

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

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

Enaladex 5, 10, 20 mg, Tablets

Each tablet contains Enalapril maleate at a dosage of 5, 10 or 20 mg, respectively.

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

Read the entire leaflet carefully before you start using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask your doctor or pharmacist. This medicine has been prescribed for the treatment of your illness. Do not pass it on to others. It might harm them, even if you think that their medical condition is similar to yours.

1. What is the medicine intended for?

This medicine causes the blood vessels to dilate and thus assists in lowering blood pressure. In addition, the medicine is intended to treat heart failure (reduction in heart function).

Some people will require several weeks of treatment until the best effect on their blood pressure is achieved.

Therapeutic group: vasodilator of the angiotensin converting enzyme inhibitor type (ACE Inhibitor).

2. Before using the medicine:

Do not use the medicine if:
<ul style="list-style-type: none">You are hypersensitive (allergic) to the active ingredient (Enalapril maleate), other medicines similar to Enalapril from the ACE inhibitor group or to any of the other ingredients the medicine contains (see section 6).A member of your family has had an allergic reaction to Enalapril or to any of the other medicines from the ACE inhibitor group or if you ever suffered from swelling of the face, eyelids, lips, mouth, tongue or throat, which caused difficulty in swallowing or breathing (angioedema) due to an unknown cause or it was hereditary.You have diabetes or suffer from kidney problems and are taking a medicine that contains aliskiren for lowering of blood pressure.You are more than three months pregnant (it is also better to avoid taking Enalapril in early pregnancy, see section 2 "Pregnancy, breastfeeding and fertility").You are taking sacubitril/valsartan, a medicine to treat chronic heart failure in adults, as the risk of angioedema (rapid swelling under the skin, for example, in the throat area) increases. <p>Do not take Enalapril if any of the above applies to you. If you are not sure, consult the doctor before taking this medicine.</p>

Special warnings regarding the use of the medicine:

- Before treatment with Enaladex, tell the doctor if:

- You have low blood pressure (may be expressed as faintness or dizziness, especially when standing up).
- You have problems involving the blood vessels in the brain.
- You suffer from a heart problem.
- You have kidney problems (including kidney transplantation), you are on a salt-restricted diet, are taking potassium supplements, potassium-sparing medicines, salt substitutes that contain potassium or other medicines that may elevate blood potassium levels (such as heparin [a medicine to prevent blood clot formation], medicines containing trimethoprim

such as co-trimoxazole [a medicine to treat infections]). These medicines may cause a high level of blood potassium, which can be serious. The doctor may need to monitor your blood potassium level or adjust the dose of Enalapril accordingly. See additional information in section "Drug interactions".

- You have a liver problem.
- You have a blood problem such as: low level or lack of white blood cells (neutropenia/agranulocytosis), low platelet level (thrombocytopenia), low red blood cell level (anemia).
- You have ever had an allergic reaction (angioedema), the symptoms include: itching, red marks on the hands, feet and throat, swelling of the face, around the eyes, lips, tongue or throat with swallowing or breathing difficulties. Note that black patients are at increased risk of these reactions with ACE inhibitor treatment.
- You are undergoing dialysis treatment.
- You have recently suffered from excessive vomiting or diarrhea.
- You suffer from diabetes. You must monitor your blood for low blood sugar levels, especially during the first month of treatment. The level of potassium in your blood can also be higher.
- You suffer from a collagen vascular disease such as: lupus erythematosus, rheumatoid arthritis, scleroderma, are taking immunosuppressant medicines, are taking the medicines allopurinol or procainamide or any combination of these factors.
- You are taking any of the following medicines, the risk of angioedema may increase:
 - Racecadotril, a medicine to treat diarrhea.
 - Medicines to prevent transplant rejection and to treat cancer (such as temsirolimus, sirolimus, everolimus).
 - Vildagliptin, a medicine to treat diabetes.
- You are taking any of the following medicines to treat high blood pressure:
 - Medicines from the angiotensin II receptor blocker group (ARBs, such as valsartan, telmisartan, irbesartan), especially if you suffer from diabetes-related kidney problems.
 - Aliskiren.

Your doctor may periodically monitor your kidney function, blood pressure and blood electrolytes level (such as potassium). Also see in section 2 "Do not use the medicine if".

Tell your doctor if you think you may be pregnant or planning to conceive. This medicine is not recommended in early pregnancy. Do not take the medicine after the third month of pregnancy, since using the medicine at this stage may cause serious harm to the baby (see in section 2 "Pregnancy, breastfeeding and fertility" and "Do not use the medicine if").

Note that the medicine lowers the blood pressure in black patients less effectively compared to other patients.

If you are not sure if the above applies to you, consult the doctor or pharmacist before taking the medicine.

If you are about to have surgery
Tell the attending doctor about taking this medicine prior to undergoing the following procedures: any type of surgery or anesthetic (even at the dentist), treatment to remove blood cholesterol (LDL apheresis) or treatment to reduce an allergic reaction to bee or wasp stings.

If one or more of the above applies to you, consult the doctor or dentist prior to procedure.

Drug interactions:

If you are taking, have recently taken or might

take other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist, because Enalapril can affect the way some medicines work and some medicines can affect the way Enalapril works. The doctor may change the dosage of Enalapril and/or take additional safety measures.

Tell the doctor or pharmacist especially if you are taking:

- potassium supplements (including salt substitutes), potassium-sparing diuretics, such as spironolactone, triamterene or amiloride and other medicines that may elevate blood potassium levels (such as trimethoprim and co-trimoxazole for the treatment of bacterial infections; cyclosporine, an immunosuppressant medicine to prevent transplant rejection, and heparin, a medicine used to thin blood to prevent blood clot formation). See additional information in section "Special warnings regarding use of the medicine".

- other medicines used to lower blood pressure such as: beta blockers, diuretics (such as thiazides, furosemide, bumetanide), or medicines to treat chest pain (angina pectoris), such as nitrates. Taking these medicines concomitantly with Enalapril may cause low blood pressure.
- angiotensin II receptor blockers (ARB) or aliskiren. See also in section 2 "Do not use the medicine if" and "Special Warnings regarding the use of the medicine".
- lithium (to treat some types of mental illness).
- tricyclic antidepressants, antipsychotic medicines (to treat serious mental illness), anesthetics, narcotics, such as morphine (to relieve severe pain). Taking these medicines concomitantly with Enalapril may cause low blood pressure.
- medicines used to treat stiffness and inflammation associated with painful conditions, particularly those affecting the muscles, bones and joints:
 - Non-steroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors (used to reduce inflammation, to help relieve pain).
 - Gold salts therapy, which can cause flushing of the face, nausea, vomiting and low blood pressure, if given concomitantly with Enalapril.
- mTOR inhibitors (such as temsirolimus, sirolimus, everolimus: medicines used to treat certain types of cancer or to prevent the body's immune system from rejecting a transplanted organ). See also in section 2 "Special Warnings regarding the use of the medicine".

- medicine containing neprilysin inhibitor, such as sacubitril (available in a combined product with valsartan), racecadotril or vildagliptin. The risk of angioedema (swelling of the face, lips, tongue or throat with swallowing or breathing difficulties) may increase. See also in section 2 "Do not use the medicine if" and "Special Warnings regarding the use of this medicine".
- aspirin (acetylsalicylic acid).
- medicines used to dissolve blood clots (thrombolytics).
- cough and cold medicines and weight reducing medicines, which contain sympathomimetic agent.
- medicines for diabetes (including oral medicines and insulin). Enalapril may cause a sharp decrease in blood sugar levels when taken concomitantly with these medicines, especially during the first weeks of treatment and in patients with kidney problems. You should closely monitor your blood sugar level during the first month of treatment with Enalapril.

If you are not sure if the information above applies to you, consult the doctor or pharmacist before taking the medicine.

If you are about to receive anesthesia (for surgery), tell the doctor or dentist you are taking Enalapril.

The dosage will be determined by your doctor and adjusted, depending on your kidney function.

Use of this medicine and food:

You can take this medicine with or without food.

Use of this medicine and alcohol consumption: If you consume alcohol during treatment with Enalapril, it may cause a significant decrease in blood pressure and feeling dizzy or fainting. Be careful with the amount of alcohol you consume.

Pregnancy, breastfeeding and fertility:

If you are pregnant or breastfeeding, think you may be pregnant or are planning to conceive, consult the doctor before taking this medicine. The doctor will usually advise you to stop taking the medicine before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Enalapril. The medicine is not recommended in early pregnancy, and use of it is forbidden after the third month of pregnancy as it may cause serious harm to your baby if taken after the third month of pregnancy.

Consult your doctor if you are breastfeeding or planning to breastfeed. Breastfeeding newborn babies (during the first weeks after the birth), and especially premature babies, is not recommended whilst taking the medicine.

In the case of an older baby your doctor will advise you on the benefits and risks of taking Enalapril whilst breastfeeding, compared to alternative treatments options.

Driving and use of machinery:

The use of this medicine may cause tiredness or dizziness. In such cases, do not drive or use machinery. As for children, they should be warned against riding a bicycle or playing near roads etc.

Important information about some of the ingredients of this medicine:

This medicine contains lactose, if you have been told by the doctor that you have intolerance to some sugars, contact the doctor before starting treatment with this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, i.e. it is essentially "sodium-free".

3. How to use this medicine

Always use this medicine according to doctor's instructions. You must check with your 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, according to your medical condition and any other medicines you are taking. Swallow the medicine with water. The medicine can be taken with or without food.

Take the medicine at approximately the same time every day.

The tablet can be halved, there is no information regarding crushing/chewing.

At the beginning of treatment with the medicine, a more significant decrease in blood pressure is possible than with the doses you take after that. At the beginning of treatment with the medicine you may feel dizziness. It may help to lie down until you feel better. These effects become less likely with future doses. If you are concerned, consult the doctor or pharmacist.

The doctor will check how you respond to Enalapril by measuring your blood pressure and performing certain blood tests.

Patients with kidney problems

If you suffer from kidney problems, the doctor will adjust Enalapril dosage depending on kidney function.

If you are undergoing dialysis, the medicine dosage may vary day by day. The doctor will instruct you on the appropriate dose.

Elderly patients

The dosage will be determined by your doctor and adjusted, depending on your kidney function.

Use in children

The experience with the use of this medicine in children with high blood pressure is limited. For other indications, there is no experience at all in children.

The dosage will be determined by the doctor, according to the child's weight and the change in child's blood pressure after taking Enalapril. Use of the medicine is not recommended in infants and children with kidney problems.

Use of the medicine is not recommended in very young babies (in the first few weeks after birth).

Do not exceed the recommended dose.

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

The most common symptoms and signs of an overdose are: a sharp drop in blood pressure, stupor. Additional symptoms may include: dizziness due to decreased blood pressure, strong and rapid heartbeat, anxiety, cough, kidney failure and rapid breathing.

If you forgot to take the medicine

If you forgot to take this medicine at the designated time, do not worry. Take the next dose at the usual time. Do not take a double dose to compensate 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 the treatment with the medicine without consulting the doctor.

If you stop taking the medicine

If you stop taking the medicine, your blood pressure may elevate. If your blood pressure elevates too high, it may affect your heart and kidneys functions. Do not stop taking this medicine unless the doctor has instructed you to do so.

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 **Enaladex** can 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.

Stop taking this medicine and refer to the doctor or to a hospital emergency room immediately with the appearance of:

- Itching, red raised skin rash (hives), shortness of breath or wheezing, swelling of the hands, feet or ankles, face, eyes, mouth, lips, tongue or throat which may cause breathing or swallowing difficulties. Be aware that black patients are at increased risk of these types of reactions.
- Rash with target like lesions, blisters, skin peeling, which may also appear on the lips, eyes, mouth, nose, and/or genitals. You may also suffer from a high fever, or joint pain (erythema multiforme).
- Severe skin reaction, which is manifested by symptoms such as: skin redness, skin peeling, blisters and raw sores, detachment of the top layer of the skin (Stevens-Johnson syndrome, toxic epidermal necrolysis).
- A bloating feeling, pain and abdominal cramps (may be caused by a bowel obstruction).
- Heart attack or stroke may occur due to a very low blood pressure in certain high-risk patients (patients suffering from problems with blood circulation to the heart or brain).
- Severe abdominal pain (may be caused by inflammation of the pancreas).

- Blood disorders which may affect the cells and other elements in the blood that are usually diagnosed by blood tests (symptoms may include: tiredness, weakness, shortness of breath, inability to exercise, exhaustion, having prolonged or recurring colds, fever, chills, prolonged bleeding, hemorrhage, due to unknown cause, red or purple spots on the skin).
- Fluid in the lung, which may cause symptoms such as: cough, breathing difficulties.

- High fever, tiredness, loss of appetite, abdominal pain, nausea, jaundice (yellowing of the skin or eyes) and liver failure. These are symptoms of hepatitis (inflammation of the liver) or bile duct obstruction (a stop in bile flow from the bile duct in the liver).

At the beginning of treatment with Enalapril, you may feel faint or dizzy. If this happens, it will help to lie down. These effects are caused by lowered blood pressure and should improve as you continue to take the medicine. If you are worried, consult a doctor.

Refer to a doctor immediately if any of the following serious side effects appear:

- A combination of some or all of the following signs:
 - High fever, inflammation of blood vessels, pain and inflammation of muscles or joints
 - Blood disorders, affecting the components of blood (usually detected by blood tests)
 - Rash, hypersensitivity to sunlight and other cutaneous effects

Additional side effects:

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

- Blurred vision
- Dizziness
- Cough
- Nausea
- Weakness

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

- Headache
- Depression
- Low blood pressure, which may cause slight dizziness
- Fainting (syncope)
- Changes in heart rhythm
- Rapid heartbeat
- Chest pain or angina pectoris
- Breathing difficulties
- Diarrhea
- Abdominal pain
- Changes in the sense of taste
- Rash
- Tiredness
- An allergic reaction with swelling of the face, lips, tongue or throat with swallowing or breathing difficulties
- Increased blood potassium level, increased levels of blood creatinine (usually diagnosed by a test)

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

- Tiredness and low hemoglobin or red blood cell levels (anemia)
- Low blood sugar levels that may cause anxiety, a sense of heightened awareness or a shaky feeling
- Low blood sodium level, a high level of blood urea (measured in a blood test)
- Sudden drop in blood pressure
- Confusion
- Sleepiness or insomnia
- Nervousness
- Tringling, feeling "pins and needles", prickling, numbness in the skin
- Vertigo (spinning sensation)
- Rapid and strong or irregular heartbeat (palpitations)
- Runny nose
- Sore throat and hoarseness
- Coughing and/or wheezing and/or breathing difficulties (asthma)

- Slow transit of food through the intestine, inflammation of the pancreas, which may cause symptoms such as severe pain in the abdomen and back

- Vomiting, indigestion, constipation, loss of appetite
- Stomach irritation, dry mouth, peptic ulcer (symptoms may be: burning, pain with an empty feeling and hunger, particularly when the stomach is empty)
- Excessive sweating
- Itching
- Itchy rash or hives
- Hair loss
- Reduced kidney function or kidney failure (symptoms may be: lower back pain and reduction in the volume of urine passed)
- High level of protein in the urine, usually diagnosed by a blood test
- Impotence (sexual function problems in men)
- Muscle cramps
- Flushing
- Ringing in the ears (tinnitus)
- High fever
- Generally feeling unwell
- Low blood pressure (may cause dizziness when standing up)
- Heart attack (may occur due to a very low blood pressure in certain high-risk patients, including patients, suffering from problems with cardiac or cerebral blood circulation)
- Stroke (may occur due to a very low blood pressure in high-risk patients)

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

- Weird dreams, sleep disorders
- Raynaud's phenomenon (blood vessel spasm, usually in fingers and toes, causing paleness or red-blue patches and cold feeling in the skin)
- Changes in blood test results such as: low number of white and red blood cells, low hemoglobin, low blood platelets level
- Pulmonary infiltrate (accumulation of fluid or other substances in lungs, visible on X-ray), pneumonia (manifested by signs of cough, high fever and breathing difficulties)
- Nasal inflammation
- Pain, inflammation and/or ulceration in gums, cheeks, tongue, lips, throat
- Liver or gallbladder problems such as: decrease in liver function, inflammation of the liver, which may cause jaundice (yellowing of the skin or eyes), elevated levels of liver enzymes or bilirubin (measured in blood tests)
- Reduction in the total amount of urine, produced per day
- Breast enlargement in men
- Bone marrow depression
- Autoimmune diseases
- Exfoliative dermatitis/erythroderma (severe skin rash with peeling of the skin), pemphigus (small, fluid-filled bumps on the skin)
- Swollen lymph nodes in the neck, armpit or groin

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

- Intestinal swelling (intestinal angioedema). Signs may include abdominal pain, nausea, vomiting.

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

- Overproduction 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 symptoms: high fever, inflammation of blood vessels (serositis/

- vasculitis), muscle pain (myalgia/myositis), joint pain (arthralgia/arthritis), rash, photosensitivity or other skin reactions.

If a side effect appears, 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 via the link

"דיווח על תופעות לוואי עקב טיפול תרופתי" 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://sideeffects.health.gov.il/>

Blood tests

Enalapril may affect some of blood test results, including: blood cells or other elements in the blood, potassium levels, creatinine or urea, sodium, liver enzymes or bilirubin.

Before a blood test, it is very important you inform your doctor you are taking Enalapril.

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 and 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 התפוגה), stated on the package. The expiry date refers to the last day of that month.

- Storage conditions:** store in a dry place, below 25°C.

- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines no longer in use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:

Lactose monohydrate, starch pregelatinized, maize starch, sodium hydrogen carbonate, magnesium stearate.

Enaladex 10 mg and Enaladex 20 mg tablets also contain Iron oxide red (E172)

What the medicine looks like and content of the package:

Enaladex 5 mg: white, round tablets, curved on both sides, with a score line on one side.
Enaladex 10 mg: pink, round tablets, curved on both sides, with a score line into quarters on one side.

Enaladex 20 mg: pink, round tablets, curved on both sides, with a score line into quarters on one side.

Approved package sizes: 5, 7, 10, 14, 20, 28, 30 tablets. Not all package sizes may be marketed. Revised in January 2022 according to MOH guidelines.

Drug registration numbers at the national drug registry of the Ministry of Health:
Enaladex 5 mg: 115 84 29809 00
Enaladex 10 mg: 115 85 29810 00
Enaladex 20 mg: 115 86 29811 00

Enaladex 5, 10, 20 PIL PB0122-11

Manufacturer and registration holder:

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