

Patient package insert according to Pharmacists' Regulations (Preparations), 1986.

This medicine can be sold with a physician's prescription only.

VASODIP® COMBO, Tablets

Composition:

Each tablet of **Vasodip Combo 10** contains:
Lercanidipine hydrochloride 10 mg and Enalapril maleate 10 mg
Each tablet of **Vasodip Combo 20** contains:
Lercanidipine hydrochloride 10 mg and Enalapril maleate 20 mg
For the list of ingredients, please see section 6.

Read this entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, ask your physician or pharmacist.
This medicine has been prescribed for you only. Do not pass it to others; it may harm them, even if you think that their medical condition is similar.

Vasodip Combo is not intended for children and adolescents under the age of 18. Vasodip Combo is not intended for primary treatment of hypertension.

1. What is the medicine used for?

- Vasodip Combo 10 is used for the treatment of hypertension in patients whose blood pressure is not adequately controlled by treatment with Lercanidipine alone.
- Vasodip Combo 20 is used for the treatment of hypertension in patients whose blood pressure is not adequately controlled by treatment with Enalapril alone.

Therapeutic group:

- Enalapril belongs to the group of Angiotensin- converting enzyme (ACE) inhibitors.
- Lercanidipine belongs to the group- calcium channel blockers.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredients (Enalapril or Lercanidipine) or to any of the other ingredients that this medicine contains (see section 6) or to other medicines of the same therapeutic groups (see above).
- You are more than 3 months pregnant (It is advisable to avoid using Vasodip Combo also in the first months of pregnancy, see "Pregnancy and breastfeeding" section).
- You suffer from diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren.
- You suffer from the following heart diseases: untreated congestive heart failure, obstruction to the blood flow from the left ventricle of the heart including a narrowing of the aortic valve, unstable angina pectoris (at rest or becoming worse or happening more often), a heart attack within the last month.
- You suffer from severely impaired function of the liver or kidneys, or if you are undergoing dialysis.
- You use antifungals (e.g. ketoconazole, itraconazole), macrolide antibiotics (e.g. erythromycin, troleandomycin), antiviral medicines (e.g. ritonavir), cyclosporin or ciclosporin.
- You have suffered from angioedema (oedema of the face, mouth, lips, tongue and/or throat, causing difficulty swallowing or breathing) hereditary in type or following treatment with a medicine of the ACE-inhibitor group or due to an unknown reason.
- You eat grapefruit or drink grapefruit juice.

Special warnings regarding the use of this medicine:

Before using Vasodip Combo, tell your physician if:

- You suffer from low blood pressure (manifested by symptoms such as fainting or dizziness especially upon transition to the standing position).
- You have recently suffered from vomiting or diarrhea.
- You are on a salt restricted diet.
- You suffer from heart disease or a condition involving the cerebral blood vessels, kidney problems (including kidney transplantation), liver problems, diabetes, connective tissue diseases with involvement of blood vessels (such as lupus erythematosus, rheumatoid arthritis or scleroderma).
- You suffer from blood problems such as: if your white blood cell count is low or you have white blood cell deficiency (leucopenia, agranulocytosis), low platelet count (thrombocytopenia) or reduced red blood cell count (anemia).
- You have dark skin, you should be aware of the fact that patients with dark skin are at high risk of developing an allergic reaction including swelling of the face, lips, tongue or throat with difficulties swallowing or breathing while taking ACE inhibitors.
- You develop a persistent dry cough.

- You are taking potassium supplements, potassium sparing medicines or potassium containing salt substitutes.
- You think you are pregnant or might become pregnant or breastfeeding (see "Pregnancy and breastfeeding" section).
- If you have intolerance to certain sugars (lactose).
- If you are taking any of the following medicines used to treat high blood pressure:
 - Angiotensin II receptor-blocker (ARBs)(also known as sartans for example Valsartan, Telmisartan, Irbesartan) especially if you have kidney problems due to diabetes.
 - aliskiren.
- Inform your treating physician about taking this medicine before undergoing: surgery or anesthesia (including dental), mechanical treatment to remove cholesterol from your blood (LDL apheresis) or treatment for reduction of allergic reactions to insect venom (e.g. bees or wasps).

If you are taking or have recently taken other medicines, including non-prescription medicines and nutrition supplements, tell the physician or the pharmacist. Especially if you are taking:

- Cyclosporin or Ciclosporin (for suppression of immune system), oral antifungal medicines (e.g. ketoconazole and itraconazole), antiviral medicines (e.g. ritonavir), antibiotics of the macrolide family (e.g. erythromycin, troleandomycin). See section 2 "Do not use this medicine if".
- Cimetidine (for stomach ulcers, at a daily dosage higher than 800 mg).
- Other medicines to treat high blood pressure such as: Angiotensin II receptor-blockers, diuretics or aliskiren, vasodilators (e.g nitroglycerin, or other organic nitrates, anaesthetics)
- Digoxin (for heart treatment), anti-arrhythmic medicines (e.g amiodarone, quinidine).
- Antidepressants (e.g. of the class of tricyclic antidepressants, lithium), antipsychotic medicines,
- Non-steroidal anti-inflammatory drugs –NSAIDs, analgesics or medicines for the treatment of rheumatoid arthritis including treatment with gold.
- Medicines for epilepsy (e.g phenytoin, carbamazepine), rifampicin (for tuberculosis),
- Medicines containing potassium or potassium supplements,
- Medicines for the treatment of cough and cold, medicines for weight loss containing a sympathomimetic component.
- Anti-diabetic medicines (including oral anti-diabetic medicines and insulin).
- Astemizole or terfenadine (medicines for allergic treatment).
- Midazolam (a medicine for sleep disorders)
- Beta blockers (medicines for the treatment of hypertension and heart problems).

Your physician may need to change your dosage and/or take other precautions if you are taking Angiotensin II receptor blockers or aliskiren (see "Special warnings" and "Do not use this medicine if" sections).

Use of this medicine and food

- Do not take this medicine with grapefruit or grapefruit juice.
- Vasodip Combo should be taken at least 15 minutes before a meal.

Use of the medicine and alcohol consumption

Alcohol may increase the effect of Vasodip Combo. Therefore it is recommended to consume no alcohol or to strictly limit your alcohol intake.

Pregnancy and breastfeeding:

- **Pregnancy:** If you think you are pregnant or might become pregnant, tell your physician. The physician will usually recommend to you to stop using Vasodip Combo before getting pregnant or once you discovered that you are pregnant and to advise you to take another medicine instead of Vasodip Combo. Vasodip Combo is not recommended during pregnancy, and must not be used during advanced pregnancy (more than 3 months), as it may cause severe harm to the fetus.
- **Breastfeeding:** Tell your physician if you are breastfeeding or intend to start breastfeeding. Breastfeeding newborn babies (in the first few weeks after birth), and especially premature babies, is not recommended whilst taking Vasodip Combo. Regarding older babies, your physician will advise you on the benefits and risks of taking Vasodip Combo while breastfeeding, as compared to other treatments.

Driving and using machines

The use of this medicine may cause dizziness, weakness, tiredness or drowsiness. If you suffer from these effects avoid driving, operating dangerous machinery or engaging in any other activity which requires alertness.

Important information about some of the ingredients of this medicine

This medicine contains lactose, if you have been previously told by a physician that you have intolerance to certain sugars, consult a physician before taking this medicine.

3. How should you use the medicine?

Always use according to the physician's instructions.
You should check with the physician or the pharmacist if you are unsure. Vasodip Combo is not intended for children and adolescents under 18 years of age.
The dosage and treatment will be determined only by the physician. The usual dosage is 1 tablet per day, taken at the same time each day.

Do not exceed the recommended dose.

The tablet should be swallowed whole with a glass of water. Vasodip Combo should be taken at least 15 minutes before a meal, preferably before breakfast.

Do not halve the tablets. There is no information about crushing/chewing.

Patients with kidney problems/ elderly: Medicine dosage will be determined by the physician and will be based on how well your kidneys are working.

Tests and follow up

The physician may examine your renal function, blood pressure and electrolyte levels (e.g. potassium) in your blood at regular time intervals.

If you forget to take your medicine at the specified time, skip the forgotten dose and take the next dose at the usual time. Never take a double dose on the same day!

If you have accidentally taken an overdose, an excessive reduction in blood pressure and rapid or irregular heart rate may occur. If you took an overdose or by mistake a child swallowed this medicine, immediately contact a physician or go to the hospital emergency room and bring the package of the medicine with you.

Persist with the treatment as recommended by the physician. Even if your condition has improved, do not discontinue treatment with the medicine without consulting the physician.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have any further questions regarding the use of this medicine, contact a physician or the pharmacist.

4. Side Effects:

Like any medicine, the use of **Vasodip Combo** may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not suffer from any of them.

Some of the side effects may be severe.

Contact your physician immediately in case of an allergic reaction with swelling of the face, lips, tongue or throat, which may cause difficulties breathing or swallowing.

At the beginning of treatment with Vasodip Combo, you may feel weak or dizzy or have blurred vision. This happens due to a sudden blood pressure drop. In such case, lie down. If you are still worried, tell your physician.

Common side effects (appear in 1 to 10 users out of 100):

Headache, dizziness, cough

Uncommon side effects (appear in 1 to 10 users out of 1000):

Changes in blood parameters such as reduction in platelet count, increase in blood potassium level, irritability (anxiety), dizziness when standing up, vertigo, fast or irregular heart rate (palpitations), sudden redness of the face, neck or chest (flushing), low blood pressure, abdominal pain, constipation, nausea, high levels of liver enzymes, skin redness, joint pain, increased urination frequency, weakness, tiredness, sensation of warmth, ankle swelling.

Rare side effects (appear in 1 to 10 users out of 10,000):

Anemia, allergic reaction, tinnitus, fainting, dry throat, sore throat, indigestion, sensation of saltiness in the tongue, diarrhea, dry mouth, swelling of the gums, allergic reaction accompanied by swelling of the face, lips, tongue or throat with difficulties swallowing or breathing, skin rash, hives, getting up at night to urinate, producing large amount of urine, impotence.

Additional side effects resulting from taking Enalapril or Lercanidipine alone

Enalapril

Very common side effects (appear in more than 1 in 10 users):

Blurred vision

Common side effects (appear in 1 to 10 users out of 100):

Depression, chest pain, changes in heart rhythm, angina pectoris, shortness of breath, altered taste sensation, increase in blood creatinine level (usually can be diagnosed in laboratory tests).

Uncommon side effects (appear in 1 to 10 users out of 1000):

Anemia (including aplastic and hemolytic anemia), sudden blood pressure drop, confusion, difficulty in sleeping or sleepiness, feeling your skin prickling or being numb, heart attack (possibly resulting from very low blood pressure in patients at risk, including those with problems of blood flow in the heart or brain), stroke (possibly resulting from very low blood pressure in patients at risk), nasal discharge, sore throat and hoarseness, asthma, slow movement of food through your intestine, inflammation of your pancreas, vomiting, gastric irritation, ulcer, anorexia, increased sweating, itching or rash, hair loss, impaired kidney function, kidney failure, high urinary protein levels (measured in a test), muscle cramps, generally feeling unwell, high fever, low blood levels of sugar or sodium, high blood levels of urea (measured in blood tests).

Rare side effects (appear in 1 to 10 users out of 10,000):

Changes in blood parameters such as decrease in white blood cell count, bone marrow suppression, autoimmune diseases, strange dreams or sleep disorders, Raynaud phenomenon (cold and pale hands and feet due to reduced blood flow), pulmonary infiltrates, nasal inflammation, pneumonia, liver problems such as reduced liver function, inflammation of your liver, jaundice (yellowing of the skin or the eyes), high bilirubin levels (measured in blood tests), erythema multiforme (red spots of various shapes on the skin), Stevens Johnson's syndrome (a serious skin condition with skin redness and peeling, blisters and raw sores, or detachment of the upper skin layer from the lower layers), reduced urine output, enlargement of the mammary glands in males.

Very rare side effects (appear in less than 1 users out of 10,000):

Intestinal swelling (intestinal angioedema).

Lercanidipine

Rare side effects (appear in 1 to 10 users out of 10,000):

Angina pectoris (chest pain due to deficient blood supply to the heart), vomiting, heartburn, muscle pain.

Very rare side effects (appear in less than 1 users out of 10,000):

Chest pain.

Patients with pre-existing angina pectoris may experience an increase in the frequency, duration or severity of the attacks due to the use of medicines of the class to which Lercanidipine belongs. Isolated cases of heart attack may occur.

Side effects can be reported to the Ministry of Health by clicking on the link [לדווח על תופעות לוואי עקב טיפול תרופתי](https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il) that can be found on the home page of the Ministry of Health website (www.health.gov.il) directing to the online form of adverse events reporting or via the following link: <https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il>.

5. How to store the medicine?

- **Avoid poisoning!** This medicine and any other medicine should be kept in a safe place out of the reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the physician.
- Do not use the medicine after the expiration date (Exp. Date) appearing on the package. The expiration date refers to the last day of that month.
- Store this medicine in its original package at a temperature below 25°C.
- Do not store different medicines in the same package.

6. Additional information

In addition to the active ingredients, the medicine also contains:
Lactose monohydrate, Cellulose microcrystalline, Sodium starch glycolate, Povidone, Sodium hydrogen carbonate, Hypromellose, Magnesium stearate, Titanium dioxide (E171), Talc, Macrogol 6000.

Vasodip Combo 20 contains in addition:

Quinoline yellow aluminium lake (E104), Iron oxide yellow (E172)

Each Vasodip Combo 10 tablet contains about 97 mg lactose.

Each Vasodip Combo 20 tablet contains about 87 mg lactose.

What does the medicine look like and what is the content of the package:

Vasodip Combo 10: White, round biconvex tablets.

Vasodip Combo 20: Yellow, round biconvex tablets.

Approved pack sizes: 10, 14, 15, 20, 28, 30 tablets. Not all pack sizes may be marketed.

This leaflet was checked and approved by the Ministry of Health on: 10/2015

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Vasodip Combo 10: 141 06 31726 00

Vasodip Combo 20: 141 05 31727 00

For simplicity and to make the reading easier, this leaflet has been formulated in the male language. However, the medicine is intended for both sexes.

Name and address of the manufacturer and Marketing Authorization Holder: Dexcel Ltd., 1 Dexcel St., Or-Akiva 3060000, Israel

Manufacturer and registration holder: **Dexcel® Ltd**

1 Dexcel St., Or-Akiva 3060000, Israel