SUMMARY OF PRODUCT CHARACTERISTICS

1. **Name of the pharmaceutical product**
   Cilniday ® 5

2. **Qualitative and Quantitative composition**
   Each film coated tablet contains:
   Cilnidipine 5 mg

   Colour: Approved colour used

   For the full list of excipients, see section 6.1

3. Pharmaceutical form
   Film coated tablet
   Off-white colored, oval shaped, biconvex, film coated tablets having central break line on one side & plain on other side.

4. **Clinical particulars**

4.1 Therapeutic indications

Cilnidipine is primarily used for the treatment of high blood pressure also referred to as hypertension. Due to its calcium channel blocking nature, it also finds its use in the treatment of patients suffering from diabetes, chronic kidney ailments, and albuminuria.

4.2 Posology

Adult: The recommended adult oral dose of cilnidipine is 5-10 mg once daily. The dosage can be increased up to 20 mg; if needed. Starting dose 5-10 mg depending on individual case. Maintaining dose – physician will titrate the dose as per patient's symptoms. Maximum dose 20 mg per day.

Pediatric: The safety of Cilnidipine in pediatric patients has not been established.

Method of administration: For oral administration

4.3 Contraindications

- Aortic stenosis, advanced.
- Hypersensitivity to Cilnidipine or other calcium channel antagonists.

4.4 Special warnings and precautions for use

- Angina
- Chronic renal insufficiency
- Congestive heart failure
- Hypotension
- Liver dysfunction, or elevated liver enzymes
- Peripheral edema (confounding physical findings in congestive failure)
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4.5 Interaction with other medicinal products and other forms of interaction.

Cilnidipine is mainly metabolized by drug metabolizing enzymes CYP3A4 and CYP2C19.

Cilnidipine may interact with other antihypertensive agents, aldesleukin, and antipsychotics which may cause hypotension. Interactions may occur with quinidine, carbamazepine, phenytoin, rifampicin, cimetidine, and erythromycin.

Drugs with Antihypertensive Action	Risk of Hypotension	Additive or synergistic action
Digoxin	It has been reported that other calcium antagonists (e.g., nifedipine) increase the concentration of digoxin in the blood. If digoxin intoxication symptoms (nausea vomiting, headache, visual abnormality, arrhythmia etc.) are observed, the dosage of digoxin should be adjusted or discontinued.	Although the mechanism has not been fully elucidated, it is believed that extrarenal clearance of digoxin is reduced.
Cimetidine	May enhance the antihypertensive effect of Cilnidipine.	Cimetidine reduces hepatic blood flow and inhibits CYP3A4 enzymes which metabolize Cilnidipine while decreasing gastric acid and increasing absorption of calcium antagonists.
Rifampicin	The antihypertensive effect of cilnidipine may be attenuated.	Rifampicin induces CYP3A4 and may promote metabolism and clearance of Cilnidipine.
Azole antifungal agents i.e., itraconazole, miconazole, etc.	May enhance the antihypertensive effect of Cilnidipine.	Azole antifungal agent inhibits CYP3A4, a drug metabolizing enzyme of Cilnidipine.
Grapefruit juice	May enhance the antihypertensive effect of Cilnidipine.	Mechanism of action is unknown but components contained in grapefruit juice likely suppress CYP3A4 activity which metabolizes Cilnidipine.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no human clinical or animal data concerning the safety of Cilnidipine during pregnancy. Until data are available, administration of Cilnidipine during pregnancy should be avoided.

Breast-feeding
Nursing mothers should consult a physician before taking cilnidipine.

4.7 Effects on ability to drive and use machines
There are no data on the effects of Cilnidipine on the ability to drive or use machines. As with other calcium channel blockers, dizziness and hypotension are known adverse reactions associated with the use of Cilnidipine. Patients should not drive a vehicle or operate a machine or perform tasks that require alertness if they experience these symptoms.

4.8 Undesirable effects
- Abdominal pain
- Swelling in the ankles
- Dizziness
- Edema
- Pain or irritation in the eyes
- Fatigue
- Flushing of the face, ears and neck
- Headache
- Nausea
- Pain in the chest area
- Palpitations
- Drowsiness

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose.
Overdose can cause hypotension. Treatment must be instituted based on symptoms. If reduction in blood pressure is remarkable, appropriate measures such as lifting lower extremities, fluid therapy and administration of vasopressors should be taken.

5. Pharmacological properties
5.1 Pharmacodynamic properties
ATC code: C08CA14
Pharmacotherapeutic group: Dihydropyridine derivatives.

Mechanism of action

Cilnidipine is a third generation dihydropyridine calcium antagonist with a slow onset and long duration of action. Calcium antagonists inhibit influx of extracellular calcium ions into the cells resulting in decreased vascular smooth muscle tone and vasodilation, leading to reduction in blood pressure. In vitro and animal studies suggest that cilnidipine blocks both the L and N type calcium channels. Cilnidipine inhibits the pressor to cold stress by suppressing sympathetic nerve activity in spontaneously hypertensive rats. It does not induce tachycardia caused by hypotensive baroreflexes. In vitro, cilnidipine inhibits norepinephrine release in electrically stimulated rabbit mesenteric arteries.
In human studies, cilnidipine had weak inotropic effects and suppressed cardiac sympathetic overactivity. Therefore, it may decrease the risk and mortality from long term cardiovascular complication. Once daily cilnidipine was associated with less reflex tachycardia and had fewer effect on the autonomic nervous system in hypertensive patients. In contrast to other long acting calcium channel blockers, cilnidipine and amlodipine did not increase plasma renin activity, thus they may decrease the risk of cardiovascular complications due to metabolic imbalances. Cilnidipine may inhibit norepinephrine and dopamine production, thereby improving insulin resistance in patients with diabetes. It also had beneficial effects on lipid profiles in hypertensive patients by decreasing total cholesterol, triglyceride, and very low-density lipoprotein cholesterol level, and increasing high density lipoprotein cholesterol and the ratio of high-density lipoprotein cholesterol to total cholesterol.

5.2 Pharmacokinetic properties
Cilnidipine has a slow onset and long duration of action of 24 hours, partly explained by its high lipophilicity.
Cilnidipine has a half-life of 2 – 8 hrs After administration of 5 – 20 mg

5.3 Preclinical safety data
None available

6. Pharmaceutical particulars
6.1 List of Excipients:
Base Granules
Colloidal Silicon Dioxide
Talc
Croscarmellose Sodium
Magnesium Stearate
Film coating (Titanium Dioxide)
Methylene dichloride

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months.

6.4 Special precautions for storage

Store below 30°C, Protect from direct sunlight, heat & moisture.

6.5 Nature and contents of container

Cilniday® 5 and Cilniday® 10 are available in the Pack of 3 x 10 Tablets.

6.6 Special precautions for disposal and other handling

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

7. Marketing Authorization Holder

Krishna Chemists Ltd.
P.O. Box 3328-00506 Nairobi, Kenya.

8. Marketing Authorisation Number(S)

H2009/24060/308

9. Date of first Registration/ Renewal of Registration

11-11-2021

10. Date of revision of text

11-11-2021