

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

Keep this leaflet. You may need to read it again. If you have more questions, ask your doctor or pharmacist. This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours. If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

ENOX PLUS 2.5 mg+12.5 mg tablets
ENOX PLUS 5 mg+25 mg tablets
Ramipril+Hydrochlorothiazide

In this leaflet

- 1 What **ENOX PLUS** is and what it is used for
- 2 Before you take **ENOX PLUS**
- 3 How to take **ENOX PLUS**
- 4 Possible side effects
- 5 How to store **ENOX PLUS**
- 6 Further information

1. What ENOX PLUS is and what it is used for

ENOX PLUS is a combination of two medicines called ramipril and hydrochlorothiazide.

Ramipril belongs to a group of medicines called "ACE inhibitors" (Angiotensin Converting Enzyme Inhibitors). It works by:

- Decreasing your body's production of substances that raise your blood pressure
- Making your blood vessels relax and widen
- Making it easier for your heart to pump blood around your body.

Hydrochlorothiazide belongs to a group of medicines called "thiazide diuretics" or water tablets. It works by increasing the amount of water (urine) you produce. This lowers your blood pressure.

ENOX PLUS is used to treat high blood pressure. The two active substances work together to lower your blood pressure. They are used together when treatment with just one did not work.

2. Before you take ENOX PLUS

Do not take ENOX PLUS:

- If you are allergic (hypersensitive) to ramipril, hydrochlorothiazide or any of the other ingredients of **ENOX PLUS** (see section 6)
- If you are allergic (hypersensitive) to medicines similar to **ENOX PLUS** (other ACE inhibitors or sulphonamide derived medicines). Signs of an allergic reaction may include a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue
- If you have ever had a serious allergic reaction called "angioedema". The signs include itching, hives (urticaria), red marks on the hands, feet and throat, swelling of the throat and tongue, swelling around the eyes and lips, difficulty breathing and swallowing
- If you are having dialysis or any other type of blood filtration.

Depending on the machine that is used, **ENOX PLUS** may not be suitable for you

- If you have severe liver problems
- If you have abnormal amounts of salt substances (calcium, potassium, sodium) in your blood
- If you have kidney problems where the blood supply to your kidney is reduced (renal artery stenosis)

During the last 6 months of pregnancy (see section below on "Pregnancy and breast-feeding")

- If you are breast-feeding (see section below on "Pregnancy and breast-feeding")

Do not take **ENOX PLUS** if any of the above apply to you. If you are not sure, talk to your doctor before taking **ENOX PLUS**.

Take special care with ENOX PLUS

Check with your doctor or pharmacist before taking your medicine:

- If you have heart, liver or kidney problems
- If you have lost a lot of body salts or fluids (through being sick (vomiting), having diarrhoea, sweating more than usual, being on a low salt diet, taking diuretics (water tablets) for a long time or having had dialysis)
- If you are going to have treatment to reduce your allergy to bee or wasp stings (desensitization)
- If you are going to receive an anaesthetic. This may be given for an operation or any dental work.

You may need to stop your **ENOX PLUS** treatment one day beforehand; ask your doctor for advice

- If you have high amounts of potassium in your blood (shown in blood test results)
- If you have a collagen vascular disease such as scleroderma or systemic lupus erythematosus

You must tell your doctor if you think that you are (or might become) pregnant.

ENOX PLUS is not recommended in the first 3 months of pregnancy and may cause serious harm to your baby after 3 months of pregnancy (see section below on "Pregnancy and breast-feeding").

Children

ENOX PLUS is not recommended for children and young people under the age of 18 years. This is because the drug has never been used in these age groups.

If any of the above apply to you (or you are not sure), talk to your doctor before taking **ENOX PLUS**

Taking ENOX PLUS with other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription (including herbal medicines). This is because **ENOX PLUS** can affect the way some other medicines work. Also some medicines can affect the way **ENOX PLUS** works.

Please tell your doctor if you are taking any of the following medicines. They can make **ENOX PLUS** work less well:

- Medicines used to relieve pain and inflammation (e.g. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) such as ibuprofen or indometacin and aspirin)
- Medicines used for the treatment of low blood pressure, shock, cardiac failure, asthma or allergies such as ephedrine, noradrenaline or adrenaline.

Your doctor will need to check your blood pressure.

Please tell your doctor if you are taking any of the following medicines. They can increase the chance of getting side effects if you take them with **ENOX PLUS**:

- Medicines used to relieve pain and inflammation (e.g. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) such as ibuprofen or indometacin and aspirin)
- Medicines which can lower the amount of potassium in your blood. These include medicines for constipation, diuretics (water tablets), amphotericin B (used for fungal infections) and ACTH (used to test if your adrenal glands are working properly)
- Medicines for cancer (chemotherapy)
- Medicines for heart problems, including problems with your heartbeat
- Medicines to stop the rejection of organs after a transplant such as ciclosporin
- Diuretics (water tablets) such as furosemide
- Medicines which can increase the amount of potassium in your blood such as spironolactone, triamterene, amiloride, potassium salts, and heparin (for thinning blood)
- Steroid medicines for inflammation such as prednisolone
- Calcium supplements
- Allopurinol (used to lower the uric acid in your blood)
- Procainamide (for heart rhythm problems)
- Colestyramine (for reducing fat amounts in your blood)
- Carbamazepine (for epilepsy).

Please tell your doctor if you are taking any of the following medicines. They may be affected by **ENOX PLUS**:

- Medicines for diabetes such as oral glucose lowering medicines and insulin. **ENOX PLUS**
- May lower your blood sugar amounts. Check your blood sugar amounts closely while taking **ENOX PLUS**
- Lithium (for mental health problems). **ENOX PLUS** may increase the amount of lithium in your blood. Your lithium amount will need to be closely checked by your doctor
- Medicines to relax your muscles
- Quinine (for malaria)
- Medicines that contain iodine, these may be used when you are having a scan or X-ray in hospital
- Penicillin (for infections)
- Medicines to thin the blood that you take by mouth (oral anticoagulants) such as warfarin.

If any of the above apply to you (or you are not sure), talk to your doctor before taking **ENOX PLUS**.

Tests

Check with your doctor or pharmacist before taking your medicine:

- If you are having a test for parathyroid function. **ENOX PLUS** might affect the results of the test
- If you are sports person having an anti-doping test. **ENOX PLUS** might give you a positive result.

Taking ENOX PLUS with food and alcohol

Drinking alcohol with **ENOX PLUS** may make you feel dizzy or light-headed.

If you are concerned about how much you can drink while you are taking **ENOX PLUS**, discuss this with your doctor as medicines used to reduce blood pressure and alcohol can have additive effects.

ENOX PLUS may be taken with or without food.

Pregnancy and breast-feeding

You must tell your doctor if you think that you are (or might become) pregnant. You should not take **ENOX PLUS** in the first 12 weeks of pregnancy, and you must not take them at all after the 13th week as their use during pregnancy may possibly be harmful to the baby. If you become pregnant while on **ENOX PLUS**, tell your doctor immediately. A switch to a suitable alternative treatment should be carried out in advance of a planned pregnancy. You should not take **ENOX PLUS** if you are breast-feeding. Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

You may feel dizzy, while taking **ENOX PLUS**. This is more likely to happen when you start taking **ENOX PLUS** or start taking a higher dose. If this happens, do not drive or use any tools or machines.

3. HOW TO TAKE ENOX PLUS

Always take **ENOX PLUS** exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Taking this medicine

Take this medicine by mouth at the same time of day each day, usually in the morning.

Swallow the tablets with liquid.

Do not crush or chew the tablets.

How much to take

Treatment of high blood pressure

Your doctor will adjust the amount you take until your blood pressure is controlled.

Elderly

Your doctor will reduce the initial dose and adjust your treatment more slowly.

If you take more ENOX PLUS than you should

Tell a doctor or go to the nearest hospital casualty department straight away. Do not drive to the hospital, get somebody else to take you or call for an ambulance. Take the medicine pack with you. This is so the doctor knows what you have taken.

If you forget to take ENOX PLUS

If you miss a dose, take your normal dose when it is next due. Do not take a double dose to make up for a forgotten tablet.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, **ENOX PLUS** can cause side effects, although not everybody gets them. Stop taking **ENOX PLUS** and see a doctor straight away, if you notice any of the following serious side effects - you may need urgent medical treatment:

- Swelling of the face, lips or throat which make it difficult to swallow or breathe, as well as itching and rashes. This could be a sign of a severe allergic reaction to **ENOX PLUS**
- Severe skin reactions including rash, ulcers in your mouth, worsening of a pre-existing skin disease, reddening, blistering or detachment of skin (such as Stevens-Johnson syndrome, toxic epidermal necrolysis or erythema multiform).

Tell your doctor immediately if you experience:

- Faster heart rate, uneven or forceful heartbeat (palpitations), chest pain, tightness in your chest or more serious problems including heart attack and stroke
- Shortness of breath, cough fever lasting 2 to 3 days and feeling less hungry.

These could be signs of lung problems including inflammation
- Bruising more easily, bleeding for longer than normal, 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 having pale skin. These can be signs of blood or bone marrow problems.

- Severe stomach pain which may reach through to your back. This could be a sign of pancreatitis (inflammation of the pancreas)
- Fever, chills, tiredness, loss of appetite, stomach pain, feeling sick, yellowing of your skin or eyes (jaundice). These can be signs of liver problems such as hepatitis (inflammation of the liver) or liver damage.

Other side effects include: Please tell your doctor if any of the following gets serious or lasts longer than a few days.

Common (affects less than 1 in 10 people)

- Headache, feeling weak or tired
- Feeling dizzy. This is more likely to happen when you start taking **ENOX PLUS** or start taking a higher dose
- Dry tickly cough or bronchitis
- Blood test showing a higher amount of sugar than usual in your blood. If you have diabetes, this may make your diabetes worse
- Blood test showing a higher amount of uric acid or more fat than usual in your blood
- Painful, red, and swollen joints

Uncommon (affects less than 1 in 100 people)

- Skin rash with or without raised area
- Flushing, fainting, hypotension (abnormally low blood pressure), especially when you stand or sit up quickly
- Balance problems (vertigo)
- Itching and unusual skin sensations such as numbness, tingling, pricking, burning or creeping on your skin (paraesthesia)
- Loss or change in the way things taste
- Sleep problems
- Feeling depressed, anxious, more nervous or shaky than usual
- Blocked nose, inflammation of your sinuses (sinusitis), shortness of breath
- Inflammation of the gums (gingivitis), swollen mouth
- Red, itchy, swollen or watery eyes
- Ringing in your ears
- Blurred vision
- Hair loss
- Chest pain
- Pain in your muscles- Constipation, stomach or gut pain
- Indigestion or feeling sick
- Passing more water (urine) than usual over the day
- Sweating more than usual or feeling thirsty
- Loss or decrease of appetite (anorexia), feeling less hungry
- Increased or irregular heartbeat
- Swollen arms and legs. This may be a sign of your body holding onto more water than usual
- Fever
- Sexual inability in men
- Blood tests showing a decrease in the number of red blood cells, white blood cells or platelets or in the amount of haemoglobin
- Blood tests showing changes in the way your liver, pancreas or kidneys are working
- Blood tests showing less potassium than usual in your blood.

Very rare (affects less than 1 in 10,000 people)

- Being sick, getting diarrhoea or heartburn
- Red swollen tongue or dry mouth
- Blood tests showing more potassium than usual in your blood.

Other side effects reported:

Please tell your doctor if any of the following gets serious or lasts longer than a few days.

- Difficulty concentrating, feeling restless or confused
- Fingers and toes changing colour when cold and then tingling or painful when you warm up.
This could be Raynaud's phenomenon
- Breast enlargement in men
- Blood clots
- Disturbed hearing
- Your eyes watering less than usual
- Objects looking yellow
- Dehydration
- Swelling, pain and redness in your cheek (inflammation of a salivary gland)
- A swelling in your gut called "intestinal angioedema" presenting with symptoms like abdominal pain, vomiting and diarrhoea
- Being more sensitive to the sun than usual
- Severe flaking or peeling of the skin, itchy, lumpy rash or other skin reactions such as red rash on your face or forehead
- Skin rash or bruising
- Blotches on your skin and cold extremities
- Nail problems (e.g. loosening or separation of a nail from its bed)
- Musculoskeletal rigidity or not being able to move your jaw (tetany)
- Weakness or cramps in your muscles
- Reduced sexual desire in men or women
- Blood in your water (urine). This could be a sign of a kidney problem (interstitial nephritis)

- More sugar than usual in your water (urine)
 - An increased number of certain white blood cells (eosinophilia) found during a blood test
 - Blood tests showing too few blood cells in your blood (pancytopenia)
 - Blood tests showing a change in the amount of salts such as sodium, calcium, magnesium and chloride in your blood
 - Slowed or impaired reactions
 - Change in the way things smell
 - Difficulty breathing or worsening of asthma
- If you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. How to store ENOX PLUS

Do not store above 25°C. Store in the original package. Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

6. Further Information

What ENOX PLUS contains

The active substances are ramipril and hydrochlorothiazide.
One tablet contains 2.5 mg ramipril and 12.5 mg hydrochlorothiazide or 5 mg ramipril and 25 mg hydrochlorothiazide.
The other ingredients are: lactose monohydrate, pregelatinized corn starch, sodium bicarbonate, glyceryl dibehenate, sodium stearyl fumarate, purified water.

Contents of the pack

30 (3x10) tablets of 2,5+12,5 mg in blister pack, in box.

30 (3x10) tablets of 5+25 mg in blister pack, in box.

Manufacturer and marketing authorization holder:

ZADA Pharmaceuticals Ltd.
Donji Bistarac without number
75 300 Lukavac
Bosnia and Herzegovina

Date and number of marketing authorization:

ENOX Plus, tablet, 30 x (2,5 + 12,5) mg:

Number: 04-07.3-2-4837/15

Date: 30.09.2015.

ENOX Plus, tablet, 30 x (5 + 25) mg:

Number: 04-07.3-2-4838/15

Date: 30.09.2015.

This leaflet was last approved in September, 2015.