
- Sodium hydroxide
- Crospovidone
- Colloidal anhydrous silica
- Magnesium stearate
- Mannitol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 Months.

6.4 Special precautions for storage

Store below 30°C. Store in the original package in order to protect from moisture. Keep the blister sealed until immediately before administration. Keep out of the sight and reach of children.

6.5 Nature and contents of container

Aluminium-Aluminium Blister pack 10 Tablets are Blister packed with Aluminium-Aluminium Foil; such 3 Blisters are packed in monocarton along with packaging insert.

Pack Size: 3x10 Tablets

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Eastleigh Pharmaceuticals Co. Ltd P.O Box 167-00610 Nairobi, Kenya

8. MARKETING AUTHORISATION NUMBER(S)

CTD10316

9. DATE OF FIRST / RENEWAL OF THE

17th October 2023

10. DATE OF REVISION OF THE TEXT

17th October 2023