APPROVED PIL

For

Cosyrel

Registration No.:

Cosyrel 5 mg/5 mg: 51/7.1.3/0495
Cosyrel 5 mg/10 mg: 51/7.1.3/0496
Cosyrel 10 mg/5 mg: 51/7.1.3/0497
Cosyrel 10 mg/10 mg: 51/7.1.3/0498

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Confidential Information

SCHEDULING STATUS S3

Cosyrel 5/5 mg, film-coated tablets

Cosyrel 5/10 mg, film-coated tablets

Cosyrel 10/5 mg, film-coated tablets

Cosyrel 10/10 mg, film-coated tablets

bisoprolol fumarate/perindopril arginine

Read all of this leaflet carefully before you start taking Cosyrel.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist, nurse or other healthcare provider.
- **Cosyrel** has been prescribed to 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 **Cosyrel** is and what it is used for
2. What you need to know before you take **Cosyrel**
3. How to take **Cosyrel**
4. Possible side effects
5. How to store **Cosyrel**
6. Contents of the pack and other information

1. What Cosyrel is and what it is used for

Cosyrel contains two active ingredients, bisoprolol fumarate and perindopril arginine in one tablet.

- Bisoprolol fumarate belongs to a group of medicines called beta-blockers. Beta-blockers slow down the heart rate and make the heart more efficient at pumping blood around the body.
- Perindopril arginine is an angiotensin converting enzyme (ACE) inhibitor. It works by widening the blood vessels, which makes it easier for your heart to pump blood through them.

Cosyrel is used to treat high blood pressure (hypertension) and/or stable chronic heart failure (a condition where the heart is unable to pump enough blood to meet the body's needs resulting in breathlessness and swelling) and/or to reduce the risk of cardiac events, such as heart attack, in patients with stable coronary artery disease (a condition where the blood supply to the heart is reduced or blocked) and who have already had a heart attack and/or an operation to improve the blood supply to the heart by widening the vessels that supply it.
Instead of taking bisoprolol fumarate and perindopril arginine as separate tablets, you will take only one tablet of **Cosyrel** which contains both active ingredients in the same strength.

2. What you need to know before you take Cosyrel

Do not take Cosyrel if you

- are allergic to bisoprolol or any other beta-blocker, to perindopril or any other ACE-inhibitor, or to any of the other ingredients of this medicine (listed in section 6),
- have heart failure that suddenly becomes worse and/or that may require hospital treatment,
- have a cardiogenic shock (a serious heart condition caused by very low blood pressure),
- have a heart disease characterised by a slow or irregular heart rate (atrioventricular block second or third degree, sinoatrial block, sick sinus syndrome),

- have a slow heart rate,
- have very low blood pressure,
- have severe asthma or severe chronic lung disease,
- have severe blood circulation problems in your limbs (such as Raynaud's syndrome), which may cause your fingers and toes to tingle or turn pale or blue,
- have an untreated phaeochromocytoma, which is a rare tumour of the adrenal gland (medulla),
- have metabolic acidosis, a condition where your blood contains too much acid,
- have experienced symptoms such as wheezing, swelling of the face, tongue or throat, with or without breathing difficulty, 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),
- are pregnant or breastfeeding your baby (see pregnancy section),
- have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren,
- are having dialysis or any other type of blood filtration. Depending on the machine that is used, **Cosyrel** may not be suitable for you,
- have kidney problems where the blood supply to one or both of your kidneys is reduced (renal artery stenosis), or you have only one kidney with a reduced blood supply to the kidney,
- if you are being treated with sacubitril/valsartan, a medicine for heart failure (see "Warning and Precaution" and "Other medicines and **Cosyrel**").
- If you are treated with lithium**.**

Warnings and precautions

Talk to your doctor or pharmacist before taking **Cosyrel**, if you

- have diabetes,

- have kidney problems (including kidney transplantation) or if you are receiving dialysis,
- have a liver problem/disease,
- have aortic and mitral stenosis (narrowing of the main blood vessel (aorta) leading from the heart) or narrowing of the aortic and/or mitral heart valves, or hypertrophic cardiomyopathy (heart muscle disease) or renal artery stenosis (narrowing of the artery supplying the kidney with blood),
- have abnormally increased levels of a hormone called aldosterone in your blood (primary aldosteronism),
- have heart failure or any other heart problems such as minor disturbances in heart rhythm or severe chest pain at rest (Prinzmetal's angina),
- suffer from a collagen vascular disease (disease of the connective tissue) such as systemic lupus erythematosus or scleroderma,
- are on a salt restricted diet or use salt substitutes which contain potassium (too much potassium in the blood can cause changes in the heart rates),
- have recently suffered from diarrhoea or vomiting, or are dehydrated (**Cosyrel** may cause a fall in blood pressure),
- are to undergo LDL apheresis (which is removal of cholesterol from your blood by a machine),
- have current antiallergic treatment or are going to have 5esensitization treatment to reduce the effects of an allergy to bee or wasp stings,
- are under strict fasting or diet,
- are to undergo anaesthesia and/or major surgery,
- have any problems with the circulation in your limbs,
- have asthma or chronic lung disease,
- have (or have had) psoriasis,
- have a tumour of the adrenal gland (phaeochromocytoma),

- have thyroid disorders **Cosyrel** can hide symptoms of an overactive thyroid),
- have angioedema (severe allergic reaction with swelling of the face, lips, tongue or throat with difficulty in swallowing or breathing). This may occur at any time during treatment. If you develop such symptoms, you should stop taking **Cosyrel** and see a doctor immediately,
- 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,
- 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 **Cosyrel**”.
- are taking any of the following medicines, the risk of angioedema is increased
  - racecadotril (used to treat diarrhoea),
  - sirolimus, everolimus, temsirolimus and other medicines belonging to the class of so-called mTor inhibitors (used to avoid rejection of transplanted organs),
  - sacubitril (available as fixed-dose combination with valsartan), used to treat long-term heart failure.

Do not suddenly stop taking **Cosyrel** since this can cause severe worsening of your heart condition. Treatment should not be discontinued abruptly, especially if you have coronary artery disease.

Children and adolescents

Cosyrel is not recommended for use in children and adolescents younger than 18 years of age.

Other medicines and Cosyrel

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

There are some medicines that may change the effect of **Cosyrel** or their effect may be changed by **Cosyrel**. This type of interaction could make one or both of the medicines less effective. Alternatively, it could increase the risk or severity of side effects.

Make sure to tell your doctor if you are taking any of the following medicines:

- medicines used to control blood pressure or medicines for heart problems (such as amiodarone, amlodipine, clonidine, digoxin, diltiazem, disopyramide, felodipine, flecainide, lidocaine, methyldopa, moxonidine, procainamide, propafenone, quinidine, rilmenidine, verapamil),
- other medicines used to treat high blood pressure, including angiotensin II receptor blocker (ARB), aliskiren (see also information under the headings “Do not take **Cosyrel**” and “Warnings and precautions”) or diuretics (medicines which increase the amount of urine produced by the kidneys),
- potassium-sparing medicines (e.g. triamterene, amiloride), potassium supplements or potassium-containing salt substitutes, other medicines which can increase potassium in your body (such as heparin and co-trimoxazole also known as trimethoprim/sulfamethoxazole),
- potassium-sparing medicines used in the treatment of heart failure eplerenone and spironolactone at doses between 12,5 mg to 50 mg by day,
- sympathomimetics agents to treat clinical shock (adrenaline, noradrenaline, dobutamine, isoprenaline, ephedrine),
- estramustine used in cancer therapy,

- 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 so-called mTor inhibitors). See section “Warnings and precautions”,
- sacubitril/valsartan (used to treat long-term heart failure). See sections “Do not take **Cosyrel**” and “Warnings and precautions”.
- lithium used to treat mania or depression,
- certain medicines used to treat depression such as imipramine, amitriptyline, monoamine oxidase (MAO) inhibitors (except MAO-B inhibitors),
- certain medicines used to treat schizophrenia (antipsychotics),
- certain medicines used to treat epilepsy (phenytoin, barbiturates such as phenobarbital),
- anaesthetic agents used for surgery,
- vasodilators including nitrates (products that make the blood vessels become wider),
- trimethoprim used to treat infections,
- immunosuppressants (medicines which reduce the defense mechanism of the body) such as ciclosporin, tacrolimus, used for the treatment of auto-immune disorders or following transplant surgery,
- allopurinol used to treat gout,
- parasympathomimetics medicines used to treat conditions such as Alzheimer’s disease or glaucoma,
- topical beta-blockers used to treat glaucoma (increase pressure in the eye),
- mefloquine used to prevent or treat malaria,
- baclofen used to treat muscle stiffness in diseases such as multiple sclerosis,
- gold salts, especially with intravenous administration (used to treat symptoms of rheumatoid arthritis),
- medicines to treat diabetes such as insulin, metformin, linagliptin, saxagliptin, sitagliptin, vildagliptin,

- non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen or diclofenac or high dose of aspirin used to treat arthritis, headache, pain or inflammation.

Contact your doctor to re-evaluate your treatment if you are treated with ACE-inhibitors/Angiotensin blockers together with a fluoroquinolone antibiotic.

Cosyrel with food, drink and alcohol

It is preferable to take **Cosyrel** before a meal.

Pregnancy, breastfeeding and fertility

You should not be treated with **Cosyrel** if you are pregnant or planning to become pregnant.

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking **Cosyrel**.

Pregnancy

You must tell your doctor if you think you are (or might become) pregnant. Your doctor will stop **Cosyrel** and will prescribe another medicine instead of **Cosyrel**.

Breastfeeding

You should not be treated with **Cosyrel** if you are breastfeeding your baby.

Tell your doctor if you are breastfeeding or about to start breastfeeding. Your doctor will prescribe another treatment for you if you wish to breastfeed, especially if your baby is a newborn, or was born prematurely.

Driving and using machines

Cosyrel may interfere with your ability to drive and use machines. You should not drive and use machines until you know how treatment with **Cosyrel** affects you. **Cosyrel** may cause hypotension (a low blood pressure), dizziness and disturbances of vision.

Cosyrel contains sodium

Cosyrel contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Cosyrel

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

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

The recommended dose is one tablet once daily. Swallow your tablet with a glass of water in the morning before a meal.

In some cases, your doctor may prescribe one half tablet of **Cosyrel** once daily in the morning before a meal.

Patient with kidney disease

Your doctor may prescribe one half tablet of **Cosyrel** if you suffer from moderate kidney disease.

Cosyrel is not recommended if you suffer from severe kidney disease.

Use in children and adolescents

Cosyrel should not be used in children and adolescents less than 18 years of age.

If you take more Cosyrel than you should

In the event of overdosage, consult your doctor or pharmacist without any delay. If neither is available contact the nearest hospital or poison control centre. Take your pack(s) of medicine with you.

The most likely effect in case of overdose is low blood pressure which can make you feel dizzy or faint (if this happens, lying down with the legs raised can help), severe difficulty in breathing, tremors (due to decreased blood sugar) and slow heart rate.

If you forget to take Cosyrel

It is important to take your medicine every day as regular treatment works better.

However, if you forget to take a dose of **Cosyrel**, take the next dose at the usual time.

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

If you stop taking Cosyrel

Do not suddenly stop taking **Cosyrel** or change the dose without consulting your doctor since this can cause severe worsening of your heart condition. Treatment should not be discontinued abruptly, especially in patients with coronary artery disease.

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

4. Possible side effects

Cosyrel can have side effects.

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

Stop taking Cosyrel and see a doctor immediately, if you experience any of the following side effects

- severe dizziness or fainting due to low blood pressure,
- worsening of heart failure causing increased breathlessness and /or retention of fluid (swelling),
- swelling of the face, lips, mouth, tongue or throat, difficulty in breathing (angioedema),
- sudden wheeziness, chest pain, shortness of breath, or difficulty in breathing (bronchospasm),
- unusual fast or irregular heart beat, chest pain (angina) or 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,
- skin rash which often starts with red itchy patches on your face, arms or legs (erythema multiforme).

Cosyrel is usually well tolerated but, you can experience different side effects, particularly when treatment is first started.

If you notice any of the side effects listed below or any not listed, please tell your doctor or pharmacist immediately

Frequent

- slow heart beat.
- headache,
- dizziness,
- vertigo,
- taste disturbances,

- pins and needles,
- tingling or numbness of the hands of feet,
- vision disturbances,
- tinnitus (sensation of noises in the ears),
- feeling of coldness in hands or feet,
- cough,
- shortness of breath,
- gastro-intestinal disorders such as nausea, vomiting, abdominal pain, difficulty of digestion or dyspepsia, diarrhoea, constipation,
- allergic reactions such as skin rashes, itching,
- muscle cramps,
- feeling of tiredness,
- fatigue,
- mood swings,
- sleep disturbances,
- depression,
- dry mouth,
- intense itching or severe skin rashes,
- formation of blister clusters over the skin,
- increased sensitivity of the skin to sun (photosensitivity reaction),
- sweating,
- kidney problems,
- impotence,
- an excess of eosinophils (a type of white blood cells),
- somnolence,
- fainting,
- palpitations,
- tachycardia (fast heart/pulse rate),

- irregular heart rate (AV-conduction disturbances inflammation of blood vessels (vasculitis),
- dizziness when standing up,
- muscle weakness,
- arthralgia (joint pain),
- myalgia (muscle pain),
- chest pain,
- malaise,
- localised swelling (oedema peripheral),
- fever,
- fall,
- changes in laboratory parameters high blood level of potassium reversible on discontinuation, low level of sodium, very low blood sugar level (hypoglycaemia) in case of diabetic patients, increased blood urea, increased blood creatinine.

Less frequent

- 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).
- decreased or absent urine output,
- flushing,
- nightmares, hallucinations,
- reduced tear flow (dry eyes),
- hearing problems,
- erection problems,
- inflammation of the liver which can cause yellowing of the skin or the whites of the eyes,

- allergic runny nose, sneezing,
- allergy-like reactions such as itching, flush, rash,
- psoriasis worsening,
- changes in laboratory parameters increased level of liver enzymes, high level of serum bilirubin, fat levels differing from normal.
- confusion,
- irritation and redness of the eye (conjunctivitis),
- eosinophilic pneumonia (a rare type of pneumonia),
- inflammation of the pancreas (which causes severe pain in the abdomen and the back),
- hair loss,
- appearance or worsening of scaly skin rash (psoriasis), psoriasis-like rash,
- acute renal failure,
- changes in blood values such as a lower number of white and red blood cells, lower haemoglobin, lower number of blood platelets.
- discoloration, numbness and pain in fingers or toes (Raynaud's phenomenon).

If you have these symptoms contact your doctor as soon as possible.

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

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 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 **Cosyrel**.

5. How to store Cosyrel

Store at or below 30 °C.

Store all medicine out of reach of children.

Do not store in bathrooms.

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

Return all unused medicine to your pharmacist.

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

Once opened, **Cosyrel** should be used within 60 days.

6. Contents of the pack and other information

What Cosyrel contains

The active substances are bisoprolol fumarate and perindopril arginine.

Cosyrel 5/5 mg One film-coated tablet contains 5 mg of bisoprolol fumarate (equivalent to 4,24 mg bisoprolol) and 5 mg of perindopril arginine (equivalent to 3,395 mg perindopril).

Cosyrel 5/10 mg One film-coated tablet contains 5 mg of bisoprolol fumarate (equivalent to 4,24 mg bisoprolol) and 10 mg of perindopril arginine (equivalent to 6,790 mg perindopril).

Cosyrel 10/5 mg One film-coated tablet contains 10 mg of bisoprolol fumarate (equivalent to 8,49 mg bisoprolol) and 5 mg of perindopril arginine (equivalent to 3,395 mg perindopril).

Cosyrel 10/10 mg One film-coated tablet contains 10 mg of bisoprolol fumarate (equivalent to 8,49 mg bisoprolol) and 10 mg of perindopril arginine (equivalent to 6,790 mg perindopril).

The other ingredients are cellulose microcrystalline PH 102 (E460), calcium carbonate (E170), pregelatinised maize starch, sodium starch glycolate type A (E468), silica colloidal

anhydrous (E551), magnesium stearate (Liga E572), croscarmellose sodium (E468), glycerol (E422), Hypromellose (E464), Macrogol 6000, titanium dioxide (E171), Iron oxide yellow (E172), Iron oxide red (E172) and water purified.

What Cosyrel looks like and contents of the pack

Cosyrel 5/5 mg Pink beige, oblong, bilayer scored film-coated tablet of 8,3 mm length and 4,5 mm width, engraved with ‘ ’ on one face and ‘5/5’ on the other face. The tablet can be divided into equal halves.

Cosyrel 5/10 mg Pink beige, oblong, bilayer scored film-coated tablet of 9,8 mm length and 5,4 mm width, engraved with ‘ ’ on one face and ‘5/10’ on the other face. The tablet can be divided into equal halves.

Cosyrel 10/5 mg Pink beige, round, bilayer film-coated tablet with a diameter of 7 mm and a curvature radius of 12,7 mm, engraved with ‘ ’ on one face and ‘10/5’ on the other face.

Cosyrel 10/10 mg Pink beige, oblong, bilayer film-coated tablet of 10 mm length and 5,7 mm width, engraved with ‘ ’ on one face and ‘10/10’ on the other face.

Tablet container of 30 film-coated tablets white polypropylene tablet container equipped with a low-density polyethylene flow reducer and a white opaque stopper containing a desiccant gel.

Holder of Certificate of Registration

Servier Laboratories South Africa (Pty) Ltd

Building Number 4

Country Club Estate

21 Woodlands Drive

Woodmead

2191

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Cosyrel 5/10 mg: 51/7.1.3/0496

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