PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Ramitens 10

Capsules

Active ingredient:

Each Ramitens 10 capsule contains: Ramipril 10 mg.

Inactive ingredients: see section 6. See also 'Important information about some of the medicine's ingredients' in section 2.

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

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

1. What is the medicine intended for?

The medicine is used to treat hypertension, to reduce the risk of heart attack or stroke, to reduce the risk or to delay the worsening of kidney problems (in diabetic or nondiabetic patients), to treat heart failure, as treatment following a heart attack complicated with heart failure.

Therapeutic Group: Antihypertensive, belongs to the ACE inhibitors group.

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient ramipril or to another medicine from the ACE inhibitors group, or to any of the additional ingredients the medicine contains (see section 6). Signs of an allergic reaction may include: rash, swallowing or breathing difficulties, swelling of the lips, face, throat or tongue.
- You suffered in the past from a serious allergic reaction called angioedema, whose signs include: itching, hives (urticaria), red spots on the hands, feet and throat, swelling of the throat and tongue, swelling around the eyes and of the lips, breathing and swallowing difficulties.
- You have taken or are currently taking sacubitril/valsartan, a medicine used to treat a type of chronic heart failure in adults.
- You are undergoing dialysis or another type of blood filtration. Depending on the type of machine in use, Ramitens may not be suitable for you.
- You suffer from a kidney problem where the blood supply to the kidney is reduced - renal artery stenosis.
- You are in the last six months of pregnancy (see 'Pregnancy, breastfeeding and fertility' section).
- You suffer from low or unstable blood pressure. This will be evaluated by the doctor.
- You suffer from diabetes or impaired kidney function and are treated with a blood pressure lowering medicine containing aliskiren.

Do not take Ramitens if the mentioned above applies to you. In case of doubt, consult with the doctor before taking Ramitens.

Special warnings regarding the use of this medicine:

Before beginning treatment with the medicine, tell your doctor if:

- You suffer from heart, liver or kidney problems.
- You suffer from a large loss of salts or fluids (as a result of vomiting, diarrhea, excessive sweating, low-salt diet, taking diuretics for a long time or if you have undergone dialysis).
- You are about to undergo treatment to reduce allergy to bee or wasp stings (desensitization).
- You are about to receive anesthetics during surgery or dental treatment. You may have to stop treatment with Ramitens one day beforehand; consult with the doctor.
- Your blood potassium level is high (as per blood test results).
- You are taking medicines that may lower your blood sodium level or you suffer from a medical condition that may lower your blood sodium level. Your doctor may refer you for periodic blood sodium level tests, especially if you are elderly.
- You are taking medicines that may increase the risk of a serious allergic reaction called angioedema, such as mTOR inhibitors (e.g. temsirolimus, everolimus, sirolimus), vildagliptin, neprilysin (NEP) inhibitors (such as racecadotril) or sacubitril/valsartan. For sacubitril/valsartan, see also section 'Do not use the medicine'.
- You suffer from connective tissue diseases such as scleroderma or systemic lupus erythematosus.
- You need to tell your doctor if you think you are pregnant or might be pregnant. Ramitens is not recommended in the first 3 months of pregnancy and may cause serious harm to the fetus after the third month (see 'Pregnancy, breastfeeding and fertility' section).
- You are taking any of the following medicines used for lowering blood pressure:
  Aliskiren and angiotensin-II receptor blockers (also known as sartans). For example: valsartan, telmisartan, irbesartan, especially if you suffer from diabetes-related kidney problems.

Your doctor may perform periodic tests of kidney function, blood pressure and your blood electrolyte levels (e.g., potassium). See also section 'Do not use the medicine'.

Children and adolescents:

Ramitens is not recommended for use in children and adolescents below 18 years of age, since the efficacy and safety of the medicine in children have not yet been established.

If the above-mentioned applies to you (or in case of doubt), please consult with the doctor before taking Ramitens.

Drug interactions:

If you are taking, or have recently taken any other medicines, including non-prescription medicines and nutritional supplements, please tell your doctor or pharmacist. This is because Ramitens may affect the action of other medicines and other medicines may affect the action of Ramitens.

Especially inform your doctor or pharmacist if you are taking:

<u>Combination with the following medicines can cause reduced efficacy of Ramitens:</u>

- Medicines to relieve pain and inflammation (for example, NSAIDs such as ibuprofen or indomethacin and aspirin).
- Medicines to treat low blood pressure, shock, heart failure, asthma or allergies, such as ephedrine, noradrenaline or adrenaline. The doctor needs to closely monitor your blood pressure.

<u>Combination with the following medicines can increase the chance of side effects:</u>

- Sacubitril/valsartan - a medicine for treating a type of chronic heart failure in adults (see also section 'Do not use the medicine')
- Medicines to relieve pain and inflammation (for example, NSAIDs such as ibuprofen or indomethacin and aspirin).
- Medicines to treat cancer (chemotherapy)
- Medicines to prevent rejection of organ transplant, such as cyclosporine
- Diuretics, such as furosemide
- Medicines that can raise the blood potassium level, such as spironolactone, triamterene, amiloride, potassium salts, trimethoprim alone or in combination with sulfamethoxazole (for infections) and heparin (for blood thinning)
- Steroids for treatment of inflammation such as prednisolone
- Allopurinol (to reduce the level of uric acid in the blood)
- Procainamide (for treatment of heart rhythm problems)
- Temsirolimus (to treat cancer)
- Sirolimus, everolimus (for prevention of graft rejection)
- Vildagliptin (to treat type 2 diabetes)
- Racecadotril (against diarrhea)
- The doctor may need to change your dosage, and/or take other precautions if you are taking angiotensin-II receptor blockers (ARBs) or aliskiren (see also sections "Do not use the medicine" and "Special warnings regarding use of the medicine").

Combination with the following medicines can affect their action:
- Medicines for diabetes, such as oral medicines to lower sugar and insulin. Ramitens may lower your blood sugar level; monitor your blood sugar level closely while taking Ramitens.
- Lithium (given for treatment of mental health problems). Ramitens can cause an increase in the level of lithium in the blood. The doctor must closely monitor lithium levels while Ramitens is being taken.

If the above-mentioned applies to you (or in case of doubt), please consult with the doctor before taking Ramitens.

Use of the medicine and food:

The medicine may be taken with or without food.

Use of the medicine and alcohol consumption:

Drinking alcohol during the course of treatment with Ramitens can cause dizziness. Consult with your doctor regarding the possibility of drinking alcohol during the course of treatment with Ramitens, since alcohol can also have an additional effect on lowering blood pressure.

Pregnancy, breastfeeding and fertility:

Pregnancy

You need to tell your doctor if you think you are pregnant or might become pregnant. Ramitens is not recommended during the first 12 weeks of pregnancy and must not be used at all from the 13th week, since its use during pregnancy may harm the baby. If you became pregnant while being treated with Ramitens, tell your doctor immediately. The doctor may decide on alternative treatment that is safe for use during pregnancy. If required, the switch to an appropriate alternative treatment should be done before a planned pregnancy.

Breastfeeding

Before you receive Ramitens, tell your doctor if you are breastfeeding or are planning to breastfeed since there is limited information on use of Ramitens during breastfeeding. Ramitens is not recommended for use when breastfeeding.

Driving and use of machinery:
You may feel dizzy while taking Ramitens. This is more likely to happen at the beginning of treatment or when increasing the dosage. If this happens, do not drive or operate machinery.

Important information about some of the medicine's ingredients:

The capsules contain the sunset yellow dye, which might cause an allergic reaction.

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 regarding the dosage and manner of treatment with the medicine.
The generally recommended dosage is: The dosage and manner of treatment will be determined by the doctor only.

Elderly patients
Your doctor may lower the initial dosage and adjust the dosage more slowly.

Do not exceed the recommended dose.

Method of administration:
Take the medicine at a fixed time every day.
Swallow the medicine in its entirety with water, regardless of mealtimes.
There is no information regarding opening and dispersion of the capsule.

If you accidentally took a higher dosage or if a child has accidentally swallowed the medicine:
Refer immediately to a doctor or a hospital emergency room and bring the medicine package with you, so that the doctor knows what you have taken. Do not drive by yourself, ask someone else to drive you or call an ambulance.

If you forgot to take the medicine:
If you forgot to take this medicine at the required time, take the next dose at the next scheduled time and consult the doctor. Do not take a double dose to make up for a forgotten dose!

Adhere to the treatment as recommended by 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 concerning the use of the medicine, consult the doctor or pharmacist.

4. Side effects

As with any medicine, the use of Ramitens may cause side effects in some users. Do not be alarmed while reading the list of side effects. You may not suffer from any of them.

Discontinue treatment with Ramitens and refer to a doctor immediately if you experience any of the following serious side effects - you may need urgent medical treatment.

- Swelling of the face, lips or throat that causes swallowing or breathing difficulties, as well as itching and rash - these can be signs of a severe allergic reaction to Ramitens.
- A severe skin reaction including rash, mouth ulcers, worsening of a pre-existing

skin disease, redness, blistering or detachment of skin (such as Stevens-Johnson syndrome, toxic epidermal necrolysis or erythema multiforme).

Report to the doctor immediately if you experience any of the following side effects:

- Increased heart rate, forceful or irregular heartbeat (palpitations), chest pain, tightness in the chest or a more serious problem such as heart attack or stroke.
- Shortness of breath or coughing - these can be signs of a lung problem.
- Bruising more easily, bleeding for longer than usual, any sign of bleeding (e.g. bleeding from the gums), purple spots, blotching on the skin or getting infections more easily than usual, sore throat and fever, feeling tired, faint, dizzy or pale skin - these can be signs of blood or bone marrow problems.
- Severe abdominal pain which may radiate to the back - could be a sign of pancreatitis.
- Fever, chills, tiredness, loss of appetite, abdominal pain, nausea, yellowing of the skin or eyes (jaundice) - these can be signs of liver problems such as liver inflammation or liver damage.

Additional side effects include:

Please inform your doctor if one of the following effects worsen or last longer than a few days.

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

- Headache or feeling tired
- Feeling of dizziness - likely to appear at the beginning of Ramitens treatment or when the dosage of Ramitens is raised
- Fainting, abnormally low blood pressure, particularly when standing up or sitting up quickly
- Dry cough, sinus infection or bronchitis, shortness of breath
- Abdominal or intestinal pain, diarrhea, indigestion, nausea and vomiting
- Skin rash with or without raised areas
- Chest pain
- Muscle cramps or pain
- Blood test results showing a higher potassium level than usual.

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

- Balance problems (vertigo)
- Itching and unusual skin sensations such as numbness, tingling, pricking, burning or creeping on your skin (paresthesia)
- Loss or change in sense of taste
- Sleep problems
- Feeling depressed, anxious, more nervous than usual or restless
- Stuffed nose, breathing difficulties or worsening of asthma
- Swelling in the intestines (intestinal angioedema), manifested by abdominal pain, vomiting or diarrhea
- Heartburn, constipation or dry mouth
- Urinating more than usual
- Sweating more than usual
- Decrease or loss of appetite
- Increase or change in heart rate
- Swelling of the arms and legs - can be a sign of the body retaining more fluid than usual
- Flushing
- Blurred vision
- Joint pain
- Fever

- Impotence in men, reduced sexual desire in men or women
- Increase in certain white blood cells (eosinophilia) which is observed in blood tests
- Blood test results indicating changes in liver, pancreas or kidney function.

Rare side effects (appear in 1-10 users out of 10,000):
- Feeling unstable or confused
- Redness and swelling of the tongue
- Severe peeling of the skin, itching, lumpy rash
- Nail problems (for instance, loosening or detachment of the nail from its bed)
- Skin rash or bruises
- Blotches on the skin and sensation of cold in the limbs
- In the eyes - redness, itching, swelling or tearing
- Hearing disturbances and ringing in the ears
- Feeling weak
- Blood test results showing a reduction in the number of red blood cells, white blood cells or platelets or in the amount of hemoglobin.

Very rare side effects (appear in less than 1 user out of 10,000);
- Increased sensitivity to sunlight.

Additional reported side effects:
Please inform your doctor if any of the following effects worsen or last longer than a few days:
- Concentration difficulties
- Swelling in the mouth
- Blood test results showing too few blood cells in your blood
- Blood test results showing a lower sodium level than usual in your blood
- Concentrated urine (dark in color), nausea or vomiting, muscle cramps, confusion and fits which may be a result of a disturbance in secretion of the hormone which regulates secretion of urine (ADH). If you experience these effects, refer to the doctor as soon as possible.
- Change in color of the fingers and toes when you are cold and then a feeling of tingling pain when you warm up (Raynaud's phenomenon)
- Breast enlargement in men
- Slowed or changed reactions
- Burning sensation
- Change in the way things smell
- Hair loss.

If a side effect appears, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult the doctor.
Side effects may be reported to the Ministry of Health by clicking on the link "Report on side effects following medicinal treatment" on the homepage of the Ministry of Health website (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering 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 and sight of children and/or babies, 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 (exp. date) stated on the package. The expiry date refers to the last day of that month.

Storage conditions:
Store in the original package, below 25°C.

6. Additional information
In addition to the active ingredient, the medicine also contains:

Starch, gelatin, titanium dioxide, brilliant blue FCF, D&C Red 33, sunset yellow FCF.

What does the medicine look like and what does the package contain:
Blister packs of 30 white/blue capsules containing white powder.

This leaflet does not contain all the information on the product. If you have any question or are unsure about anything, refer to the doctor.

Manufacturer and Registration Holder: Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 9100301.

Medicine registration number in the National Medicines Registry of the Ministry of Health: 131-58-30972

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