

Applicant: AstraZeneca Pharmaceuticals (Pty) Ltd
Product Name: ZESTORETIC
Strength and Dosage Form: 10 mg and 20 mg

Module 1.5.5 PI and PIL updates
Date of amendment: 22 October 2021

1.5.5 PATIENT INFORMATION LEAFLET (AMENDED PROPOSED CLEAN)

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S3

ZESTORETIC[®] 10; ZESTORETIC[®] 20 Tablets

Lisinopril and Hydrochlorothiazide

Contains sugar: mannitol 17,7 mg per ZESTORETIC 10 tablet and 40 mg per ZESTORETIC 20 tablet

Read all of this leaflet carefully before you start taking ZESTORETIC

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- ZESTORETIC has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

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 contains two active substances, lisinopril and hydrochlorothiazide. They both lower blood pressure but by a different mechanism. Hydrochlorothiazide is a diuretic. Diuretics act on the kidney to remove water from the blood into the urine. Lisinopril belongs to a group of medicines called ACE inhibitors (Angiotensin Converting Enzyme inhibitors). Lisinopril works by widening your blood vessels, which helps reduce your blood pressure and makes it easier for your heart to pump blood to all parts of your body. Your doctor has prescribed ZESTORETIC because your blood pressure is too high.

2. What you need to know before you take ZESTORETIC

Do not take ZESTORETIC:

- If you are hypersensitive (allergic) to lisinopril, hydrochlorothiazide or to any of the other ingredients of ZESTORETIC.
- If you have previously been treated with a medicine in the same group as lisinopril (ACE inhibitors) and have had allergic reactions with itching, hives, sudden fall in blood pressure, swelling of the hands, feet or ankles, the face, lips, tongue and/or throat with difficulty in swallowing or breathing or if you or a member of your family have had a similar reaction.
- If you have ever shown an allergic type reaction to hydrochlorothiazide diuretics, which are medicines similar to sulphonamides (a type of antibiotic) or to any of ZESTORETIC's ingredients.
- If you have a kidney condition called anuria, where you fail to produce urine.
- If you have a heart condition called aortic stenosis (narrowing of the aorta) or hypertrophic cardiomyopathy (increase in the thickness of the heart muscle).
- If you are pregnant, trying to fall pregnant or are 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.
- if you have hereditary angioedema (a condition that makes you more prone to the swelling described above).

The safety in children has not been proven.

Warnings and precautions

Take special care with ZESTORETIC:

Tell your doctor if you have or have had any medical condition, especially the following:

- If you are pregnant or trying to fall pregnant.
- If you are dehydrated or have less electrolytes (salt) in your blood (shown on blood tests), or on other water pills (diuretics)
- If you have had a previous heart attack or stroke.
- If you have a narrowing of the aorta (aortic stenosis), the kidney artery (renal artery stenosis) or an increase in the thickness of the heart muscle (hypertrophic cardiomyopathy).

- If you have low blood pressure (you may notice this as dizziness or light-headedness especially when standing).
- If you have kidney disease or on dialysis.
- If you have liver disease.
- If you experience swelling of the face, finger and toes, lips, tongue, and difficulty breathing (angio-oedema).
- If you have asthma or lupus (SLE).
- If you have diabetes or high cholesterol.
- If you have gout.
- If you have diarrhoea or vomiting
- If you are on a salt-restricted diet
- If you have a persistent cough.

If you are taking medicines called mTOR inhibitors (for example temsirolimus, everolimus, sirolimus) or medicines containing NEP inhibitors (for example racecadotril) as they may increase the risk of angioedema. Signs of angioedema include swelling of the face, lips, tongue and/or throat with difficulty in swallowing or breathing.

If you have had skin cancer or if you develop a suspicious 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). Limit exposure to sunlight and protect your skin when exposed to sun while taking ZESTORETIC.

If you are undergoing/or will undergo desensitisation treatment for an allergy, for example, to insect stings. The desensitisation treatment reduces the effects of the allergy (e.g. bee or wasp stings) but sometimes it can cause a more severe allergic reaction if you are taking ACE inhibitors during the desensitisation treatment.

If you are going into hospital for an operation. Tell your doctor or dentist that you are taking ZESTORETIC before you are given a local or general anaesthetic. ZESTORETIC, combined with some anaesthetics, may cause a short-term drop in blood pressure soon after taking the tablets.

Take special care when taking the first dose of ZESTORETIC. It may cause a greater fall in blood pressure than will occur following continued treatment. You may notice this as dizziness or light headedness and it may help to lie down. If you are concerned, please consult your doctor.

Other medicines and ZESTORETIC

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines).

If you are taking any of the following medicines tell your doctor, pharmacist or health care professional:

- Diuretics (water tablets)
- Other medicines for your high blood pressure
- Medicines for diabetes, including insulin. Your dose of anti- diabetic may need to be changed.
- Non-steroidal anti-inflammatory medicines (NSAIDs), e.g. indomethacin that you may use for arthritis or muscle pain.
- Gold injections (such as sodium aurothiomalate), usually used to treat rheumatoid arthritis.
- Medicines for mental disorders such as lithium.
- Potassium tablets or potassium-containing salt substitutes.
- 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).
- Racecadotril used to treat diarrhoea.
- Tissue plasminogen activator (TPA) that is used to dissolve blood clots that have formed in blood vessels
- Muscle relaxants such as tubocurarine.
- Corticosteroids and adrenaline
- Desensitisation treatment such as treatment for a bee sting, grass allergy, mites etc.

ZESTORETIC with food, drink and alcohol

Tablets may be taken before, during or after meals.

Pregnancy and breastfeeding

Before taking ZESTORETIC, tell your doctor if you are pregnant, trying to become pregnant or are breastfeeding.

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

ZESTORETIC must not be taken during pregnancy.

Driving and using machines

ZESTORETIC can cause dizziness or tiredness. You should not perform such tasks which require special attention until you know how your medicine will affect you.

ZESTORETIC contains mannitol

ZESTORETIC contains mannitol and may have a laxative effect

3. How to take ZESTORETIC

Do not share medicines prescribed for you with any other person.

Always take ZESTORETIC exactly as your doctor or pharmacist has instructed you. Check with your doctor or pharmacist if you are not sure.

The usual recommended dose is 1 tablet taken once daily. The dosage may be increased to a maximum of 2 tablets taken once a day.

Your doctor will tell you how many tablets to take each day.

The dosage is individual and it is important that you take it as prescribed by your doctor. Your starting dose and long-term dose will depend on your medical condition and whether you are taking any other medicines.

Your doctor will tell you how long your treatment with ZESTORETIC will last. Do not stop treatment early.

If you have the impression that the effect of ZESTORETIC is too strong or too weak, tell your doctor or pharmacist.

- Swallow your tablets whole with a drink of water.
- You can take your tablet at any time of the day, with or without food. However, try to take your tablets at the same time each day, this will help you to remember to take it.
- Remember, the first dose of ZESTORETIC may cause a greater fall in blood pressure than will occur following continued treatment. You may notice this as dizziness or light-headedness and it may help to lie down. If concerned, please consult your doctor as soon as possible.

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

If you take more ZESTORETIC than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take ZESTORETIC

If you miss a dose, take the dose as soon as you remember, but do not take your next dose at the same time. Take the next dose as usual.

Do not take a double dose to make up for forgotten individual doses.

4. Possible side effects

ZESTORETIC can have side effects.

Not all side effects reported for ZESTORETIC are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking ZESTORETIC, please consult your health care provider for advice.

If any of the following happens, stop taking ZESTORETIC and tell your doctor immediately or go to the casualty department at your nearest hospital:

- If you develop difficulty in breathing with or without swelling of the face, lips, tongue and/or throat.
- If you develop swelling of the face, lips, tongue and/or throat which may cause difficulty in swallowing.
- If you develop severe itching of the skin (with raised lumps).

These are all very serious side effects. If you have them, you may have had a serious reaction to ZESTORETIC. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- anaemia
- muscle weakness
- inflammation of the pancreas, shown in blood tests
- changes in the way things smell
- low levels of sodium, shown in blood tests (the symptoms may be tiredness, headache, nausea, vomiting).
- yellow skin and/or eyes (jaundice)
- inflammation of the liver, shown in blood tests.

These are all serious side effects. You may need urgent medical attention.

There may be changes to some of the cells or other parts of your blood. It is possible that your doctor may occasionally take blood samples to check whether ZESTORETIC has had any effect on your blood. Sometimes these changes may show themselves as tiredness or a sore throat, or they may be accompanied by a fever, joint and muscle pains, swelling of the joints or glands or sensitivity to sunlight.

Tell your doctor if you notice any of the following:

Frequent side effects:

- dizziness or light-headedness especially when standing up quickly,
- headache,
- cough,
- tiredness,
- diarrhoea,
- nausea,
- vomiting,
- skin rash,
- muscle cramps,
- weakness (loss of strength),
- numbness or tingling in the fingers or toes,

- impotence,
- fainting.

Less frequent side effects:

- dry mouth,
- gout,
- rapid heartbeat,
- chest discomfort,
- signs of depression.

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

- serious allergic reaction

Other side effects associated with the lisinopril component:

Effects on the heart and blood vessels: An excessive drop in blood pressure may be experienced in patients with coronary heart disease, or those with a narrowing of the aorta, the kidney artery or the heart valves, or those patients with an increase in the thickness of the heart muscle. This could cause a heart attack or stroke.

Effects on the stomach, bowel and liver: Stomach pain and indigestion

Effects on your nervous system: Mood changes, confusion, dizziness. Changes in the way things taste. Feeling sleepy or difficulty in going to sleep, strange dreams.

Effects on your respiratory system: Wheezing, running nose, sinus pain.

Effects on your skin: Hair loss, sweating, rash, itching. Psoriasis and severe skin disorders (symptoms of which include redness, blistering and peeling).

Effects on your urinary system: ZESTORETIC may affect the kidneys causing an abnormally low or no urine to be passed.

Other side effects associated with the hydrochlorothiazide component:

Effects on the blood vessels: Inflammation of the blood vessels.

Effects on the stomach and bowel: Loss of appetite, upset stomach, *constipation, inflammation of the salivary glands.*

Effects on your nervous system: Restlessness.

Effects on your respiratory system: Lung problems.

Effects on your skin: Bruising and discolouration to the skin.

Effects on your sight: Visual changes that make objects look yellow, transient visual disturbance, severe eye pain accompanied by redness and sudden blurred vision. Patients with an acute painful red eye should seek medical attention immediately; if left untreated this condition could lead to permanent vision loss.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: <https://www.sahpra.org.za/Publications/Index/8>. By reporting side effects, you can help provide more information on the safety of ZESTORETIC.

5. How to store ZESTORETIC

Store all medicines out of reach of children.

Store at or below 25 °C

ZESTORETIC should be stored away from light in a dry place

Do not use ZESTORETIC after the expiry date stated on the container

Return all unused medicines to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What ZESTORETIC contains

The active substances are lisinopril dihydrate and hydrochlorothiazide.

Each ZESTORETIC 10 tablet contains 10 mg lisinopril as the dihydrate and 12,5 mg of hydrochlorothiazide

Each ZESTORETIC 20 tablet contains 20 mg lisinopril as the dihydrate and 12,5 mg of hydrochlorothiazide

The other ingredients are calcium hydrogen phosphate dihydrate, iron oxide, magnesium stearate, maize starch, mannitol, pregelatinised starch.

What ZESTORETIC looks like and contents of the pack

ZESTORETIC 10 Tablets: Peach-coloured, round, biconvex, uncoated tablet. Intagliated with "Zt" and "10" on one side and plain on the other.

ZESTORETIC 20 Tablets: White, round, biconvex uncoated tablet intagliated ZESTORETIC on one side and bisected on the other.

ZESTORETIC tablets are packed in plastic bottles containing 30 tablets or cartons containing 30 tablets in blister strips.

Not all pack sizes may be marketed

Holder of Certificate of Registration

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Access to the corresponding Professional Information

TBA