For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

TORCILIN

1. Generic Name

Cilnidipine Tablets IP 5 mg, 10 mg and 20 mg

2. Qualitative and quantitative composition

TORCILIN 5

Each film coated tablet contains:

Cilnidipine I.P. ……..5 mg

Excipients…… q.s.

Colour: Titanium Dioxide I.P.

The excipients used are Microcrystalline cellulose, Lactose, Polyethylene glycol glycol, Croscarmellose sodium, Polyvinyl pyrrolidine Hypromellose phthalate, Purified Talc, Magnesium stearate, Ethylcellulose, Titanium dioxide.

TORCILIN 10

Each film coated tablet contains:

Cilnidipine I.P. ……..10 mg

Excipients…… q.s.

Colour: Titanium Dioxide I.P.

The excipients used are Microcrystalline cellulose, Lactose, Polyethylene glycol glycol, Croscarmellose sodium, Polyvinyl pyrrolidine Hypromellose phthalate, Purified Talc, Magnesium stearate, Ethylcellulose, Titanium dioxide.

TORCILIN 20

Each film coated tablet contains:

Cilnidipine I.P. ……..20 mg

Excipients…… q.s.

Colour: Titanium Dioxide I.P.

The excipients used are Microcrystalline cellulose, Dibasic Calcium Phosphate Starch, Lactose, Hydroxy propyl cellulose, Magnesium stearate, Sodium starch Glycolate, Colloidal silicon dioxide, Hydroxy propyl methyl cellulose, Talcum, Polyethylene glycol, Titanium dioxide.

3. Dosage form and strength

Dosage form: Film coated tablet

Strength: 5mg, 10 mg and 20 mg

4. Clinical particulars

4.1 Therapeutic Indication

TORCILIN is indicated for the treatment of mild to moderate hypertension.

4.2 Posology and Method of Administration

Posology

The usual dose of cilnidipine is 5 to 10 mg once daily; if necessary, dosage may be increased to 20 mg once daily. TORCILIN Tablets can be administered regardless of meal.

The tablet should be swallowed whole with water.

Or, as directed by physician.

Method of administration

Tablet for oral administration.

4.3 Contraindications

- Hypersensitivity to the active substance, Cilnidipine or to any of the excipients.
- Cardiogenic shock.
- Severe aortic stenosis.
- Recent history of unstable angina or acute myocardial infarction, heart failure,
- hypotension.

4.4 Special Warnings and Precautions for Use

Cardiovascular Disorders: Cilnidipine should be used with caution in patients with hypotension, heart failure, and poor cardiac reserve. Cilnidipine should be discontinued immediately in patients who feel chest pain following the administration of the drug.

Abrupt Cessation of Therapy: In case of angina, cilnidipine should not be discontinued abruptly to avoid withdrawal symptoms.

Grapefruit Juice: Grapefruit juice may intensify the effect of cilnidipine. Thus, avoid drinking grapefruit juice as much as possible while on cilnidipine therapy.

Laboratory Test: Cilnidipine therapy may interfere with the results of vanillyl mandelic acid test which is used to detect tumour's such as pheochromocytoma and neuroblastoma. Therefore, cilnidipine should be avoided for 72 hours before sample collection, but the patient should be monitored intensively in a clinical setting.

4.5 Drugs Interactions

Antipsychotic Drugs: Co-administration of antipsychotic drugs with cilnidipine may result in low blood pressure. Thus, caution should be exercised while concomitant use of these drugs with cilnidipine.

Antidiabetic Drugs: Co-administration of cilnidipine with antidiabetic drugs may result in changes in glucose levels, thus, monitoring of blood glucose levels may be required.

Other Drugs: Antiepileptic drugs (such as phenytoin and carbamazepine), rifampin, quinidine, erythromycin, other anti-hypertensive drugs, and aldesleukin should also be used with caution along with cilnidipine.

4.6 Use in Special Populations (Such as Pregnant Women, Lactating Women, Paediatric Patients, Geriatric Patients Etc.)

Pregnant Women:

Hypertension in pregnancy increases the maternal risk for pre-eclampsia, gestational diabetes, premature delivery, and delivery complications (e.g., need for cesarean section, post-partum hemorrhage). Hypertension increases the fetal risk for intrauterine growth restriction and intrauterine death. Thus, pregnant women with hypertension should be carefully monitored and

managed accordingly. The safety of cilnidipine in human pregnancy has not been established. Thus, TORCILIN Tablets are not recommended during pregnancy.

Lactating Women:

It is not known whether cilnidipine is secreted in breast milk. As a precautionary measure, it is advised that the nursing mother not breastfeed her child while on cilnidipine therapy. Accordingly, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Paediatric Patients:

Safety and efficacy of cilnidipine in paediatric patients has not been established. Thus, TORCILIN Tablets are not recommended in children.

Geriatric Patients:

In general, a lower starting dose is recommended in elderly patients given their greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease and/or other drug therapy. Dosage up-titration, if required, should be done with caution.

4.7 Effects on Ability to Drive and Use Machines

For cilnidipine, studies have not been performed on effects on the ability to drive and use machines. Dizziness has been reported in patients with deceased blood pressure. It is advised not to operate machinery or drive a vehicle if patient experience drowsiness, dizziness, fatigue, headache or hypotension as side-effects of cilnidipine therapy.

4.8 Undesirable Effects

Cilnidipine may cause following adverse reactions:

General: Edema (face, limb, etc.), facial flush, thickening of gums, heat sensation, lethargy, generalized fatigue, frequent urination, impotence, liver dysfunction, jaundice, thrombocytopenia (nose/gum bleeding), allergic reaction, etc.

Gastrointestinal: Nausea, vomiting, anorexia, stomachache, gastrointestinal reflux disease (GERD).

Eye: Transient blindness, eye pain.

Musculoskeletal: Muscle ache, tremors.

Cardiovascular System: Hypotension, palpitations, ischemic chest pain.

Central Nervous System: Dizziness, headache, depression, cerebral ischemia.

Dermatological: Rashes, itching, photosensitivity.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 any point of contact of Torrent Pharma available at: https://tplapp.com/aer/ComplaintForm/new_Complaint_intimation_tp.aspx?Flag=T

4.9 Overdose

In humans, experience with cilnidipine overdose is limited. Overdose symptoms include confusion, dizziness, headache, fatigue, and sedation. If overdose occurs, it might cause excessive peripheral vasodilation with marked hypotension. If overdose should occur, initiate

active cardiac and respiratory monitoring. Frequent blood pressure measurements are essential. Should hypotension occur, provide cardiovascular support including elevation of the extremities and judicious administration of fluids. If hypotension remains unresponsive to these conservative measures, consider administration of vasopressors (such as phenylephrine) with attention to circulating volume and urine output.

5. Pharmacological properties

5.1 Mechanism of action

Cilnidipine is a novel dihydropyridine class of calcium-channel blocker (CCB)/antagonist used for the management of hypertension. Cilnidipine inhibits the transmembrane influx of calcium ions (Ca++) into cardiac and vascular smooth muscle. However, it has greater selectivity for vascular smooth muscle. Antihypertensive action of cilnidipine is due to a direct relaxant effect on vascular smooth muscle. Cilnidipine has little or no action at the SA or AV nodes and negative inotropic activity is rarely seen at therapeutic doses. Like most of the other CCBs, cilnidipine acts on the L-type of calcium channels present on blood vessels.

Cilnidipine blocks entry of calcium ions and thus, suppresses contraction of blood vessels, thereby reducing blood pressure. Cilnidipine possesses both, L- and N-type calcium channel blocking activity. Since N-type calcium channels are distributed along the sympathetic nerve endings and in the brain, cilnidipine exerts specific antisympathetic effect i.e., it inhibits the release of norepinephrine, a sympathomimetic hormone. Thus, cilnidipine reduces blood pressure which is associated with sympathetic overactivity.

5.2 Pharmacodynamic Properties

Cilnidipine is a calcium channel blocker class of antihypertensive agent. Cilnidipine decreases blood pressure safely and effectively without excessive blood pressure reduction or tachycardia. With chronic once daily oral administration of cilnidipine, antihypertensive effectiveness is maintained for about 24 hours.

5.3 Pharmacokinetic Properties

Absorption: After oral administration of cilnidipine, absorption is very rapid with peak plasma concentration reached after 2 hours.

Distribution: Distribution of cilnidipine tends to be higher in the liver as well as in kidneys, plasma, and other tissues. Cilnidipine has a large volume of distribution. Plasma protein binding of cilnidipine is very high i.e., 98% of the administered dose.

Metabolism: Cilnidipine is metabolized by both liver and kidney. It is rapidly metabolized by liver microsomes by a dehydrogenation process. The major enzymatic isoform involved in cilnidipine dehydrogenation of the dihydropyridine ring is CYP3A.

Excretion: Approximately 20% of the administered dose of cilnidipine gets eliminated through the urine, with the remainder (about 80%) being eliminated in feces.

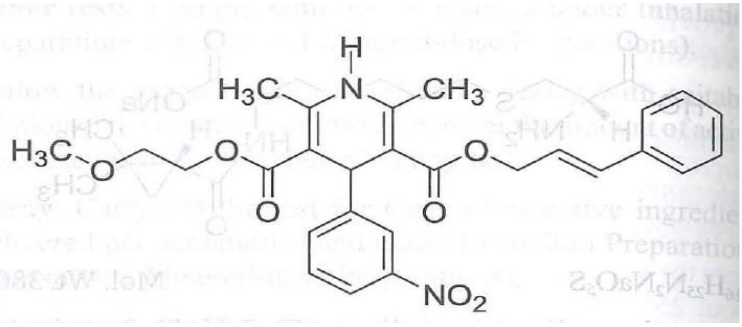
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

No relevant information available.

7. Description

Cilnidipine is l, 4-Dihydro-2, 6-dimethyl-4-(3-nitrophenyl)-3,5-pyridine dicarboxylic acid 2-methoxyethyl (2*E*)-3-phenyl-2-propenyl ester. The empirical formula is $C_{27}H_{28}N_2O_7$ and its molecular weight is 492.5 g/mol. The chemical structure of Cilnidipine is:



TORCILIN 5 and TORCILIN 10 are white to off white coloured circular film coated tablets

TORCILIN 20 is white to off white coloured, round, biconvex, plain on both sides & film coated tablets.

8. Pharmaceutical particulars

8.1 Incompatibilities

Not Available

8.2 Shelf-life

Do not use later than the date of expiry.

8.3 Packaging information

TORCILIN 5 and TORCILIN 10 are available in strip of 10 Tablets

TORCILIN 20 is available in Aluminum- PVDC blister of 10 tablets.

8.4 Storage and Handing Instructions

Store protect from light & moisture, at a temperature not exceeding 30°C.

Keep all medicines out of reach of children.

9. Patient counselling information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10. Details of manufacturer

TORCILIN 5, TORCILIN 10

Hetero Labs Ltd. (Unit-II)

Village: Kalyanpur, Chakkan Road, Baddi (Tehsil),

Solan (Distt.), Himachal Pradesh- 173 205

TORCILIN 20

Akums Drugs & Pharmaceuticals Ltd

19, 20, 21 Sec. 6-A, IIE, SIDCUL, Ranipur, Haridwar -249403

11. Details of permission or licence number with date

TORCILIN 5, TORCILIN 10 – MNB/09/780 issued on 22.01.2018

TORCILIN 20 - 10/UA/2004 issued on 10.01.2018

12. Date of revision

Jan-2025

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/TORCILIN 5, 10 and 20 mg/Jan-2025/02/PI