

Package leaflet: Information for the patient

Cosimprel 5 mg/10 mg, film-coated tablets

bisoprolol fumarate/perindopril arginine

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, pharmacist or nurse.
- 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 or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Cosimprel is and what it is used for

Cosimprel contains two active ingredients, bisoprolol fumarate and perindopril arginine in one tablet:

- Bisoprolol fumarate belongs to a group of medicine 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.

Cosimprel is used to treat high blood pressure (hypertension) 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 Cosimprel which contains both active ingredients in the same strength.

2. What you need to know before you take Cosimprel

Do not take Cosimprel 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 characterized 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, 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 more than 3 months pregnant (it is also better to avoid Cosimprel in early pregnancy - 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, Cosimprel may not be suitable for you,
- have kidney problems where the blood supply to your kidneys is reduced (renal artery stenosis),
- if you have taken or are currently taking sacubitril/valsartan, a medicine for heart failure, as the risk of angioedema (rapid swelling under the skin in an area such as the throat) is increased (see “Warning and Precaution” and “Other medicines and Cosimprel”).

Warnings and precautions

Talk to your doctor or pharmacist before taking Cosimprel, if you:

- have diabetes,
- have kidney problems (including kidney transplantation) or if you are receiving dialysis,
- have a liver problem,
- have aortic and mitral stenosis (narrowing of the main blood vessel leading from the heart) 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 diarrhea or vomiting, or are dehydrated (Cosimprel 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 desensitisation 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 (Cosimprel 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 Cosimprel 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 Cosimprel”.

- are taking any of the following medicines, the risk of angioedema is increased:
 - racecadotril (used to treat diarrhea),
 - sirolimus, everolimus, temsirolimus and other drugs belonging to the class of so-called mTor inhibitors (used to avoid rejection of transplanted organs and for cancer),
 - sacubitril (available as fixed-dose combination with valsartan), used to treat long-term heart failure.
 - linagliptin, saxagliptin, sitagliptin, vildagliptin and other drugs belonging to the class of the also called gliptins (used to treat diabetes).

Do not suddenly stop taking Cosimprel since this can cause severe worsening of heart condition. Treatment should not be discontinued abruptly, especially in patients with coronary artery disease.

You must tell your doctor if you think you are (or might become) pregnant. Cosimprel 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).

Children and adolescents

Cosimprel is not recommended for use in children and adolescents younger than 18.

Other medicines and Cosimprel

Please tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

There are some medicines that may change the effect of Cosimprel or their effect may be changed by Cosimprel. 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, digitalis glycosides, diltiazem, disopyramide, felodipine, flecainide, lidocaine, methyl dopa, 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 Cosimprel” and “Warnings and precautions”) or diuretics (medicines which increase the amount of urine produced by the kidneys),
- potassium-sparing drugs (e.g. triamterene, amiloride), potassium supplements or potassium-containing salt substitutes, other drugs which can increase potassium in your body (such as heparin, a medicine used to thin blood to prevent clots; trimethoprim and co-trimoxazole also known as trimethoprim/sulfamethoxazole for infections caused by bacteria),
- potassium-sparing drugs 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 diarrhea (racecadotril) or avoid rejection of transplanted organs (sirolimus, everolimus, temsirolimus and other drugs 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 Cosimprel” and “Warnings and precautions”.
- lithium used to treat mania or depression,
- certain medicines used to treat depression such as imipramine, amitriptylin, 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 defence 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 acetylsalicylic acid used to treat arthritis, headache, pain or inflammation.

Cosimprel with food, drink and alcohol

It is preferable to take Cosimprel before a meal.

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 Cosimprel before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Cosimprel. Cosimprel 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. Cosimprel 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 a newborn, or was born prematurely.

Driving and using machines

Cosimprel usually does not affect alertness but dizziness or weakness due to low blood pressure may occur in some patients, particularly at the start of treatment or upon change of medication as well as in conjunction with alcohol. If you are affected in this way, your ability to drive or to operate machinery may be impaired.

Cosimprel contains sodium

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

3. How to take Cosimprel

Always take this medicine exactly as your doctor or pharmacist has told you. 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 Cosimprel once daily in the morning before a meal.

Patient with kidney disease

Cosimprel is not recommended if you suffer from moderate and severe kidney disease.

Use in children and adolescent

Use in children and adolescent is not recommended.

If you take more Cosimprel than you should

If you take more tablets than prescribed, contact your doctor or pharmacist immediately.

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 Cosimprel

It is important to take your medicine every day as regular treatment works better. However, if you forget to take a dose of Cosimprel, take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Cosimprel

Do not suddenly stop taking Cosimprel or change the dose without consulting your doctor since this can cause severe worsening of 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 this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

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

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

- severe dizziness or fainting due to low blood pressure (common - may affect up to 1 in 10 people),
- worsening of heart failure causing increased breathlessness and /or retention of fluid (common - may affect up to 1 in 10 people),
- swelling of the face, lips, mouth, tongue or throat, difficulty in breathing (angioedema) (uncommon - may affect up to 1 in 100 people),
- sudden wheeziness, chest pain, shortness of breath, or difficulty in breathing (bronchospasm) (uncommon - may affect up to 1 in 100 people),
- unusual fast or irregular heart-beat, chest pain (angina) or heart attack (very rare - may affect up to 1 in 10,000 people),
- weakness of arms or legs, or problems speaking which could be a sign of a possible stroke (very rare - may affect up to 1 in 10,000 people),
- inflamed pancreas which may cause severe abdominal and back pain accompanied with feeling very unwell (very rare - may affect up to 1 in 10,000 people),
- yellowing of the skin or eyes (jaundice) which could be a sign of hepatitis (very rare - may affect up to 1 in 10,000 people),
- skin rash which often starts with red itchy patches on your face, arms or legs (erythema multiforme) (very rare - may affect up to 1 in 10,000 people).

Cosimprel is usually well tolerated but, as with any medicine, people 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:

Very common (may affect more than 1 in 10 people):

- slow heart beat.

Common (may affect up to 1 in 10 people):

- headache,
- dizziness,
- vertigo,
- taste disturbances,
- pins and needles,
- tingling or numbness of the hands or 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.

Uncommon (may affect up to 1 in 100 people):

- 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,
- 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.

Rare (may affect up to 1 in 1000 people):

- 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.

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

- 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,
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- changes in blood values such as a lower number of white and red blood cells, lower haemoglobin, lower number of blood platelets.

Frequency not known (frequency cannot be estimated from the available data):

- discoloration, numbness and pain in fingers or toes (Raynaud's phenomenon).

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

Reporting of side effects

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

HPRRA 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 Cosimprel

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 carton. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Once opened, Cosimprel should be used within 20 days for tablet containers of 10 film-coated tablets, 60 days for tablet containers of 28 or 30 film-coated tablets and 100 days for tablet containers of 100 film-coated tablets.

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 Cosimprel contains

- The active substances are bisoprolol fumarate and perindopril arginine. Each tablet of Cosimprel contains 5 mg bisoprolol fumarate equivalent to 4.24 mg bisoprolol and 10 mg 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 Cosimprel looks like and contents of the pack

Cosimprel is a pink beige, oblong, bilayer scored film-coated tablet engraved with ‘’ on one face and ‘5/10’ on the other face. The tablet can be divided into equal halves.

The tablets are available in box of 10, 28, 30, 84 (3 tablet containers of 28), 90 (3 tablet containers of 30), 100 and 120 (4 tablet containers of 30) film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Les Laboratoires Servier
50, rue Carnot
92284 Suresnes cedex
France

Manufacturer

Les Laboratoires Servier Industrie (LSI)
905, route de Saran
45520 Gidy
France

and

Servier (Ireland) Industries Ltd (SII)
Moneylands, Gorey Road
Arklow - Co. Wicklow
Ireland

and

Anpharm Przedsiębiorstwo Farmaceutyczne S.A.
03-236 Warszawa, ul. Annopol 6b
Poland

and

EGIS Pharmaceuticals PLC
H- 9900 Körmend, Mátyás király u. 65,
Hungary

This medicinal product is authorised in the Member States of the EEA under the following names:

Belgium	Bipressil 5mg/10mg comprimé pelliculé
Bulgaria	Prestilol 5mg/10mg филмирани таблетки
Croatia	Prestilol 5mg/10mg filmom obložene tablete
Cyprus	Cosyrel 5mg/10mg επικαλυμμένα με λεπτό υμένιο δισκία
Czech Republic	Cosyrel 5mg/10mg, potahované tablety

Estonia	Prestilol
Finland	Cosyrel 5mg/10mg Tabletti, kalvopäällysteinen
France	Cosimprel 5mg/10mg, comprimé pelliculé
Greece	Cosyrel 5mg/10mg επικαλυμμένα με λεπτό υμένιο δισκία
Hungary	Cosyrel 5mg/10mg filmtabletta
Ireland	Cosimprel 5mg/10mg film-coated tablet
Italy	Cosyrel
Latvia	Prestilol 5mg/10mg apvalkotās tabletes
Lithuania	Prestilol 5mg/10mg plėvele dengtos tabletės
Luxembourg	Bipressil 5mg/10mg comprimé pelliculé
Netherlands	Cosimprel 5 mg/10 mg filmomhulde tabletten
Poland	Prestilol
Portugal	Cosyrel 5mg/10mg
Romania	Cosyrel 5mg/10mg comprimate filmate
Slovakia	Prestilol 5mg/10mg filmom obalené tablety
Slovenia	Cosyrel 5mg/10mg filmsko obložene tablete

This leaflet was last revised in

Detailed information on this medicine is available on the web site of Health Products Regulatory Authority:
www.hpra.ie.