Package leaflet: Information for the patient

Pendrex Plus 4 mg/1.25 mg tablets

perindopril erbumine/indapamide

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 any further 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. See section 4.

What is in this leaflet

1. What Pendrex Plus is and what it is used for

Pendrex Plus tablets are a combination of two active substances, perindopril and indapamide. This medicine **is used in the treatment of high blood pressure (hypertension).**
- Perindopril belongs to a class of medicines called ACE inhibitors. These work by widening the blood vessels, which makes it easier for your heart to pump blood through them.
- Indapamide is a diuretic. Diuretics increase the amount of urine produced by the kidneys and are sometimes called water tablets. However, indapamide is different from other diuretics, as it only causes a slight increase in the amount of urine produced.

Each of the active substances reduces blood pressure and they work together to control your blood pressure.

2. What you need to know before you take Pendrex Plus

Do not take Pendrex Plus:
- if you are **allergic** to perindopril or any other ACE inhibitor, or indapamide or other sulphonamides or any of the other ingredients of this medicine (listed in section 6 and end of section 2)
- if you have experienced symptoms such as **wheezing, swelling of the face or tongue, intense itching or severe skin rashes** with previous ACE inhibitor treatment or if you or a member of your family have had these symptoms in any other circumstances (a condition called **angioedema**)
- if you have a **severe liver disease** or suffer from a condition called **hepatic encephalopathy** (degenerative disease of the brain)
- if you have a **severe kidney disease** where the blood supply to your kidneys is reduced (renal artery stenosis)
- if you are **receiving dialysis**, or any other type of blood filtration. Depending on the machine that is used, Pendrex Plus may not be suitable for you.
- if you have **diabetes or impaired kidney function** and you are treated with a blood pressure lowering medicine containing **aliskiren**

- if you have **low or high blood potassium**
- if you are suspected of having untreated **decompensated heart failure** (severe water retention, difficulty in breathing)
- if you are more than **3 months pregnant**. (It is also better to avoid Pendrex Plus in early pregnancy – see pregnancy section.)
- if you are **breast-feeding** (see breast-feeding)
- if you have taken or are currently taking **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.

Warnings and precautions
Talk to your doctor **before** taking Pendrex Plus:
- if you have **narrowing of the main blood vessel** leading from the heart (aortic stenosis)
- if you have **narrowing of heart's left valve** (mitral valve stenosis)
- if you have **heart muscle disease** (hypertrophic cardiomyopathy)
- if you have **narrowing of the artery supplying the kidney** with blood (renal artery stenosis)
- if you have heart failure or any other **heart problems**
- if you have problems with **your kidneys,** or if you are receiving dialysis
- if you have abnormally **increased levels of a hormone called aldosterone** in your blood (primary aldosteronism)
- if you have **liver problems**
- if you suffer from a **collagen disease** (skin disease) such as *systemic lupus erythematosus* or scleroderma
- if you have **atherosclerosis** (hardening of the arteries)
- if you suffer from **hyperparathyroidism** (dysfunctioning of the parathyroid gland)
- if you suffer from **gout**
- if you have **diabetes**
- if you are on a **salt restricted diet** or use salt substitutes which contain **potassium**
- if you take **lithium** or **water tablets** called potassium-sparing diuretics (spironolactone, triamterene) or potassium supplements as their use with Pendrex Plus should be avoided (see "Other medicines and Pendrex Plus")
- if you have **a severe allergic reaction** with swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema). This may occur at any time during treatment. If you develop such symptoms, you should stop taking the treatment and see a doctor immediately.
- if you are taking any of the following medicines used to treat high blood pressure:
  - an angiotensin II receptor blocker (ARBs) (also known as sartans - for example valsartan, telmisartan, irbesartan), in particular if you have diabetes-related kidney problems.
  - 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 information under the heading "Do not take Pendrex Plus".
- if you are a **haemodialysis patient** dialysed with high-flux membranes
- if you are taking any of the following medicines, the risk of angioedema (rapid swelling under the skin in an area such as the throat) may be increased:
  - racecadotril, a medicine used to treat diarrhoea
  - medicines used to prevent organ transplant rejection and for cancer (e.g. temsirolimus, sirolimus, everolimus and other medicines belonging to the class of mTOR inhibitors)
  - vildagliptin, a medicine used to treat diabetes.
- if you are more than **70 years** old
- if **you are of black origin** since you may have a higher risk of angioedema and this medicine may be less effective in lowering your blood pressure than in non-black patients.

- if you think you are (or might become) **pregnant**. Pendrex Plus is not recommended in early pregnancy, and must not be taken if you are more than 3 months pregnant, as it may cause serious harm to your baby if used at that stage (see pregnancy section).

You should also inform your doctor or pharmacist that you are taking this medicine:
- if you are to **undergo anaesthesia** and/or **surgery**
- if you have recently suffered from **diarrhoea** or **vomiting,** or are **dehydrated**
- if you have noticed increased sensitivity of the skin to **sunlight**
- if you have a persistent **dry cough**
- if you have **abdominal pain with or without nausea or vomiting;** these may be symptoms of serious allergic reaction called intestinal angioedema
- if you are to undergo **dialysis** or **LDL aphaeresis** (removal of cholesterol from your blood by a machine)
- if you are going to have **desensitisation treatment** to reduce the effects of an allergy to bee or wasp stings
- if you are to undergo a medical test that requires injection of an **iodinated contrast agent** (a substance that makes organs like kidney or stomach visible on an X-ray)
- if you experience **a decrease in vision or pain in one or both of your eyes** while taking this medicine. These could be symptoms of fluid accumulation in the vascular layer of the eye (choroidal effusion) or an increase of pressure in your eye (glaucoma) and can happen within hours to weeks of taking Pendrex Plus. This can lead to permanent vision loss, if not treated. If you previously have had a penicillin or sulphonamide allergy, you can be at higher risk of developing this. You should discontinue treatment with this medicine and seek medical attention.

Children and adolescents
Do not give this medicine to children and adolescents.

Other medicines and Pendrex Plus
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Avoid taking this medicine with:
- **lithium** (used to treat depression)
- **potassium supplements** (including salt substitutes), **potassium-sparing diuretics** (such as eplerenone, spironolactone, triamterene, amiloride) and other medicines that can increase the amount of potassium in your blood (e.g. **trimethoprim** and **co-trimoxazole** also known as trimethoprim/sulfamethoxazole for infections caused by bacteria; **ciclosporin**, an immunosuppressant medicine used to prevent organ transplant rejection; and **heparin**, a medicine used to thin blood to prevent clots)
- **estramustine** (used in cancer therapy).

In particular, **before taking** this medicine check with your doctor if you are taking any of the following:

- other medicines for treating **high blood pressure**
  If you are taking an angiotensin II receptor blocker (ARB) or aliskiren (Your doctor may need to change your dose and/or to take other precautions; see also information under the headings “Do not take Pendrex Plus” and “Warnings and precautions”) or diuretics (medicines which increase the amount of urine produced by the kidneys)
- medicines used for **heart rhythm problems** (e.g. procainamide, digoxin, hydroquinidine, disopyramide, quinidine, amiodarone, sotalol, diphemanil)
- potassium-sparing medicines used in **the treatment of heart failure**: eplerenone and spironolactone at doses between 12.5 mg to 50 mg per day

- **sacubitril/valsartan** (used to treat long-term heart failure). See sections "Do not take Pendrex Plus" and "Warnings and precautions".
- **antihistamines** for hay fever or allergies e.g**.** terfenadine, astemizole, mizolastine
- **bepridil** (for angina pectoris)
- **benzamides** (for psychotic disorders e.g. sultopride)
- **butyrophenones** (for psychotic disorders e.g. haloperidol)
- anaesthetic medicines
- iodinated contrast agent
- **cisapride** (used to treat gastric and digestive problems)
- **erythromycin** by injection (an antibiotic)
- **moxifloxacin** or **sparfloxacin** (antibiotics)
- **methadone** (anti-addiction medicine)
- **allopurinol** (for gout)
- **corticosteroids** used to treat various conditions including severe asthma and rheumatoid arthritis
- **immunosuppressants** used for the treatment of auto-immune disorders or following transplant surgery (e.g. ciclosporin, tacrolimus)
- medicines for treating **cancer**
- **halofantrine** (for malaria)
- **pentamidine** (for pneumonia)
- **vincamine** (for symptomatic cognitive disorders in elderly)
- **baclofen** (for muscle stiffness occurring in diseases such as multiple sclerosis)
- **diabetes medicines** such as insulin, metformin, glimepiride, vildagliptin and other gliptins
- **calcium** including calcium supplements
- **stimulant laxatives** (e.g. senna)
- non-steroidal anti-inflammatory medicines (NSAIDs) for **pain relief** (e.g. ibuprofen) or high dose salicylates (e.g. **acetylsalicylic acid**)
- **amphotericin B** by injection (for severe fungal disease)
- medicines to treat mental disorders such as depression, anxiety, schizophrenia (e.g. **tricyclic antidepressants**, **neuroleptics**)
- **tetracosactide** (to treat Crohn's disease)
- **gold** (sodium aurothiomalate) by injection (medicine for rheumatic disorders)
- **vasodilatators** including nitrates (products that make the blood vessels become wider)
- medicines used for the **treatment of low blood pressure, shock or asthma** (e.g. ephedrine, noradrenaline or adrenaline)
- medicines, which are most often used to treat diarrhoea (**racecadotril**) or avoid rejection of transplanted organs (**sirolimus, everolimus, temsirolimus and other medicines belonging to the class of mTOR inhibitors**). See section "Warnings and precautions".

Ask your doctor if you are not sure what these medicines are.

Pendrex Plus with food and drink
Take special care if you are on a salt-restricted diet. See your doctor before you take this medicine.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy
You must tell your doctor if you think you are (or might become) pregnant. Your doctor will normally advise you to stop taking Pendrex Plus before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Pendrex Plus. Pendrex Plus is not recommended in early pregnancy, and must not be taken when more than 3 months pregnant, as it may cause serious harm to your baby if used after the third month of pregnancy.

Breast-feeding
You must not take Pendrex Plus if you are breast-feeding.
Tell your doctor immediately if you are breast-feeding or about to start breast-feeding.

Driving and using machines
This medicine does not affect your alertness but you may feel dizzy or weak due to a decrease in your blood pressure, especially at the beginning of treatment or when increasing the dose. If this happens, your ability to drive or to operate machinery may be affected.

Pendrex Plus contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Pendrex Plus

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Take your tablet with a glass of water preferably in the morning and before a meal.

Adults
The recommended dose is one tablet once a day.

Elderly
Your doctor will decide on the best dose for you.

Patients with kidney insufficiency
Your doctor may decide to modify the dose regimen if you suffer from kidney impairment.

Use in children and adolescents
This medicine should not be given to children and adolescents (see "Warnings and precautions").

If you take more Pendrex Plus than you should
If you take too many tablets, contact your nearest hospital or tell your doctor immediately. The most likely effect in case of overdose is low blood pressure. If marked low blood pressure occurs (symptoms such as dizziness or faintness), lying down with your legs raised can help.

If you forget to take Pendrex Plus
It is important to take your medicine every day as regular treatment is more effective. However, if you forget to take one or more doses, take another as soon as you remember and then go on as prescribed. Do not take a double dose to make up for a forgotten dose.

If you stop taking Pendrex Plus
Always consult your doctor, if you wish to stop taking this medicine. Even if you feel well, it may be necessary to continue taking this medicine.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you notice any of the following side effects, STOP taking the tablets and contact your doctor immediately. These are symptoms of a serious **allergic reaction** and must be treated **immediately**, usually in a **hospital**.

- swelling of the face, eyes, lips, mouth, tongue or throat, which may cause difficulty in swallowing or breathing (angioedema) (see section 2 "Warnings and precautions") (uncommon – may affect up to 1 in 100 people)
- tightening of the chest, wheezing and shortness of breath (bronchospasm) (uncommon – may affect up to 1 in 100 people)
- severe dizziness or fainting due to low blood pressure (common – may affect up to 1 in 10 people)
- severe skin reactions including erythema multiforme (a skin rash which often starts with red itchy patches on your face, arms or legs) or intense skin rash, hives, reddening of the skin over your whole body, severe itching, blistering, peeling and swelling of the skin, inflammation of mucous membranes (Stevens Johnson Syndrome) or other allergic reactions (very rare – may affect up to 1 in 10,000 people).

Also contact your doctor immediately if you notice any of the following side effects:

Rare: may affect up to 1 in 1,000 people:
- kidney disorder with severely decreased or absent urine output which can also occur with a high temperature (fever), nausea, tiredness, pain in your sides, swelling of your legs, ankles, feet, face and hands or blood in your urine (acute renal failure)
- dark urine, feeling sick (nausea) or being sick (vomiting), muscle cramps, confusion and seizures. These may be symptoms of a condition called SIADH (inappropriate antidiuretic hormone secretion).

Very rare: may affect up to 1 in 10,000 people
- unusual fast or irregular heartbeat
- chest pain
- heart attack
- weakness of arms or legs, or problems speaking which could be a sign of a possible stroke
- inflamed pancreas which may cause severe abdominal and back pain accompanied with feeling very unwell
- yellowing of the skin or eyes (jaundice) which could be a sign of hepatitis.

Not known: frequency cannot be estimated from the available data
- life-threatening irregular heartbeat
- disease of the brain caused by liver illness (hepatic encephalopathy)
- sudden short sightedness (myopia)
- decrease in vision or pain in your eyes due to high pressure (possible signs of fluid accumulation in the vascular layer of the eye (choroidal effusion) or acute angle-closure glaucoma).

Other side effects

Common: may affect up to 1 in 10 people
- constipation
- nausea
- vomiting
- stomach discomfort after meal (dyspepsia)
- abdominal pains
- diarrhoea
- taste disturbance

- dry cough
- difficulty breathing
- vision disturbances
- ringing or buzzing in the ears
- muscle cramps
- feeling of weakness (asthenia)
- headache
- feelings of dizziness
- sensations of tickling, itching or tingling without an apparent cause (paresthesia)
- spinning sensation (vertigo)
- skin reactions (rash, raised rash eruptions, itching)
- changes in laboratory parameters seen on blood tests: low potassium levels.

Uncommon: may affect up to 1 in 100 people
- purple skin patches (purpura)
- skin itchy rash (urticaria)
- blister cluster
- mood disturbances and/or sleep disturbances
- depression
- kidney disorder (renal insufficiency)
- impotence (inability to obtain or maintain an erection)
- sweating
- an excess of eosinophils (a type of white blood cells)
- change in laboratory parameters: high blood level of potassium reversible on discontinuation, low blood level of sodium that may lead to dehydration and low blood pressure
- somnolence
- fainting
- awareness of your heartbeat (palpitations)
- fast heartbeat (tachycardia)
- very low blood sugar level (hypoglycaemia) in case of diabetic patients
- inflammation of blood vessels (vasculitis)
- dry mouth
- increased sensitivity of the skin to sun (photosensitivity reactions)
- joint pain (arthralgia)
- muscle pain (myalgia)
- chest pain
- malaise
- oedema peripheral
- fever
- increased blood urea
- increased blood creatinine
- fall.

Rare: may affect up to 1 in 1,000 people
- fatigue
- psoriasis worsening
- changes in laboratory parameters: increased level of liver enzymes, high level of serum bilirubin, low level of chloride in the blood, low level of magnesium in the blood
- decreased or absent urine output
- flushing.

Very rare: may affect up to 1 in 10,000 people
- reduction in the number of platelets
- reduction in the number of white blood cells, which makes infections more likely
- reduction in the number of red blood cells which can make the skin pale and cause weakness or breathlessness (aplastic anaemia, haemolytic anaemia)
- lower haemoglobin
- eosinophilic pneumonia (a rare type of pneumonia)
- nasal stuffiness or runny nose
- confusion
- high level of calcium in the blood
- abnormal hepatic function.

Not known: frequency cannot be estimated from the available data
- abnormal ECG heart tracing
- changes in laboratory parameters seen on blood tests: high uric acid levels and high sugar levels in the blood
- vision blurred
- discolouration, numbness and pain in fingers or toes (Raynaud's phenomenon)
- If you suffer from systemic lupus erythematosus (a type of collagen disease), this might get worse.

Disorders of the blood, kidney, liver or pancreas and changes in laboratory parameters (blood tests) can occur. Your doctor may need to give you blood tests to monitor your condition.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system: HPRA Pharmacovigilance; website www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Pendrex Plus

Keep this medicine out of the sight and reach of children.

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

Do not store above 30°C. Store in the original package in order to protect from light and moisture.

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. Contents of the pack and other information

What Pendrex Plus contains
- The active substances are perindopril erbumine and indapamide. Each tablet contains 4.00 mg of perindopril erbumine, equivalent to 3.338 mg perindopril, and 1.25 mg of indapamide.

- The other ingredients are hydroxypropylbetadex, lactose monohydrate, povidone K25, silicified microcrystalline cellulose, colloidal silica hydrated, colloidal anhydrous silica and magnesium stearate.

What Pendrex Plus looks like and contents of the pack
White, oblong, biconvex tablet debossed with PI on the one side.

The tablets are packed in Alu/Alu blister and inserted in a carton.

Pack sizes: 7, 14, 20, 28, 30, 50, 56, 60, 90, 98, 100 tablets

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturers
Marketing Authorisation Holder
Rowex Ltd., Bantry, Co. Cork, Ireland.

Manufacturers
Lek Pharmaceuticals d.d., Verovškova 57, 1526 Ljubljana, Slovenia.
Lek S.A., ul. Domaniewska 50 C, 02-672 Warszawa, Poland.
Salutas Pharma GmbH, Otto-von-Guericke-Allee 1, 39179 Barleben, Germany.
Lek Pharmaceuticals d.d., Trimlini 2D, 9220 Lendava, Slovenia.

This medicine is authorised in the Member States of the European Economic Area under the following names:
Germany: Perindopril HEXAL plus Indapamid 4 mg /1,25 mg Tabletten
Ireland: Pendrex Plus 4mg/1.25mg tablets

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