Summary of Product Characteristics (SmPC)

1. Name of the medicinal product : C D T E L - H (T e l m i s a r t a n a n d Hydrochlorothiazide Tablets USP)

2. Qualitative and Quantitative composition :

COMPOSITION:

Each uncoated tablet contains:

Telmisartan USP	40.00 mg
Hydrochlorothiazide USP	12.50 mg
Lactose BP	87.50 mg.

3. Pharmaceutical Form: Tablet.

Brown colored, round shaped, Beveled edge, biconvex, film coated tablets debossed with "I1" on one side and plain on other side.

4. Clinical Particulars:

4.1 Therapeutic Indications:

Telmisartan and hydrochlorothiazide tablets are indicated for the treatment of hypertension. This fixed dose combination is not indicated for initial therapy.

4.2 Posology and method of administration:

- The usual starting dose of Telmisartan is 40 mg once a day; blood pressure response is dose related over the range of 20-80 mg. Patients with depletion of intravascular volume should have the condition corrected or Telmisartan tablets should be initiated under close medical supervision. Hydrochlorothiazide is effective in doses of 12.5 mg to 50 mg once daily.
- To minimize dose-independent side effects, it is usually appropriate to begin combination therapy only after a patient has failed to achieve the desired effect with mono therapy.
- Telmisartan and hydrochlorothiazide tablets may be administered with other antihypertensive agents. Telmisartan and hydrochlorothiazide tablets may be administered with or without food.
- The combination may be substituted for the titrated components.

Administration

Oral route of Administration.

4.3 Contraindications:

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• Telmisartan and hydrochlorothiazide tablets are contraindicated in patients with known hypersensitivity (e.g., anaphylaxis or angioedema) to Telmisartan, hydrochlorothiazide, or any other component of this product.
• Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

4.4 Special warning and precaution for use:

- Hydrochlorothiazide/Telmisartan may cause drowsiness, dizziness, light-headedness, or fainting; alcohol, hot weather, exercise, or fever may increase these effects. To prevent them, sit up or stand slowly, especially in the morning. Sit or lie down at the first sign of any of these effects. Do not drive or perform other possibly unsafe tasks until you know how you react to it.
- Hydrochlorothiazide/Telmisartan contains a sulfonamide called hydrochlorothiazide, which can cause certain eye problems (myopia, angle-closure glaucoma). Your risk may be increased if you are allergic to sulfonamide medicines (e.g. sulfamethoxazole) or to penicillin antibiotics (e.g. amoxicillin). Untreated angle-closure glaucoma can lead to permanent vision loss. If these eye problems occur, symptoms usually occur within hours to weeks of starting hydrochlorothiazide/Telmisartan. Contact your doctor immediately if you experience symptoms, such as vision changes (e.g. decreased vision clearness) or eye pain.
- Hydrochlorothiazide/Telmisartan may cause you to become sunburned more easily. Avoid the sun, sunlamps, or tanning booths until you know how you react to hydrochlorothiazide/Telmisartan. Use a sunscreen or wear protective clothing if you must be outside for more than a short time.
- If you have high blood pressure, do not use nonprescription products that contain stimulants. These products may include diet pills or cold medicines. Contact your doctor if you have any questions or concerns.
- Your doctor may have also prescribed a potassium supplement for you. If so, follow the dosing carefully. Do not start taking additional potassium on your own or change your diet to include more potassium without first checking with your doctor.
- Check with your doctor before you use a salt substitute or a product that has potassium in it.
- Diabetes patients - Hydrochlorothiazide/Telmisartan may affect your blood sugar. Check blood sugar levels closely. Ask your doctor before you change the dose of your diabetes medicine.
- Hydrochlorothiazide/Telmisartan may raise your blood sugar. High blood sugar may make you feel confused, drowsy, or thirsty. It can also make you flush, breathe faster, or have a fruit-like breath odor. If these symptoms occur, tell your doctor right away.
- Hydrochlorothiazide/Telmisartan may interfere with certain lab tests, including parathyroid function tests. Be sure your doctor and lab personnel know you are taking hydrochlorothiazide/Telmisartan.
- Lab tests, including kidney function, blood pressure, and blood electrolytes, may be performed while you use hydrochlorothiazide/Telmisartan. These tests may be used to monitor your condition or check for side effects. Be sure to keep all doctor and lab appointments.

- Use hydrochlorothiazide/Telmisartan with caution in the elderly; they may be more sensitive to its effects.
- Hydrochlorothiazide/Telmisartan should be used with extreme caution in children; safety and effectiveness in children have not been confirmed.

4.6 Pregnancy and Lactation:

Hydrochlorothiazide/Telmisartan may cause birth defects or fetal death if you take it while you are pregnant. If you think you may be pregnant, contact your doctor right away. Hydrochlorothiazide/Telmisartan is found in breast milk. Do not breast-feed while taking hydrochlorothiazide/Telmisartan.

4.7Effects on the ability to drive and use machines:

- This drug may make you dizzy or cause vision problems. Do not drive, use machinery, or do any activity that requires alertness or clear vision until you are sure you can perform such activities safely. Limit alcoholic beverages.

4.8 Undesirable effects:

- **Get emergency medical help if you have any of these signs of an allergic reaction:** Rash; difficulty breathing; swelling of your face, lips, tongue, or throat.
- If you become dizzy or nauseated, or have pain, numbness, or tingling in your chest, arms, neck, or jaw, stop and call your doctor right away.

4.9 Overdose

If you accidentally take more tablets than you should, tell a doctor or get other medical advice straight away. Take the medicine pack with you.

Telmisartan: Limited data are available with regard to over dosage in humans. The most likely manifestation of over dosage with Telmisartan tablets 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 Particulars:

1. Pharmacodynamic properties

Pharmacotherapeutic group: Angiotensin II antagonists and diuretics,
ATC code: C09DA07

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 AT1 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. There is also an AT2 receptor found in many tissues, but AT2 is not known to be associated with cardiovascular homeostasis. Telmisartan has much greater affinity (>3,000 fold) for the AT1 receptor than for the AT2 receptor. Blockade of the renin-angiotensin system with ACE inhibitors, which inhibit the biosynthesis of angiotensin II from angiotensin I, is widely used in the treatment of hypertension. ACE inhibitors also inhibit the degradation of bradykinin, a reaction also catalyzed by ACE. Because telmisartan does not inhibit ACE (kininase II), it does not affect the response to bradykinin. Whether this difference has clinical relevance is not yet known. Telmisartan does not bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation. Blockade of the angiotensin II receptor inhibits the negative regulatory feedback of angiotensin II on renin 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 renin-aldosterone link is mediated by angiotensin II, so coadministration of an angiotensin II receptor antagonist tends to reverse the potassium loss associated with these diuretics.

Pharmacodynamics:

- The pharmacodynamics of Telmisartan & hydrochlorothiazide has been investigated in vitro and in vivo in rodents, guinea pigs, rabbits and dogs. The combination of Telmisartan with hydrochlorothiazide (40 mg/12.5 mg and 80 mg/12.5 mg) is expected to benefit patients with hypertension who are not adequately responsive to Telmisartan alone.

2. Pharmacokinetic properties

- Telmisartan is orally well absorbed and metabolized to an active metabolite which is more potent than Losartan as AT1 antagonist. Orally administered hydrochlorothiazide is rapidly absorbed and diuretic effect is seen in 1 hour and their duration lasts up to 12-24 hours. Both Telmisartan and hydrochlorothiazide has longer duration of actions. These agents are bound to plasma proteins to varying degrees and this has no correlation to their half-life.

Absorption and Distribution:

- Telmisartan: Telmisartan is highly bound to plasma proteins (>99.5%), mainly albumin and ⍰1-acid glycoprotein. Plasma protein binding is constant over the concentration range achieved with recommended doses. The volume of distribution for telmisartan is approximately 500 liters, indicating additional tissue binding.
- Hydrochlorothiazide: Hydrochlorothiazide crosses the placental but not the blood-brain barrier and is excreted in breast milk.

Metabolism and Excretion:

- Telmisartan: Following either intravenous or oral administration of 14C-labeled telmisartan, most of the administered dose (>97%) was eliminated unchanged in feces via biliary excretion; only minute amounts were found in the urine (0.91% and 0.49% of total radioactivity, respectively). Telmisartan is metabolized by conjugation to form a pharmacologically inactive acylglucuronide; the glucuronide of the parent compound is the only metabolite that has been identified in human plasma and urine. After a single dose, the glucuronide represents approximately 11% of the measured radioactivity in plasma. The cytochrome P450 isoenzymes are not involved in the metabolism of telmisartan. Total plasma clearance of telmisartan is >800 mL/min. Terminal half-life and total clearance appear to be independent of dose.
- Hydrochlorothiazide: Hydrochlorothiazide is not metabolized but is eliminated rapidly by the kidney. At least 61% of the oral dose is eliminated as unchanged drug within 24 hours.

Pharmacokinetics in Special Populations:

- **Pediatric:** Telmisartan pharmacokinetics have not been investigated in patients <18 years of age.
- Geriatric: The pharmacokinetics of telmisartan do not differ between the elderly and those younger than 65 years.
- **Gender:** Plasma concentrations of telmisartan are generally 2 to 3 times higher in females than in males. In clinical trials, however, no significant increases in blood pressure response or in the incidence of orthostatic hypotension were found in women. No dosage adjustment is necessary.
- **Renal Insufficiency:** Renal excretion does not contribute to the clearance of telmisartan. Based on modest experience in patients with mild-to-moderate renal impairment (creatinine clearance of 30 to 80 mL/min, mean clearance approximately 50 mL/min), no dosage adjustment is necessary in patients with decreased renal function. Telmisartan is not removed from blood by hemofiltration.

3. Pre-clinical Safety:

- He combination of telmisartan and hydrochlorothiazide resulted in additive placebo-adjusted decreases in systolic and diastolic blood pressures at trough of 16 to 21/9 to 11 mmHg for doses between 40 mg/12.5 mg and 80 mg/25 mg, compared with 9 to 13/7 to 8 mmHg for telmisartan 40 mg to 80 mg monotherapy and 4/4 mmHg for

hydrochlorothiazide 12.5 mg monotherapy. The antihypertensive effect was independent of age or gender.

- There was essentially no change in heart rate in patients treated with the combination of telmisartan and hydrochlorothiazide in the placebo-controlled trial.
- Four other studies of hypertensive patients of at least six months' duration allowed add-on of hydrochlorothiazide for patients who either were not adequately controlled on the randomized telmisartan monotherapy dose or had not achieved adequate blood pressure response after completing the up-titration of telmisartan. In active-controlled studies, the addition of 12.5 mg hydrochlorothiazide to titrated doses of telmisartan in patients who did not achieve or maintain adequate response with telmisartan monotherapy further reduced systolic and diastolic blood pressures.

6. Pharmaceutical Particulars:

6.1 List of Excipients:

Microcrystalline cellulose	BP
Lactose	BP
Colloidal Silicon Dioxide	USP
Magnesium Hydroxide	BP
Crospovidone	USP
Polyvinyl Pyrrolidone (PVPK 30)	BP
Magnesium Stearate	BP
Purified Talc	BP

6.2 Incompatibilities: Nil.

6.3 Shelf Life: 36 months.

6.4 Special Precautions for storage:

Store below 30°C in a dry place. Protect from light.

6.5 Nature and contents of container:

Alu- Alustrip of 10 tablets each, such 3 strips are packed in a primary carton along with pack insert.

6.6 Special precautions for disposal and other handling

None

7. Marketing Authorization Holder: Zota Healthcare Limited

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8. Marketing Authorization Number

TAN 21 HM 0103

9. Date of first Authorization /renewal of the authorization

29th March 2021

10. Date of revision of text