SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

Cilnidipine Tablets
NOVILEC-20

Strength

20 mg

Pharmaceutical form

Tablets for oral administration

2. Quality and Quantitative Composition

Each film-coated tablet contains:

Cilnidipine.....20mg

Excipient(s) with known effect: 108 mg of lactose monohydrate/tablet

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Tablets

White coloured, circular, biconvex film coated tablets

4. Clinical Particulars

4.1 Therapeutic indications

Cilnidipine is indicated for the treatment of hypertension and hypertensive associated vascular disorders.

4.2 Posology and method of administration

In general, for adults, 5~10 mg of Cilnidipine is orally administered once daily after breakfast. The dose may be adjusted according to the patient's age and symptoms. If the effect is insufficient, the dose can be increased up to 20 mg once a day. However, for severe hypertension, 10 to 20 mg once daily is orally administered after breakfast.

Administration to the elderly

Since it is generally considered un favorable for elderly people to have excessive

blood pressure reduction, when used in the elderly, it is desirable to start administration at a low dose (for example, 5 mg) and carefully observe the course.

Administration to children, etc.

Low birth weight in infant, safety evaluation has not been established for new born, infants, infants or children (do not use without proper guidance).

Method of administration: Oral administration

4.3 Contraindications

Cilnidipine is contraindicated in patients with known hypersensitivity (e.g., anaphylaxis or angioedema) to Cilnidipine or any other component of this product.
Pregnant women or women who may be pregnant (see "Administration to pregnant women, pregnant women, lactating women, etc.)

4.4 Special warning and precautions

Careful administration (Carefully administer to the following patients)

- Patients with severe liver dysfunction [Blood levels may increase]
- Patients with a history of serious side effects caused by calcium channel blockers
- Senior citizens or elderly people (See "Administration to the Elderly")

It has been reported that the symptoms worsened when the administration of calcium channel blocker was suddenly stopped. Therefore, if it is necessary to stop the administration of this drug, the dose should be gradually reduced and the patient should be carefully monitored.
If it is necessary to stop the administration of drug after 5 mg dosage, take measures such as changing to another drug.
Also, be careful with drug replacement drug with consent of patient.

Patient should be guided to be careful when operating dangerous machinery such as working at heights or driving a car, as dizziness may occur due to the antihypertensive effect.
This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp-lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interactions

This drug is mainly metabolized by the drug-metabolizing enzyme CYP3A4 and partly by CYP2C19

Drug name, etc.	**Clinical symptoms or measures**	**Mechanism or risk factors**
Drugs with antihypertensive effect	Blood pressure may drop excessively.	It is prescribed to enhance the action additively or synergistically.
Digoxin	It has been reported that other calcium channel blockers (such as nifedipine) increase blood levels of digoxin. If symptoms of digoxin toxicity (nausea or vomiting, headache, visual abnormality, arrhythmia, etc.) are observed, appropriate measures such as adjusting the dose of digoxin or discontinuing administration of this drug should be taken.	The mechanism has not been completely elucidated, but it is thought to be due to a decrease in renal and extrarenal clearance of digoxin.
Cimetidine	It has been reported that the action of other calcium channel blockers (such as nifedipine) is enhanced.	It is thought that cimetidine lowers hepatic blood flow and suppresses enzyme metabolism of calcium channel blockers in hepatic microsomes, while lowering gastric acid and increasing absorption of calcium channel blockers.
Rifampicin	It has been reported that the action of other calcium channel blockers (such as nifedipine) is attenuated.	It is thought that the hepatic drug-metabolizing enzyme (cytochrome P-450) induced by rifampicin promotes the metabolism of calcium channel blockers and increases the clearance.

Azole antifungal agents, such as itraconazole, miconazole, etc	The blood concentration of this drug may increase.	It is considered that the azole antifungal agent inhibits the drug-metabolizing enzyme CYP3A4 of this drug.
Grapefruit juice	It has been confirmed that the blood concentration of this drug increases.	Although the details of the expression mechanism are unknown, it is thought that the ingredients contained in grapefruit juice suppress the drug-metabolizing enzyme CYP3A4 of this drug.

4.6 Pregnancy and lactation

Do not administer to pregnant women or women who may be pregnant. [In animal experiments (rats), fatal toxicity and prolongation of gestation period and delivery time have been reported.
It is desirable to avoid administration to lactating women, but if administration is unavoidable, lactation should be stopped. [In animal experiments (rats), it has been reported that chemicals are transferred into breast milk.

4.7 Effects on ability to drive and use machine

The symptoms, such as dizziness may occur because of the hypotensive action from this drug. Give warning against engaging in hazardous activities requiring alertness, such as working at a height, operating machinery or driving motor vehicles.

4.8 Undesirable effects

Adverse drug reactions (including abnormal changes in laboratory test values) were observed in 414 (6.95%) out of 5,958 cases investigated at the time of approval and in the post-marketing drug use-results survey (at the end of re-examination).

Serious side effects

Liver dysfunction, jaundice (incidence unknown): Hepatic dysfunction and jaundice accompanied by elevation of AST (GOT), ALT (GPT), fu-GTP, etc. may occur. If this is the case, discontinue administration and take appropriate measures.

Thrombocytopenia (less than 0.1%): Thrombocytopenia may occur. If any abnormalities are observed, administration should be stopped immediately and appropriate measures should be taken.

Other side effects

	Less than 0.1~5%	Less than 0.1%	Frequency unknown
Liver	**Increase in AST (GOT), ALT (GPT),**	**Rise of A1-P**	
Kidney	Increased creatinine, urea nitrogen, urinary protein positive	Urine sediment positive	
Psycho-nervous system	Headache, heavy headache, dizziness, light headedness, stiff	Drowsiness, insomnia, tremor, forgetfulness	Numbness
Cardiovascular	Flushing, palpitation, heat sensation, abnormal electrocardiogram (ST depression, T wave reversal), decrease in blood pressure	Chest pain, increased cardiothoracic ratio, tachycardia, atrioventricular block, cold sensation	Extra systole, bradycardia
Digestive organ	Nausea or vomiting, abdominal pain	Constipation, bloating, mouth flatulence, gum thickening, chest burn,	
Hypersensitivity note[2)]	Rashes	Redness, itching	Photosensitivity
Blood	Fluctuations in white blood cell count, neutrophils, and haemoglobin	Changes in red blood cell count, haematocrit,	
Others	Edema (face, lower limbs, etc.), general malaise, pollakiuria, elevated serum cholesterol, CK (CPK), Fluctuations in uric acid, serum K, and serum P.	Weakness, peroneal muscle spasm, dryness around the eyes, red eye irritation, taste abnormalities, urinary glucose positive,	Tinnitus

		fasting blood glucose,	

Note 1): Carefully observe such symptoms, and discontinue administration if any abnormalities are observed.
Note 2): If such symptoms occur, administration should be discontinued.

Reporting of suspected adverse reactions
Reporting of suspected adverse reactions: 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

Over dosage of Cilnidipine may cause excessive reduction in blood pressure. If reduction in blood pressure is remarkable, appropriate measures such as lifting lower extremities, fluid therapy and administration of vasopressors should be taken. Hemodialytical removal of the drug is not effective because of its high rate of protein binding.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Cilnidipine bound to the dihydropyridine binding site of L-type voltage-gated Ca channels present in vascular smooth muscle cell membranes and suppressed Ca2 + influx from L-type voltage-gated Ca channels (rabbit, in vitro) It is thought that this relaxes and dilates vascular smooth muscle and exerts an antihypertensive effect.
Cilnidipine binds to the dihydropyridine binding site of L-type voltage-gated Ca channels present in vascular smooth muscle cell membranes, Suppressed Ca2+ influx from L-type voltage-gated Ca channels (rabbit, in vitro).
As a result, it is considered that by suppressing the release of noradrenaline from the sympathetic nerve endings, the increase in heart rate during hypotension due to the enhancement of sympathetic nerve activity and the pressurization during stress loading are suppressed.

5.2 Pharmacokinetic Properties:

The Cmax of a single oral dose of 5 mg, 10 mg, and 20 mg of this drug to 6 healthy adult males was 4.7 ng/mL, 5.4 ng/mL, 15.7 ng/mL, and AUC 0~24 was 23.7 ng or hr/mL, respectively ,
27.5 ng or hr/mL, 60.1 ng or hr/mL, and increased in a dose-dependent manner).

The pharmacokinetic parameters of 6 healthy adult males when 10 mg of this drug was orally administered once daily are as follows. After the 4th day of

administration, the steady state was reached and no accumulation was observed.

Parameters / Administration days	**C_{max} (ng/mL)**	**T_{max} (hr)**	**$T_{1/2}(\alpha)$ (hr)**	**$T_{1/2}(\beta)$ (hr)**	**$AUC_{0\sim\infty}$ (ng.hr/mL)**
Day 1 of administration	9.5 ±1.6	2.8±1.0	1.0 ± 0.2	5.2 ±2.0	51.4±12.7
Day 4 of administration	13.5±5.0	3.7±0.8	-	-	101.8±29.0
Day 7 of administration	16.5±7.9	3.0±1.3	1.1±0.6	8.1±2.7	95.5±34.5

(Mean ± standard deviation)

There was no difference in plasma concentration transition between hypertensive patients with a single oral dose of 10 mg of this drug between patients with normal renal function and patients with impaired renal function (Serum creatinine level: 1.5-3.1 mg/dL). Furthermore, even when 10 mg of this drug was orally administered once daily for 7 days to patients with impaired renal function, no effect of repeated administration was observed on the change in plasma concentration.

Metabolism and excretion

From the metabolites observed in plasma and urine in healthy adult males), the main metabolic pathway is considered to be demethylation of the methoxyethyl group, followed by hydrolysis of the cinnamyl ester group and oxidation of the dihydropyridine ring. It is considered that CYP3A4 is mainly involved in the demethylation reaction of the methoxyethyl group in the metabolic process and that CYP2C19 is partially involved (in vitro).
The calcium antagonism of the demethylated methoxyethyl group was 1/100 of the activity of the unchanged form (rabbit).
When 10 mg of this drug was orally administered to healthy adult males twice daily for 7 days, no unchanged drug was detected in urine, and 5.2% of the total dose was excreted as a metabolite). (The approved dosage for this is oral administration once daily after breakfast).
The in vitro human serum protein binding rate was 99.3%.

5.3 Preclinical safety Data

None stated

6. Pharmaceutical Particulars

6.1 List of excipients

Lactose monohydrate

Lowsub hydroxypropyl cellulose,
Tartaric acid
Microcrystalline
cellulose Magnesium
stearate
Instacoat universal white (IC U 3849) (Hydroxy Propyl Methyl Cellulose, Polyethylene Glycol, Talc & Titanium Dioxide)

6.2 Incompatibilities

None

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store protect from light and moisture, at temperatures not exceeding 30°C

6.5 Nature and contents of container

Aluminium/Aluminium blister pack of 10 tablets, such 3 blisters are packed in outer carton along with pack insert.

6.6 Special precautions for disposal and other handling

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

7. Marketing Authorization Holder

MICRO LABS LIMITED

31, race course
road Bangalore-
560001 INDIA

8. Number from the register of medicinal product.
H2024/CTD9533/21429

9. Date of authorization or of the last renewal of the authorization

31/July/2024

10. Date of revision of the text

Aug 2021