

Package leaflet: Information for the user
Zestoretic 10 mg/12.5 mg and 20 mg/12.5 mg Tablets
lisinopril, hydrochlorothiazide

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 Zestoretic is and what it is used for
2. What you need to know before you take Zestoretic
3. How to take Zestoretic
4. Possible side effects
5. How to store Zestoretic
6. Contents of the pack and other information

1. What Zestoretic is and what it is used for

Zestoretic is used to treat high blood pressure (hypertension). It contains two medicines called lisinopril and hydrochlorothiazide.

- Lisinopril belongs to a group of medicines called ACE inhibitors. It works by making your blood vessels widen.
- Hydrochlorothiazide belongs to a group of medicines called diuretics (water tablets). It helps your body to get rid of water and salts like sodium in your urine.

These medicines work together to lower your blood pressure.

2. What you need to know before you take Zestoretic

Do not take Zestoretic:

- if you are allergic to lisinopril or hydrochlorothiazide or any of the other ingredients of Zestoretic (listed in section 6).
- if you are allergic to ACE inhibitor or sulphonamide medicines. If you are not sure if this applies to you, please ask your doctor.
- if you have ever had itching, hives, sudden fall in blood pressure, sudden swelling of the hands, feet, ankles, face, lips, tongue or throat, especially if this followed treatment with an ACE inhibitor. It may also have been difficult to swallow or breathe.
- 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.
- if you have hereditary angioedema (a condition that makes you more prone to the swelling described above). If you are not sure if this applies to you, please ask your doctor.

- if you have severe kidney problems.
- if you have stopped passing water (urine).
- if you have severe liver problems.
- if you are more than 3 months pregnant. (It is also better to avoid Zestoretic in early pregnancy – see the sections on ‘Pregnancy and breast-feeding’).
- if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren.
- If you experienced breathing or lung problems (including inflammation or fluid in the lungs) following hydrochlorothiazide intake in the past. If you develop any severe shortness of breath or difficulty breathing after taking Zestoretic, seek medical attention immediately.

Do not take Zestoretic if any of the above applies to you. If you are not sure, talk to your doctor or pharmacist before taking Zestoretic.

Warnings and precautions

Talk to your doctor or pharmacist before taking Zestoretic:

- if you have had skin cancer or if you develop an unexpected skin lesion during the treatment. Treatment with hydrochlorothiazide, particularly long term use with high doses, may increase the risk of some types of skin and lip cancer (non-melanoma skin cancer). Protect your skin from sun exposure and UV rays while taking Zestoretic.
- if you have a narrowing (stenosis) of the aorta (an artery in your heart), the heart valves (mitral valves) or the kidney artery.
- if you have an increase in the thickness of the heart muscle (known as hypertrophic cardiomyopathy).
- if you have problems with your blood vessels (collagen vascular disease).
- if you have low blood pressure. You may notice this as feeling dizzy or light-headed, especially when standing up.
- if you have kidney problems or you are having kidney dialysis or you have had a kidney transplant.
- if you have liver problems.
- if you have diabetes.
- 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 of “Do not take Zestoretic”.

- if you have recently had diarrhoea or vomiting (being sick).
- if your doctor has told you to control the amount of salt in your diet.
- if you have high levels of cholesterol and you are having a treatment called ‘LDL apheresis’.
- if you have ever had a condition called systemic lupus erythematosus (SLE).
- if you are of black origin as Zestoretic may be less effective. You may also more readily get the side effect ‘angioedema’ (a severe allergic reaction with swelling of the hands, feet, ankles, face, lips, tongue or throat).
- if you are taking any of the following medicines, the risk of angioedema (rapid swelling under the skin in area such as the throat) may be increased:

- Medicines called mTOR inhibitors, used to prevent organ transplant rejections and for cancer (e.g. temsirolimus, everolimus, sirolimus)
- Racecadotril, a medicine used to treat diarrhoea;
- Vildagliptin, a medicine used to treat diabetes.

Signs of angioedema include swelling of the face, lips, tongue and/or throat with difficulty in swallowing or breathing.

- if you experience a decrease in vision or eye pain. These could be symptoms of fluid accumulation in the vascular layer of the eye (choroidal effusion) or an increase of pressure in your eye and can happen within hours to a week of taking Zestoretic. This can lead to permanent vision loss, if not treated. If you earlier have had a penicillin or sulfonamide allergy, you can be at higher risk of developing this.

You must tell your doctor if you think you are (**or might become**) pregnant. Zestoretic 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 the sections on ‘Pregnancy’ and ‘Breast-feeding’).

If you are not sure if any of the above applies to you, talk to your doctor or pharmacist before taking Zestoretic.

Treatment for allergies such as insect stings

Tell your doctor if you are having or are going to have treatment to lower the effects of an allergy such as insect stings (desensitisation treatment). If you take Zestoretic while you are having this treatment, it may cause a severe allergic reaction.

Operations

If you are going to have an operation (including dental surgery) tell the doctor or dentist that you are taking Zestoretic. This is because you can get low blood pressure (hypotension) if you are given certain local or general anaesthetics while you are taking Zestoretic.

Other medicines and Zestoretic

Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. This includes medicines that you buy without a prescription and herbal medicines. This is because Zestoretic can affect the way some medicines work and some medicines can have an effect on Zestoretic. Your doctor may need to change your dose and/or to take other precautions.

In particular, tell your doctor or pharmacist if you are taking any of the following medicines:

- Other medicines for treatment of high blood pressure (antihypertensives).
- An angiotensin II receptor blocker (ARB) or aliskiren, (see also information under the headings “Do not take Zestoretic” and “Warnings and precautions”).
- Medicines associated with low blood potassium (hypokalaemia) such as other diuretics (“water tablets” including those which conserve potassium), laxatives, corticosteroids (e.g. prednisone), ACTH (a hormone), amphotericin (an antifungal medicine) and salicylic acid derivatives.
- Non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen or indometacin, used to treat muscle pain or arthritis.
- Medicines for depression (tricyclic and tetracyclic antidepressants).
- Medicines for mental problems such as lithium.
- Aspirin (acetylsalicylic acid), if you are taking more than 3 grams each day.

- Potassium supplements (including salt substitutes), potassium-sparing diuretics and other medicines that can increase the amount of potassium in your blood (e.g. trimethoprim and co-trimoxazole 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).
- Calcium salts or Vitamin D supplements.
- Medicines for diabetes (insulin and oral antidiabetics such as sulphonylureas). Your dose of antidiabetic medicine may need to be changed when taking thiazide diuretics.
- Medicines to treat asthma.
- Medicines to treat nose or sinus congestion or other cold remedies (including those you can buy in the pharmacy).
- Medicines to suppress the body's immune response (immunosuppressants, such as ciclosporin).
- Allopurinol (for gout).
- Medicines for uneven heart beat problems (such as procainamide).
- Heart medicines (e.g. digoxin) or other medicines to control the rhythm of your heart.
- Gold injections (such as sodium aurothiomalate), usually used to treat rheumatoid arthritis.
- Amphotericin B injection (to treat fungal infections).
- Carbenoxolone (to treat ulcers or inflammation in the gullet or in and around the mouth).
- Corticosteroids (steroid medicines).
- Corticotropin (a hormone).
- Medicines to treat constipation (stimulant laxatives).
- Colestyramine and colestipol (to lower cholesterol, prevent diarrhoea or reduce itching).
- Muscle relaxants such as tubocurarine.
- Trimethoprim (an antibiotic).
- Sotalol (a beta-blocker).
- Lovastatin (to lower cholesterol).
- Dextran sulphate (used in the treatment called 'LDL apheresis' to lower cholesterol).
- Medicines used to treat cancer (e.g. cyclophosphamide, methotrexate, everolimus) and medicines given to prevent the body from rejecting a transplanted organ, e.g. kidney or liver (such as temsirolimus, sirolimus, everolimus). See section 2 'Warnings and precautions.'
- Racecadotril used to treat diarrhoea. See section 2 'Warnings and precautions.'
- Vildagliptin, a medicine used to treat diabetes. See section 2 'Warnings and precautions.'
- Tissue plasminogen activator (TPA) that is used to dissolve blood clots that have formed in blood vessels.
- Other medicines known to have an effect on the heart called Torsades de pointes.

Simultaneous treatment with tissue plasminogen activators (medicines used to dissolve clots) may increase the risk of localised swelling in your face, mouth or in other parts of your body.

Low blood pressure may be aggravated by alcohol, barbiturates or anaesthetics. You may notice dizziness when standing up.

Pregnancy and breast-feeding

Pregnancy

You must tell your doctor if you think you are (**or might become**) pregnant. Your doctor will normally advise you to stop taking Zestoretic before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Zestoretic.

Zestoretic 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

Tell your doctor if you are breast-feeding or about to start breast-feeding. Zestoretic is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed, especially if your baby is newborn, or was born prematurely.

Driving and using machines

- This medicine may have an effect on your ability to drive or use machines, especially at the start of treatment or when the dose is adjusted, or in combination with alcohol. If this happens to you, do not drive or use any tools or machines.
- You must wait to see how your medicine affects you before trying these activities.

3. How to take Zestoretic

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

Once you have started taking Zestoretic your doctor may take blood tests. Your doctor may then adjust your dose so you take the right amount of medicine for you.

Taking your medicine

- Swallow the tablet with a drink of water.
- Try to take your tablets at the same time each day. It does not matter if you take Zestoretic before or after food.
- Keep taking Zestoretic for as long as your doctor tells you to, it is a long term treatment. It is important to keep taking Zestoretic every day.

Taking your first dose

- Take special care when you have your first dose of Zestoretic or if your dose is increased. It may cause a greater fall in blood pressure than later doses.
- This may make you feel dizzy or light-headed. If this happens, it may help to lie down. If you are concerned, please talk to your doctor as soon as possible.

Adults

- The recommended dose is one tablet once a day. Your doctor will prescribe the tablet that is the right strength for you.
- If necessary, your doctor may increase your dose to two tablets once a day.

Use in children

- Zestoretic is not recommended for use in children.

If you take more Zestoretic than you should

If you take more Zestoretic than prescribed by your doctor, talk to a doctor or go to a hospital immediately. Take the medicine pack with you so that the tablets can be identified.

If you forget to take Zestoretic

- If you forget to take a dose, take it as soon as you remember. However, if it is nearly time for the next dose, skip the missed dose.
- Do not take a double dose to make up for a forgotten dose.

If you stop taking Zestoretic

Do not stop taking your tablets, even if you are feeling well, unless your doctor tells you to.

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.

Zestoretic contains two medicines: lisinopril and hydrochlorothiazide. The following side effects have been seen with these individual medicines. This means they could also happen with Zestoretic.

Your doctor may take blood samples from time to time to check whether Zestoretic has had any effect on your blood.

Possible side effects with lisinopril**Severe allergic reactions** (rare, may affect up to 1 in 1,000 people)

If you have a severe allergic reaction, **stop taking Zestoretic and see a doctor immediately.**

The signs may include sudden onset of:

- Swelling of your face, lips, tongue or throat. This may make it difficult to swallow.
- Severe or sudden swelling of your hands, feet or ankles.
- Difficulty breathing.
- Severe itching of the skin (with raised lumps).

Severe liver problems (very rare, may affect up to 1 in 10,000 people)

The signs may include:

- Yellowing of your skin or eyes, dark coloured urine or a loss of appetite.

If this happens to you, **see a doctor immediately.**

Other possible side effects:**Common (may affect up to 1 in 10 people)**

- Headache.
- Feeling dizzy or light-headed, especially if you stand up quickly.
- Fainting.
- Diarrhoea.
- Being sick (vomiting).
- Cough.
- Kidney problems (shown in a blood test).

Uncommon (may affect up to 1 in 100 people)

- Mood changes.
- Tingling feeling such as ‘pins and needles’.
- Spinning feeling (vertigo).
- Changes in the way things taste.
- Difficulty in sleeping.
- Heart attack or stroke.
- Unusual heart beat.
- Change of colour in your fingers or toes.
- Runny nose.
- Feeling sick (nausea).
- Stomach pain and indigestion.
- Changes in blood tests that check how the liver is working.
- Rash.
- Itching.
- Being unable to get an erection (impotence).
- Feeling weak.
- Feeling tired.
- Increased levels of certain substances in your blood (urea, creatinine or potassium).

Rare (may affect up to 1 in 1,000 people)

- Changes to some of the cells or other parts of your blood. The signs may include feeling tired and pale skin.
- Feeling confused.
- Changes in the way things smell.
- Dry mouth.
- Skin rash with dark red, raised, itchy bumps (hives).
- Hair loss (alopecia).
- Psoriasis (a skin problem).
- Infection of the blood.
- Kidney failure.
- Enlarged breasts in men.
- Syndrome of inappropriate antidiuretic hormone secretion (SIADH).
- Low levels of sodium in the blood, which may cause weakness, tiredness, headache, feeling sick, being sick (vomiting) and cramps.

Very rare (may affect up to 1 in 10,000 people)

- Problems with your bone marrow or a reduced number of blood cells and/or platelets in your blood. You may notice tiredness, an infection (which may be serious), fever, feeling breathless or that you bruise or bleed more easily.
- Swollen glands (lymph nodes).
- Increased immune response (autoimmune disease).
- Low levels of sugar in your blood (hypoglycaemia). The signs may include feeling hungry or weak, sweating and a fast heart beat.
- Suddenly feeling wheezy or short of breath (bronchospasm).
- Lung inflammation (which may make you feel breathless).
- Sinusitis (a feeling of pain and fullness behind your cheeks and eyes).
- Eosinophilic pneumonia. The signs include a combination of the following:
 - sinusitis

- feeling like you have flu
- feeling more and more breathless
- pain in the area of your stomach or gut
- skin rash
- a feeling of ‘pins and needles’ or numbness of your arms or legs.
- Inflammation of the pancreas. This causes moderate to severe pain in the stomach.
- Swelling of the lining of the gut. This may cause sudden stomach pain, diarrhoea or make you be sick (vomit).
- Sweating.
- Severe skin disorder or rash. The symptoms include redness, blistering and peeling of the skin which may develop quickly and may include blistering in the mouth and nose.
- Passing less water (urine) than normal or passing no water.
- Acute respiratory distress (signs include severe shortness of breath, fever, weakness, and confusion).

Not known (frequency cannot be estimated from the available data)

- Serious allergic reaction.
- Seeing, feeling or hearing things that are not there (hallucinations).
- Flushing of your skin.
- Feeling depressed.

Possible side effects with hydrochlorothiazide (frequency not known)

- Skin and lip cancer (Non-melanoma skin cancer).
- Inflammation of a salivary gland.
- A reduced number of blood cells and/or platelets in your blood. You may notice tiredness, an infection (which may be serious), fever, feeling breathless or that you bruise or bleed more easily.
- Loss of appetite.
- An increase in the amount of sugar (glucose) in your blood (hyperglycaemia).
- Sugar in your urine.
- An increase in the amount of uric acid in your blood.
- Altered levels of substances in your blood (for example low sodium and potassium). You may notice muscle weakness, thirst, ‘pins and needles’, cramps or feeling sick.
- Raised or high levels of fats in your blood (including cholesterol).
- Feeling restless.
- Depression.
- Difficulty sleeping.
- Tingling feelings such as ‘pins and needles’.
- Feeling light headed.
- Changes to your vision that can make things look yellow.
- Problems with your sight for a short time.
- Severe eye pain with redness and sudden blurred vision. If you have a suddenly painful red eye tell your doctor immediately; you may need treatment to avoid permanent loss of vision.
- 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).
- A spinning feeling (vertigo).

- Feeling faint (especially when standing up).
- Damage to blood vessels causing red or purple spots in the skin.
- Difficulty breathing. You may feel breathless if your lungs get inflamed or have fluid on them.
- Stomach irritation.
- Diarrhoea.
- Constipation.
- Inflammation of the pancreas. This causes moderate to severe pain in the stomach.
- Yellowing of your skin or the whites of your eyes (jaundice).
- Skin problems including rash caused by sensitivity to sunlight, rash, a severe rash that develops quickly with blistering or peeling of the skin and possibly blistering in the mouth, activating or worsening of existing lupus conditions or appearance of unusual skin reactions.
- Allergic reactions.
- Muscle cramps and muscle weakness.
- Kidney problems which may be severe (shown in blood tests).
- Fever.
- Weakness.

Do not be concerned by this list of possible side effects. You may not get any of them.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

Ireland

HPRA Pharmacovigilance

Website: www.hpra.ie

Malta

ADR Reporting

Website: www.medicinesauthority.gov.mt/adrportal

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Zestoretic

- 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 strip and the carton. The expiry date refers to the last day of that month.
- Store your tablets below 30°C. Always keep the blister strip in the carton in order to protect your tablets from light.
- 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 Zestoretic contains

The active substances are lisinopril (as dihydrate) and hydrochlorothiazide. Two strengths of tablets are available:

- Zestoretic 10 mg/12.5 mg Tablets contain 10 mg of lisinopril and 12.5 mg of hydrochlorothiazide.
- Zestoretic 20 mg/12.5 mg Tablets contain 20 mg of lisinopril and 12.5 mg of hydrochlorothiazide.

The other ingredients are calcium hydrogen phosphate dihydrate, magnesium stearate, maize starch, mannitol and pregelatinised starch. Zestoretic 10 mg/12.5 mg Tablets also contain iron oxide (E172).

What Zestoretic looks like and contents of the pack

Zestoretic 10 mg/12.5 mg Tablets are peach coloured and round. They have '10 12.5' on one side and a break line on the other. The break line is not intended for breaking the tablet.

Zestoretic 20 mg/12.5 mg Tablets are white and round. They have '20 12.5' on one side and a break line on the other. The break line is not intended for breaking the tablet.

They are supplied in cartons containing blister strips of 28 tablets.

Marketing Authorisation Holder and Manufacturer

The Marketing Authorisations for Zestoretic marketed in Ireland and Malta are held by Atnahs Pharma Netherlands B.V., Copenhagen Towers, Ørestads Boulevard 108, 5.tv, DK-2300 København S, Denmark.

Zestoretic is manufactured by

AstraZeneca AB, Gärtunavägen, SE- 152 57Södertälje Sweden

ROVI Pharma Industrial Services S. A.,
Vía Complutense, 140,
Alcalá de Henares, Madrid, 28805
Spain

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