



Patient package insert according to the Pharmacists' Regulations (Preparations)- 1986

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

VASODIP[®] COMBO 10, 20, Tablets

Each tablet contains Lercanidipine hydrochloride 10 mg and Enalapril maleate 10 mg or 20 mg respectively.

Inactive ingredients and allergens in the medicine – see section 6 “Additional information” and in section 2 “Important information about some of the ingredients of the medicine”.

Read this entire leaflet carefully before using the medicine. This leaflet contains concise information about this medicine. If you have any further questions, ask the doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it to others. It may harm them, even if it seems that their medical condition is similar to yours.

Vasodip Combo is not intended for primary treatment of hypertension.

1. What is the medicine intended 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 the medicine

Do not use the medicine if:

- You are hypersensitive (allergic) to the active ingredients (Enalapril maleate or Lercanidipine hydrochloride) or to any of the other ingredients this medicine contains (see section 6).
- You have ever had an allergic reaction to a type of medicine similar to those contained in **Vasodip Combo**, i.e. medicines called ACE inhibitors or calcium channel blockers.
- You have ever had swelling of your face, lips, mouth, tongue or throat which caused difficulty in swallowing or breathing (angioedema) after taking an ACE inhibitor medicine or due to an unknown reason or due to a hereditary reason.
- You take sacubitril/valsartan, a medicine used to treat a type of long-term (chronic) heart failure in adults, as the risk of angioedema (rapid swelling under the skin in an area such as the throat) is increased.
- You have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren.
- You are more than 3 months pregnant (It is advised to avoid using **Vasodip Combo** also in early pregnancy, see section "Pregnancy, breastfeeding and

fertility").

- You suffer from certain heart diseases: obstruction to the blood flow from the heart, untreated heart failure, unstable angina (chest discomfort occurring at rest or progressively increasing), a heart attack within the last month.
- You have severe liver problems.
- You have severe kidneys problems, or you are undergoing dialysis.
- You take medicines that are hepatic metabolism inhibitors, such as antifungal medicines (e.g. ketoconazole, itraconazole), macrolide antibiotics (e.g. erythromycin, troleandomycin, clarithromycin), antiviral medicines (e.g. ritonavir).
- You take a medicine called ciclosporin (used after transplants to prevent organ rejection).
- You consume grapefruits or grapefruit juice.

Special warnings regarding the use of the medicine:

Before the treatment with Vasodip Combo, tell the doctor if:

- You have low blood pressure (manifested by symptoms such as fainting or dizziness especially when standing up).
- You have recently suffered from severe vomiting or diarrhea.
- You are on a salt restricted diet.
- You have a heart problem.
- You have a condition involving the blood vessels in the brain.
- You have kidney problems (including kidney transplantation). This may lead to higher levels of potassium in your blood which can be serious. The doctor may need to adjust the dose of enalapril or monitor the blood level of potassium.
- You have a liver problem.
- You have a blood problem such as: low level or lack of white blood cells (leucopenia, agranulocytosis), low platelet count (thrombocytopenia), or decreased red blood cell count (anemia).
- You have a connective tissue disease with blood vessels involvement (e.g. lupus erythematosus, rheumatoid arthritis or scleroderma), you are on therapy that suppresses the immune system, you use the medicines allopurinol or procainamide or any combination of these.
- You are a black patient, you should be aware that black patients are at increased 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 have diabetes. You should monitor your blood sugar for low glucose levels, especially during the first month of treatment. The level of blood potassium can also be higher.
- You are taking potassium supplements, potassium sparing medicines or potassium containing salt substitutes.
- You are over 70 years of age.

If you are taking any of the following medicines, the risk of angioedema may be increased:

- Racecadotril, a medicine used to treat diarrhea;
- Medicines used to prevent organ transplant rejection and for cancer (e.g., temsirolimus, sirolimus, everolimus).
- Vildagliptin, a medicine used to treat diabetes.

If you are taking any of the following medicines used to treat high blood pressure:

- An angiotensin II receptor-blocker (ARBs) e.g.: (valsartan, telmisartan, irbesartan),

- especially if you have kidney problems due to diabetes.
- Aliskiren.

Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g. potassium) in your blood at regular intervals. See also section "Do not use the medicine if".

If you are about to have a procedure

If you are about to have any of the following, tell the doctor you are taking **Vasodip Combo**:

- Surgery or receive anesthetics (including at the dentist).
- A treatment to remove cholesterol from the blood called LDL apheresis.
- Treatment to reduce allergic reactions to bees or wasps stings.

You must tell the doctor if you think you are pregnant, might become pregnant or breastfeeding (see section "Pregnancy, breastfeeding and fertility").

Children and adolescents

The safety and efficacy of this medicine in children aged up to 18 years have not been established.

Drug interactions

Vasodip Combo must not be taken with certain medications.

If you are taking, have recently taken or might take other medicines including non-prescription medicines and nutrition supplements, tell the doctor or pharmacist. This is because when **Vasodip Combo** is taken in combination with other medicines, the effect of **Vasodip Combo** or of the other medicine may be changed, or certain side effects may occur more frequently.

Especially tell the doctor or pharmacist if you are taking:

- Other medicines to lower blood pressure.
- Potassium supplements (including salt substitutes), potassium sparing diuretics, other medicines that can increase blood potassium level (e.g. trimethoprim and co-trimoxazole to treat infections caused by bacteria; ciclosporin, an immunosuppressant medicine used to prevent organ transplant rejection; heparin, a medicine used to thin blood to prevent clots). See in section 2 "Do not use the medicine if".
- Lithium (a medicine used to treat a certain kind of depression).
- Antidepressant medicines called tricyclic antidepressants.
- Medicines for mental problems called antipsychotics.
- Non-steroidal anti-inflammatory medicines including COX-2 inhibitors (medicines to reduce inflammation and relieve pain).
- Certain medicines for pain relief or for rheumatoid arthritis, including gold therapy.
- Medicines to treat cough and cold and medicines for weight loss containing a sympathomimetic component.
- Anti-diabetic medicines (including oral medicines and insulin).
- Astemizole or terfenadine (medicines to treat allergies).
- Amiodarone, quinidine or sotalol (medicines to treat a fast heart beat).
- Phenytoin, phenobarbital or carbamazepine (medicines to treat epilepsy).
- Rifampicin (a medicine to treat tuberculosis).

- Digoxin (medicines to treat heart problems).
- Midazolam (a medicine for sleep disorders).
- Beta blockers e.g. metoprolol (a medicine to treat hypertension, heart failure and abnormal heart rhythm).
- Cimetidine (at a dose higher than 800 mg, a medicine for stomach ulcers, digestive problems or heartburn).

Do not take **Vasodip Combo** if you take sacubitril/valsartan, a medicine used to treat a type of long-term (chronic) heart failure in adults, as the risk of angioedema (rapid swelling under the skin in an area such as the throat) is increased.

If you are taking any of the following medicines, the risk of angioedema may be increased:

- Racecadotril, a medicine used to treat diarrhea.
- Medicines used to prevent organ transplant rejection and for cancer (e.g., temsirolimus, sirolimus, everolimus).
- Vildagliptin, a medicine used to treat diabetes.

The doctor may need to change your dosage and/or to take other precautions if:

- you are taking an angiotensin II receptor-blockers or aliskiren (see section "Do not use the medicine if" and "Special warnings regarding the use of the medicine").

Use of the medicine and food

- **Vasodip Combo** should be taken at least 15 minutes before a meal.
- A high fat meal significantly increases blood levels of the medicine.
- Do not take **Vasodip Combo** with grapefruit or grapefruit juice as they can increase its hypotensive effect (see "Do not use the medicine if").

Use of the medicine and alcohol consumption

Alcohol may increase the effect of **Vasodip Combo**. Do not consume alcohol during treatment with **Vasodip Combo**.

Pregnancy, breastfeeding and fertility

Pregnancy and fertility

You must tell your doctor if you think you are pregnant or might become pregnant. The doctor will usually advise you to stop taking **Vasodip Combo** before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of **Vasodip Combo**.

Vasodip Combo is not recommended during pregnancy and must not be used if you are more than 3 months pregnant, as it may cause serious harm to the fetus if used after the third month of pregnancy.

Breastfeeding

Vasodip Combo should not be used during breastfeeding.

Driving and using machines

If you feel dizziness, weakness or drowsiness while taking this medicine, do not drive a vehicle or operate machines.

Important information about some of the ingredients of the medicine

This medicine contains lactose. If you have been told by a doctor that you have an intolerance to some sugars, consult a doctor before starting treatment with this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially "sodium-free".

3. How to use the medicine?

Always use the medicine according to the doctor's instructions.

Check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.

The dosage and manner of treatment will be determined by the doctor only.

Adults: the usual recommended dosage is 1 tablet per day, at the same time. 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. See in section 2 "Use of medicine and food".

Children: the medicine is not intended for treatment of children and adolescents under 18 years of age.

Patients with kidney problems/elderly: the medicine dosage will be determined by the doctor according to the function of your kidneys.

Do not exceed the recommended dose.

Do not halve the tablets since there is no score line. There is no information about crushing/chewing.

If you have accidentally taken a higher dosage, an excessive decrease in blood pressure and irregular or rapid heart rate may occur.

If you have taken an overdose or if a child has accidentally swallowed this medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine

If you forget to take the medicine at the designated time, skip the forgotten dose. Take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

Continue with the treatment as recommended by the doctor. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

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 further questions on the use of this medicine, consult the doctor or pharmacist.

4. Side Effects:

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

Some side effects may be serious.

Refer to a doctor 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 start of **Vasodip Combo** treatment, you might feel faint or dizzy or have blurred vision. This happens due to a sudden blood pressure drop. In this case, lie down. If you are worried, tell your doctor.

Side effects observed with Vasodip Combo

Common side effects (effects that occur in 1-10 out of 100 users):

- Cough
- Dizziness, headache

Uncommon side effects (effects in 1-10 out of 1,000 users):

- Changes in blood values such as decrease in platelet count
- Increase in blood potassium level
- Nervousness (anxiety)
- Feeling dizzy when standing up, vertigo
- Fast heartbeat or heartbeat awareness (palpitations)
- Sudden reddening 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
- Feeling weak, tiredness, feeling hot, ankle swelling.

Rare side effects (effects that occur in 1-10 out of 10,000 users):

- Anemia
- Allergic reactions
- Ringing in your ears (tinnitus)
- Fainting
- Dry throat, sore throat
- Indigestion, salty sensation on 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 amounts of urine
- Impotence

Additional side effects observed with Enalapril or Lercanidipine alone

Enalapril

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

Blurred vision, dizziness, weakness or nausea and cough.

Common side effects (effects that occur in 1-10 out of 100 users):

Depression, headache, fainting (syncope), chest pain, dizziness due to low blood pressure, changes in heart rhythm, fast heartbeat, angina, shortness of breath, change in sense of taste,

increase in blood creatinine level (usually detected by a test), high level of blood potassium, diarrhea, abdominal pain, tiredness (fatigue), rash, allergic reaction with swelling of the face, lips, tongue or throat with difficulty in swallowing or breathing.

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):

Anemia (including aplastic and hemolytic anemia), sudden drop in blood pressure, confusion, nervousness, sleeplessness or sleepiness, feeling your skin prickling or being numb, heart attack (possibly due to very low blood pressure in patients at risk, including those with blood flow problems in the heart or brain), stroke (possibly due to very low blood pressure in patients at risk), runny nose, sore throat and hoarseness, asthma associated tightness in chest, slow movement of food through your intestine, pancreas inflammation, vomiting, indigestion, constipation, gastric irritation, dry mouth, ulcer, anorexia, itching or rash (hives), hair loss, impaired kidney function, kidney failure, increased sweating, high protein levels in the urine (measured in a test), muscle cramps, generally feeling unwell, high fever, low levels of blood sugar or sodium, high level of blood urea (measured in blood tests), flushing, heartbeat awareness (palpitations), vertigo (spinning sensation), ringing in the ears (tinnitus), impotence.

Rare side effects (effects that occur in 1-10 out of 10,000 users):

Changes in blood values such as decrease in white blood cell count, bone marrow suppression, autoimmune diseases, strange dreams or sleep problems, Raynaud phenomenon (cold and pale hands and feet due to reduced blood flow), nasal inflammation, pneumonia, liver problems such as decreased liver function, inflammation of the liver, jaundice (yellowing of the skin or the eyes), high levels of liver enzyme or bilirubin (measured in a blood tests), erythema multiforme (red spots of different shapes on the skin), Stevens Johnson's syndrome and toxic epidermal necrolysis (a serious skin condition with skin redness and peeling, blisters and raw sores), exfoliative dermatitis/erythroderma (severe skin rash with flaking or peeling skin), pemphigus (small fluid-filled bumps on the skin), reduced urine output, enlargement of the mammary glands in males (gynecomastia), swollen glands in neck, armpit or groin, accumulation of fluid or other substances in the lungs (as seen on X-rays), inflammation of the cheeks, gums, tongue, lips, throat.

Very rare side effects (effects that occur in less than 1 in 10,000 users):

Intestinal swelling (intestinal angioedema).

Side effects with unknown frequency (effects for which a frequency has not yet been determined):

Over production of antidiuretic hormone, which causes fluid retention, resulting in weakness, tiredness or confusion. A symptom complex has been reported which may include some or all of the following: fever, inflammation of blood vessels (serositis/vasculitis), muscle pain (myalgia/myositis), joint pain (arthralgia/arthritis). Rash, photosensitivity or other skin manifestations may occur.

Lercanidipine

Some side effects can be serious.

If any of the following happen, refer to a doctor immediately:

Rare side effects (effects that occur in 1-10 out of 10,000 users):

Angina pectoris (chest pain due to lack of blood supply to the heart), allergic reactions (symptoms include itching, rash, urticaria), fainting.

Patients with pre-existing angina pectoris may experience increased frequency, duration or severity of the attacks with the group of medicines to which Lercanidipine belongs. Isolated cases of heart attack have been observed.

Other possible side effects

Common side effects (effects that occur in 1-10 out of 100 users):

Headache, fast heart rate, heartbeat awareness (palpitations), sudden reddening of your face, neck or upper chest (flushing), ankle swelling.

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):

Dizziness, fall in blood pressure, heartburn, nausea, stomach pain, skin rash, itching, muscle pain, passage of large amounts of urine, feeling weak or feeling tired.

Rare side effects (effects that occur in 1-10 out of 10,000 users):

Sleepiness, vomiting, diarrhea, hives, increased frequency of urination, chest pain.

Side effects with unknown frequency (effects for which a frequency has not yet been determined):

Swelling of gums, changes in liver function (detected by blood tests), cloudy fluid (when performing dialysis through a tube into your abdomen), swelling of your face, lip, tongue or throat, which may cause difficulty in breathing or swallowing.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect which is not mentioned in this leaflet, consult the doctor.

Side effects can be reported to the Ministry of Health by clicking the link

"דיווח על תופעות לוואי עקב טיפול תרופתי" found on the homepage of the Ministry of Health website (www.health.gov.il) directing to the online form for reporting side effects or via the link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be stored in a closed place out of the reach of sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (תאריך תפוגה) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** Store in original package at a temperature below 25°C.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

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 also contains:

Quinoline yellow aluminium lake (E104), iron oxide yellow (E172).

What the medicine looks like and what the package contains:

Vasodip Combo 10: White, round biconvex tablets.

Vasodip Combo 20: Yellow, round biconvex tablets.

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

Revised in March 2023 according to MOH guidelines.

Drug registration number at the national drug registry of the Ministry of Health:

Vasodip Combo 10: 141-06-31726-00

Vasodip Combo 20: 141-05-31727-00

Manufacturer and registration holder: Dexcel Ltd., 1 Dexcel St., Or Akiva 3060000, Israel