PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S3

ZOFARIL CO 30 mg/12,5 mg film coated tablets

Zofenopril calcium and hydrochlorothiazide

Contains sugar (56,2 mg lactose monohydrate)

Read all of this leaflet carefully before you start taking ZOFARIL CO.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- ZOFARIL CO 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 ZOFARIL CO is and what it is used for

ZOFARIL CO contains 30 mg zofenopril calcium and 12,5 mg hydrochlorothiazide as the active ingredients.

- Zofenopril calcium is a cardiovascular medicine which belongs to a group of blood pressure-

lowering medicines called angiotensin-converting enzyme (ACE) inhibitors.

- Hydrochlorothiazide is a diuretic, that acts by increasing the amount of urine you produce.

ZOFARIL CO is used to treat mild to moderate high blood pressure (hypertension), when this is not adequately controlled by taking zofenopril alone.

2. What you need to know before you take ZOFARIL CO

Do not take ZOFARIL CO:

- if you are hypersensitive (allergic) to zofenopril, hydrochlorothiazide or any of the other ingredients of ZOFARIL CO (see section 6)
- if you are allergic (hypersensitive) to other sulphonamide-derived substances (like hydrochlorothiazide, which is a sulphonamide-derived medicine)
- if you have had any previous allergic reaction to any other ACE inhibitor, such as captopril or enalapril
- if you are pregnant or breastfeeding (see Pregnancy and breastfeeding)
- if you have a history of severe swelling and itching around the face, nose and throat (angioedema) associated with previous ACE inhibitor therapy, or if you suffer from hereditary/idiopathic angioedema (rapid swelling of the skin, tissues, digestive tract and other organs)
- 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 heart conditions called hypertrophic obstructive cardiomyopathy (abnormally thick heart muscle that can cause shortness of breath, chest pain or abnormal heart rhythms) or aortic stenosis (narrowing of the valve in the large blood vessel of the heart that can cause shortness of breath, chest pain and tiredness)
- if you suffer from severe liver or kidney problems
- if you suffer from narrowing of the arteries to the kidneys
- if you have diabetes or impaired kidney function and you are treated with a blood pressure-

lowering medicine containing aliskiren

- if you are currently taking water tablets such as spironolactone, triamterene, amiloride (used to treat high blood pressure)
- if you have a condition called porphyria (a metabolic disorder)
- simultaneous administration of ZOFARIL CO with lithium may lead to toxic blood concentrations of lithium
- if you have previously had or currently have cancer of the skin and/or lip
- if you have kidney problems or are elderly you should not take a fluoroquinolone antibiotic (used to treat bacterial infections) such as moxifloxacin or levofloxacin while taking ZOFARIL CO.

Warnings and precautions

Take special care with ZOFARIL CO:

- if you have liver or kidney problems
- if you have high blood pressure that is caused by a kidney problem or by narrowing of the artery leading to the kidney (renovascular hypertension)
- if you have recently had a kidney transplant
- if you are undergoing dialysis
- if you are on LDL apheresis (a procedure similar to kidney dialysis that clears your blood of harmful cholesterol)
- if you have abnormally high levels of the hormone aldosterone in your blood (primary aldosteronism)
- if you have a narrowing of the heart valve (aortic stenosis) or thickening of the heart walls (hypertrophic cardiomyopathy)
- if you suffer or have suffered from psoriasis (skin disease characterised by scaly pink patches)
- if you are receiving desensitisation treatment (“allergy injections”) for insect stings
- if you have lupus erythematosus (a disorder of the immune system, your body’s defence

system)

- if you tend to have low blood potassium, and especially if you suffer from prolonged QT syndrome (a kind of heart problem seen as an ECG abnormality) or you are taking digitalis (to help your heart pump)
- if you have diabetes
- if you have angina or disorders affecting the brain, since low blood pressure can lead to a heart attack or stroke
- 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, etc.), in particular if you have diabetes-related kidney problems
  - aliskiren.
- 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:
  - racecadotril, a medicine used to treat diarrhoea
  - medicines used to prevent organ transplant rejection and for cancer (e.g., temsirolimus, sirolimus, everolimus)
  - vildagliptin, a medicine used to treat diabetes
- 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 ZOFARIL CO.
- if you are elderly or have kidney problems you should not take a fluoroquinolone antibiotic (used to treat bacterial infections) such as moxifloxacin or levofloxacin while taking ZOFARIL CO as it may cause or aggravate kidney problems.

Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g. potassium) in your blood at regular intervals. See Do not take ZOFARIL CO.

The hydrochlorothiazide in ZOFARIL CO may cause your skin to be oversensitive to sunlight or

artificial UV light. Stop taking ZOFARIL CO and tell your doctor if you get a rash, itchy spots or sensitive skin during treatment (see Possible side effects).

Anti-doping test: ZOFARIL CO could cause a positive anti-doping test. Your blood pressure may get too low with ZOFARIL CO, especially after the first dose (this is more likely if you are also taking diuretics, are dehydrated or on a low-salt diet). If this happens, tell your doctor immediately and then lie down on your back.

If you are having an operation, tell your anaesthetist that you are taking ZOFARIL CO before being anaesthetised. This will help him/her to control your blood pressure and heart rate during the procedure.

You must tell your doctor if you think you are (or might become) pregnant. ZOFARIL CO is not recommended in early pregnancy and must not be taken if you are pregnant, as it may cause serious harm to your baby (see Pregnancy and breastfeeding).

Children and adolescents

Do not give ZOFARIL CO to children under the age of 18 years as safety and efficacy have not been established.

Other medicines and ZOFARIL CO:

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

Tell your doctor if you are taking, have recently taken or might take any other medicines, e.g.:

- sacubitril/valsartan (a combination product used to treat high blood pressure
- sirolimus (used to prevent organ rejection after a kidney transplant)
- temsirolimus (used to treat a type of cancer that begins in the kidney)
- everolimus (used to prevent organ rejection after a transplant)

- racecadotril (used to treat diarrhoea)
- medicines that increase blood potassium levels (trimethoprim, potassium supplements, potassium-sparing diuretics, such as spironolactone, triamterene, amiloride), potassium-containing salt substitutes
- fluoroquinolone antibiotics (used to treat bacterial infections) such as moxifloxacin or levofloxacin
- other medicines that affect the levels of blood chemicals (adrenocorticotropic hormone - ACTH - used to stimulate the production of some hormones by the body, amphotericin B injections, carbenoxolone, stimulant laxatives)
- lithium (used to treat mood disorders)
- anaesthetics
- narcotics (such as morphine)
- antipsychotics (used to treat schizophrenia and similar illnesses)
- antidepressants of the tricyclic type, e.g. amitriptyline and clomipramine
- barbiturates (used to treat anxiety, insomnia, and seizure disorders)
- other high blood pressure medicines and vasodilators (including beta-blockers, alpha-blockers and diuretics such as hydrochlorothiazide, furosemide, torasemide)
  Your doctor may need to change your dose and/or take other precautions if you are taking an angiotensin II receptor blocker (ARB) or aliskiren (see also information under the headings Do not take ZOFARIL CO and Warnings and precautions.)
- nitroglycerin and other nitrates used for chest pain (angina)
- antacids including cimetidine (used to treat heartburn and stomach ulcers)
- ciclosporin (used after organ transplants) and other immunosuppressants (medicines that suppress your body’s defence system)
- heparin (used to thin your blood and prevent blood clots from forming)
- medicines for gout (e.g. probenecid, sulfinpyrazone and allopurinol)
- insulin or oral anti-diabetic medicines such as vildagliptin (used to treat high sugar levels)
- cytostatics (used to treat cancer or diseases which affect the body’s defence system)

- corticosteroids (powerful anti-inflammatory medicines)
- procainamide (used to control an irregular heartbeat)
- nonsteroidal anti-inflammatory medicines (NSAIDs, such as aspirin or ibuprofen)
- sympathomimetics (medicines that act on the nervous system, including some used to treat asthma or hay fever, and pressor amines, e.g. adrenaline)
- calcium salts
- digitalis (used to help the heart pump)
- colestyramine and colestipol resins (used to lower cholesterol)
- medicines used to relax muscles (e.g. tubocurarine)
- amantadine (an antiviral medicine).

ZOFARIL CO with food, drink and alcohol:

ZOFARIL CO can be taken with food or on an empty stomach, but always with some water.

Alcohol increases the hypotensive (lowering of blood pressure) effect of ZOFARIL CO; ask your doctor for further advice on drinking alcohol whilst on ZOFARIL CO.

Pregnancy and 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 ZOFARIL CO.

Pregnancy:

You should not take ZOFARIL CO if you are pregnant.

You should use contraception while taking ZOFARIL CO.

If you become pregnant while taking ZOFARIL CO tell your doctor immediately. If you are planning to have a baby tell you docter, he/she will switch your medicine to a suitable alternative.

Breastfeeding:

You should not breastfeed your baby if you take ZOFARIL CO.

Driving and using machines:

ZOFARIL CO may cause dizziness or tiredness. If this happens to you, do not drive a vehicle or operate machinery.

ZOFARIL CO contains lactose monohydrate:

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking ZOFARIL CO.

3. How to take ZOFARIL CO

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

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

Adults (18 to 65 years)

The recommended dose of ZOFARIL CO is one tablet per day.

ZOFARIL CO may be taken with food or on an empty stomach. The tablet is best taken with some water. To ease swallowing, you may break the tablet in two and swallow one half right after the other.

Paediatric population (under 18 years)

Do not give ZOFARIL CO to children under the age of 18 years.

Elderly patients (over 65 years)

If you are over 65 years and suffer from an impaired kidney function, ZOFARIL CO may not be suitable for you (see Warnings and precautions).

Your doctor will tell you how long your treatment with ZOFARIL CO will last. Do not stop treatment early. If you have the impression that the effect of ZOFARIL CO is too strong or too weak, tell your doctor or pharmacist.

If you take more ZOFARIL CO than you should:

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre. Always take the labelled medicine package with you, whether there are any ZOFARIL CO tablets left or not.

The most frequent symptoms and signs of an overdose are low blood pressure with fainting (hypotension), very slow heart beat (bradycardia), changes in blood chemicals (electrolytes), kidney dysfunction, excessive urination with consequent dehydration, nausea and somnolence, muscle spasms, heart rhythm disturbances (especially if you are also taking digoxin or medicines for heart rhythm problems).

If you forget to take ZOFARIL CO:

If you forgot to take a dose, take it as soon as you remember. However, if your next dose is nearly due, skip the forgotten dose and take the next scheduled normal dose at the usual time. Do not take a double dose to make up for forgotten individual doses.

If you stop taking ZOFARIL CO:

Do not stop taking ZOFARIL CO unless your doctor tells you to. Should you need to stop taking ZOFARIL CO, your doctor will decide which is the best method for you. Always consult your doctor before stopping treatment with ZOFARIL CO.

4. Possible side effects

ZOFARIL CO can have side effects.

Not all side effects reported for ZOFARIL CO are included in this leaflet. Should your general

health worsen or if you experience any untoward effects while taking ZOFARIL CO, please consult your doctor, pharmacist or other healthcare professional for advice.

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

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

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

Tell your doctor if you notice any of the following:

Frequent side effects:

- dizziness
- headache
- cough.

Less frequent side effects:

- infection, bronchitis
- sore throat
- increase in blood cholesterol and/or other lipids, increased blood glucose, potassium, uric acid, creatinine and liver enzymes
- decrease in blood potassium
- sleeplessness (insomnia) or sleepiness (somnolence), fainting, muscle tightness (hypertonia)
- angina (chest pain), heart attack, atrial fibrillation, fast irregular heartbeat
- flushing, low blood pressure, high blood pressure
- nausea, indigestion (heartburn), gastritis, inflammation of the gums, dry mouth, stomach pain

- skin disease characterised by scaly pink patches (psoriasis), acne (problem skin), dry skin, itching, hives
- back pain
- increased urine (polyuria)
- general weakness (asthenia), flu-like symptoms, peripheral swelling (usually around the ankles)
- impotence.

In addition to the side effects reported with ZOFARIL CO, the following have generally been reported with ACE inhibitors:

- Tiredness (fatigue). Severe low blood pressure at the start of treatment or when the dosage is increased, with dizziness, impaired vision, fainting (syncope), low blood pressure on standing.
- Chest pain, muscle aches and/or cramps.
- Impaired consciousness, sudden dizziness, suddenly impaired vision or weakness and/or loss of sense of touch on one side of the body (transient ischaemic attack or stroke).
- Reduced kidney function, changes in the amount of daily urine, presence of proteins in the urine (proteinuria).
- Vomiting (being sick), nausea (feeling sick), diarrhoea, constipation.
- Allergic skin reaction with peeling, redness, loosening and blistering of the skin (toxic epidermal necrolysis), worsening of psoriasis, hair loss (alopecia).
- Increased sweating.
- Mood changes, depression, sleep disorders.
- Altered skin sensations such as burning, prickling, or tingling (paraesthesia).
- Disorders of balance, confusion, ringing in the ears (tinnitus), taste disturbances, blurred vision.
- Difficulty in breathing, narrowing of the airways in the lung (bronchospasm), sinusitis, runny or stuffy nose (rhinitis), inflammation of the tongue (glossitis).

- Yellowing of the skin (jaundice), inflammation of the liver or pancreas (hepatitis, pancreatitis), bowel obstruction (ileus).
- Changes in blood tests, such as red blood cell, white blood cell or platelet count or a reduction in all kinds of blood cells (pancytopenia): **Contact your doctor if you find that you bruise easily or develop an unexplained sore throat or fever.**
- Increased blood levels of bilirubin, increased blood urea.
- Anaemia due to rupture of red blood cells (haemolytic anaemia), which may occur if you suffer from G6PD (glucose 6-phosphate dehydrogenase) deficiency.

The following side effects were not reported in clinical trials with ZOFARIL CO, but they have been reported with hydrochlorothiazide, so they may also occur with the use of ZOFARIL CO:

- Skin and lip cancer (Non-melanoma skin cancer).
- Impaired production of new blood cells by the bone marrow (bone marrow failure).
- Altered levels of body fluids (dehydration) and blood chemicals (electrolytes), gout, diabetes, metabolic alkalosis.
- Apathy, nervousness, restlessness.
- Convulsions, depressed level of consciousness, coma, paresis.
- Yellow vision (xanthopsia), worsening of myopia, decreased lacrimation.
- Vertigo (spinning sensation).
- Heart rhythm disturbances (dysrhythmias), changes in the electrocardiogram.
- Formation of blood clots in veins (thrombosis) and embolism, circulatory collapse (shock).
- Respiratory distress, lung inflammation (pneumonitis), formation of fibrous tissue in the lungs (interstitial lung disease), fluid accumulation in the lung (pulmonary oedema).
- Thirst, lack of appetite (anorexia), absence of bowel movements (paralytic ileus), excessive gas in the stomach, inflammation of the glands that produce saliva (sialadenitis), increased blood amylase (a pancreatic enzyme, hyperamylasaemia), inflammation of the gall bladder (cholecystitis).
- Purple spots/blotches on the skin (purpura), increased sensitivity of your skin to sunlight,

rash (especially facial) and/or patchy redness that can cause scarring (cutaneous lupus erythematosus), inflammation of blood vessels with consequent death of tissue (necrotising vasculitis).

- Acute kidney failure (with reduced urine production and build-up of fluid and waste materials in your body), inflammation of the connective tissue within the kidneys (interstitial nephritis), sugar in the urine.

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 ZOFARIL CO.

5. How to store ZOFARIL CO

- Store at or below 30 °C.
- Keep blister strips in outer carton until required for use.
- STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
- Do not use after the expiry date printed on the carton.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What ZOFARIL CO contains:

The active substances are 30 mg zofenopril calcium and 12,5 mg hydrochlorothiazide.

The other ingredients are the following:

Hypromellose, iron oxide red (E172), lactose monohydrate, macrogol 400, macrogol 6000,

magnesium stearate, maize starch, microcrystalline cellulose, silica colloidal anhydrous, titanium dioxide (E171).

What ZOFARIL CO looks like and contents of the pack:

Pastel-red, round, slightly biconvex tablets with a score line on one side.

The score line is to facilitate breaking for ease of swallowing and not to divide into equal doses.

Transparent PVC/PVDC/silver aluminium blister strips packed into a cardboard carton.

Pack size: 28 tablets.

Holder of Certificate of Registration:

LeBasi Pharmaceuticals (Pty) Ltd

San Domenico Building, Unit 6, Ground Floor

10 Church Street

Durbanville

7551

087 551 3245

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