CINLICIAN 5
Cilnidipine Tablets 5 mg

QUALITATIVE AND QUANTITATIVE COMPOSITION:
Label Claim:
Each film coated tablet contains:
Cilnidipine 5 mg
Excipients q.s.
Colour: Titanium Dioxide BP

List of Excipients:
Microcrystalline Cellulose BP
Maize Starch BP
Purified Talc BP
Magnesium Stearate BP
Colloidal Anhydrous Silica BP
Sodium Starch Glycolate BP
Crospovidone BP
Fine Coat
Titanium Dioxide BP
Macrogols (PEG-6000) BP

INDICATION:
Cilnidipine, a novel calcium-channel blocker, is prescribed in the treatment, control, prevention & improvement of the following diseases, conditions and symptoms: High blood pressure.

PHARMACEUTICAL FORM
White coloured, round, biconvex, film coated tablet plain on both side.

DOSAGE AND ADMINISTRATION
The recommended adult oral dosage of Cilnidipine is 5-10 mg once daily. The dosage can be increased up to 20 mg, if needed. Cilnidipine can be taken before or after food intake.
Method of Administration: Oral

CONTRAINDICATION:
Hypersensitivity to cilnidipine or to any of the excipients of Cinlician Tablets. Cilnidipine is contraindicated in patients with severe aortic stenosis, cardiogenic shock, cardiac ischaemia, recent history of unstable angina or MI, heart failure and hypotension.

SPECIAL WARNING AND PRECAUTION FOR USE:
Hypotension, poor cardiac reserve, heart failure. Sudden withdrawal may exacerbate angina. Discontinue in patients who experience ischemic pain following administration.

ADVERSE REACTION:
Adverse reactions, including abnormalities in laboratory data, were observed in 414 (6.95%) of 5,958 patients in the investigations at the time of approval and the post marketing studies (at the end of the re-examination period).
Clinically Significant Adverse Reactions: Hepatic Dysfunction and Jaundice (Frequency Unknown): Hepatic function disorder and jaundice accompanied with increased aspartate aminotransferase (AST) [glutamic oxaloacetic transaminase (GOT)], alanine aminotransferase (ALT) [glutamic pyruvic transaminase (GPT)] and γ-glutamyl transpeptidase (GTP) may occur. Therefore, close observation should be made, and if any abnormality is observed, appropriate measures e.g. discontinuation of Cilnidipine Tablet, should be taken.
Thrombocytopenia (Incidence: <0.1%): Since thrombocytopenia may occur, close observation should be made and if any abnormality is observed, appropriate measures eg, discontinuation of Cilnidipine Tablet should be taken.
If any of the following adverse reactions occur, appropriate measures should be taken depending on the symptoms.

- Peripheral oedema
- Headache
- Dizziness
- Flushing
- Low blood pressure
- Abnormally rapid heart rate
- Palpitations
- Gastrointestinal disturbances
- Increased micturition frequency
- Lethargy
- Eye pain
- Depression
- Ischaemic chest pain
- Cerebral ischaemia
- Blindness
- Rashes
- Fever
- Abnormal liver function
- Myalgia
- Impotence

INTERACTION WITH OTHER MEDICINE AND CONCOMITANT USE:
Cilnidipine can interact with aldesleukin, quinidine, phenytoin, rifampicin, erythromycin, cimetidine, carbamazepine, other anti-hypertensive drugs and anti-psychotic drugs.

PREGNANCY AND LACTATION:
Pregnancy
Cilnidipine should not be administered to pregnant women or women having possibilities of being pregnant. It has been reported that Cinlician prolongs the gestation period and delivery time in animal experiments (in rats).
Lactation
It is advisable to avoid the administration of Cilnidipine to nursing mothers. However, if the administration is indispensable, the patient should be instructed to discontinue lactation. Transfer of Cilnidipine Tablet to mother's milk has been reported in animal experiments (in rats).

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
The symptoms e.g. dizziness may occur because of the hypotensive action from Cilnidipine. Give warning against engaging in hazardous activities requiring alertness e.g. working at a height, operating machinery or driving motor vehicles.

OVERDOSE:
Overdosage of Cilnidipine Tablet may cause excessive reduction in blood pressure. If reduction in blood pressure is remarkable, appropriate measures e.g. lifting lower extremities, fluid therapy and administration of vasopressors should be taken. Hemodialytical removal of Cilnidipine is not effective because of its high rate of protein-binding.

PHARMACOLOGICAL PROPERTIES
PHARMACOKINETICS:
Plasma Drug Levels:
When a single dose of cilnidipine 5-, 10- or 20 mg was orally administered to 6 healthy male volunteers, the peak plasma concentration (C_{max}) was found to be 4.7 ng/mL, 5.4 ng/mL and 15.7 ng/mL, respectively and the area under the concentration-time curve (AUC_{0-24}) to be 23.7 ng·hr/mL, 27.5 ng·hr/mL and 60.1 ng·hr/mL, respectively. Thus, both parameters increased in a dose dependent manner. When a single dose of cilnidipine 10 mg was repeatedly administered once a day to 6 healthy male volunteers, pharmacokinetic parameters of cilnidipine were indicated as follows.
The plasma concentration reached a steady-state from Day 4 of the administration and there was no evidence of the accumulation. The pharmacokinetics of Cilnidipine Tablet have also been evaluated in patients with impaired renal function (serum creatinine: 1.5-3.1 mg/dL) following a single oral dose of 10 mg in the hypertensive patients and no significant differences were found in the pharmacokinetic profile of Cilnidipine Tablet compared with that in patients with normal renal function. Repeated oral administration of Cilnidipine Tablet at a dose of 10 mg once a day for 7 days in patients with impaired renal function caused no differences in the pharmacokinetic profile compared with that in patients with normal renal function.
Metabolism and Excretion:
From the metabolites identified in the plasma and urine of healthy male volunteers, it is considered that the major route of cilnidipine metabolism is demethylation of the methoxyethyl group followed by hydrolysis of the cinnamyl ester and oxidation of the dihydropyridine ring. It is considered that CYP3A4 is mainly involved and CYP2C19 is partly involved in the demethylation of the methoxyethyl group (in vitro). The calcium channel blocking action of the metabolite with the demethylated methoxyethyl group was only $1_{/100}$ of that of the parent compound (in rabbits). When a single oral dose of cilnidipine 10 mg was repeatedly administrated to healthy male volunteers once a day for 7 days, no unchanged compound of cilnidipine but 5.2% of the dose was excreted in the urine as metabolites. (The approved administration of Cilnidipine Tablet is orally once a day after breakfast.) An in vitro experiment showed that cilnidipine was 99.3% bound to human serum protein.

PHARMACODYNAMICS:
Pharmacotherapeutic group: Antihypertensive
ATC code: G03BG02
Cilnidipine, a novel calcium-channel blocker, is prescribed for the medical management of hypertension in adults. It acts by blocking the activity of calcium channels in the blood vessels and increasing the blood supply to the heart.
Pharmacodynamic effects:
Cilnidipine is a dihydropyridine class of calcium-channel blocker. Cilnidipine prevents intracellular calcium influx and results in vasodilatation. Cinlician is prescribed for patients at risk of vascular damage caused by hypertension. It comes in the form of a tablet, and helps to control hypertension (high blood pressure) by reduce the functioning of the body`s angiotensin receptors. Cilnidipine possesses superior selectivity for vascular smooth muscle cells.

PACKAGING:
10 tablets are packed in Alu-Alu blister & such 3 blisters are packed in a printed carton along with pack insert.

STORAGE CONDITION:
Store in dry place below 30°C. Keep out of reach of children.

SHELF LIFE:
36 months

MANUFACTURED BY:
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