Package leaflet: Information for the user

Bifril 30mg 7.5mg 15mg 60mg film-coated tablets
(zofenopril calcium)

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. 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 Bifril is and what it is used for

Bifril contains zofenopril calcium 30 mg 7.5 mg 15 mg 60 mg which belongs to a group of blood pressure lowering medicines called angiotensin converting enzyme (ACE) inhibitors.
Bifril is used to treat the following conditions:
- high blood pressure (hypertension).
- heart attack (acute myocardial infarction) in people who may or may not show signs and symptoms of heart failure, and who have not received treatment that helps dissolve blood clots (thrombolytic therapy).

2. What you need to know before you take Bifril

Do not take Bifril if you:
- are allergic to zofenopril calcium or any of the other ingredients of this medicine (listed in section 6)
- have had any previous allergic reaction to any other ACE inhibitor such as captopril or enalapril
- have a history of severe swelling and itching around the face, nose and throat (angioneurotic edema) associated with previous ACE inhibitor therapy, or if you suffer from hereditary/idiopathic angioneurotic oedema (rapid swelling of the skin, tissues, digestive tract and other organs)
- 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
- suffer from severe liver problems
- suffer from narrowing of the arteries to the kidneys
- are more than 3 months pregnant (It is also better to avoid Bifril in early pregnancy – see pregnancy section.)
- are a woman of child-bearing age unless using effective contraception.
- have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren

Warnings and precautions
Talk to your doctor before taking Bifril.
Tell your doctor if you:

- have **high blood pressure** and **liver** or **kidney problems**
- have high blood pressure that is caused by a kidney problem or by narrowing of the artery leading to the kidney (renovascular hypertension)
- have recently had a **kidney transplant**
- are undergoing **dialysis**
- are on **LDL apheresis** (a procedure similar to kidney dialysis that clears your blood of harmful cholesterol)
- have **abnormally high levels** of the hormone **aldosterone** in your blood (primary aldosteronism) or **decreased levels** of the hormone **aldosterone** in your blood (hypoaldosteronism)
- have a **narrowing of the heart valve (**aortic stenosis) or **thickening of the heart walls** (hypertrophic cardiomyopathy)
- suffer or have suffered from **psoriasis** (skin disease characterised by scaly pink patches)
- are receiving **desensitization** treatment ('allergy injections') for insect stings.
- 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 areas 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

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 Bifril"

Your **blood pressure may get too low** with Bifril, 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 Bifril before being anaesthetised. This will help him/her to control your blood pressure and heart rate during the procedure.

In addition if you suffer from **heart attack** (acute myocardial infarction) and you:

- have low blood pressure (< 100mmHg) or are in a state of circulatory shock (as a result of your heart problem) – Bifril is not recommended for you
- are over 75 years of age – Bifril should be used with special care.

You must tell your doctor if you think you are (or might become) pregnant. Bifril 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
Do not give this medicine to children and adolescents under the age of 18 years because it is unlikely to be safe.

Other medicines and Bifril
Tell your doctor if you are taking, have recently taken or might take any other medicines.
In particular, tell your doctor if you are taking:

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- 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; cyclosporin, an immunosuppressant medicine used to prevent organ transplant rejection; and heparin, a medicine used to thin blood to prevent clots)
- lithium (used to treat mood disorders)
- anaesthetics
- narcotic drugs (such as morphine)
- antipsychotic drugs (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 to take other precautions:
  If you are taking an angiotensin II receptor blocker (ARB) or aliskiren (see also information under the headings "Do not take Bifril" and "Warnings and precautions")
- nitroglycerine and other nitrates used for chest pain (angina)
- antacids including cimetidine (used to treat heartburn and stomach ulcers)
- cyclosporin (used after organ transplants) and other immunosuppressant drugs (medicines that suppress your body's defence)
- allopurinol (used to treat gout)
- insulin or oral anti-diabetic medicines
- cytostatic agents (used to treat cancer or diseases which affect the body's defence system)
- corticosteroids (powerful anti-inflammatory drugs)
- procainamide (used to control an irregular heart beat)
- nonsteroidal anti-inflammatory drugs (NSAIDs, such as aspirin or ibuprofen)
- sympathomimetic drugs (medicines that act on the nervous system, including some used to treat asthma or hay fever and pressor amines, e.g. adrenalin).
- racecadotril (a medicine used to treat diarrhoea), medicines used to prevent organ transplant rejection and for cancer (e.g. temsirolimus, sirolimus, everolimus), and vildagliptin (a medicine used to treat diabetes). The risk of angioedema may be increased.

Bifril with food, drink and alcohol
Bifril can be taken with food or on an empty stomach, but the tablet is best taken with water. Alcohol increases the hypotensive (lowering of blood pressure) effect of Bifril; ask your doctor for further advice on drinking alcohol whilst on this medication.

Pregnancy and breast-feeding

Pregnancy
If you are pregnant, if you think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. Your doctor will normally advise you to stop taking Bifril before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Bifril.
Bifril 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
If you are breast-feeding or about to start breast-feeding ask your doctor for advice before taking this medicine. Bifril 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

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This medicine may cause dizziness or tiredness. If this happens to you, do not drive or operate machinery.

Bifril contains lactose
This product contains **lactose.** If you know you have an intolerance to some sugars, contact your doctor before taking this medicine.

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

3. How to take Bifril

Always take Bifril exactly as your doctor has told you. Check with your doctor if you are not sure.
Bifril may be taken with food or on an empty stomach. The tablet is best taken with water.

[*for 30 mg, 15 mg, 60 mg only*]
The tablet can be divided into equal doses.

Treatment of high blood pressure (hypertension)
The normal starting dose of Bifril is 15mg, once a day. Your doctor will gradually adjust the dosage (usually at four weeks intervals) to find the dose that suits you best. Long-term antihypertensive effects are usually obtained with 30mg of Bifril, once a day. The maximum dose is 60mg per day, taken in a single or two divided doses.
If you are dehydrated, have a salt deficiency or are taking diuretics (water pills), it may be necessary to start your treatment with 7.5mg of Bifril.

Liver or kidney problems
If you have mild to moderate liver impairment or moderate to severe kidney impairment, your doctor will start your treatment with half the therapeutic dose of Bifril (15mg). If you are receiving dialysis, one-quarter of the usual therapeutic dose (7.5mg) is needed at the start of your treatment.

Heart attack (acute myocardial infarction)
Bifril treatment should begin within the first 24 hours after the onset of symptoms.
You will receive Bifril tablets twice a day in the morning and evening, as follows:

- 7.5mg twice a day, on the first and second day of treatment
- 15mg twice a day, on the third and fourth day of treatment
- From the fifth day onwards, the dose should be increased to 30mg, twice a day
- Your doctor may adjust your dose or the maximum dose you receive on the basis of your blood pressure measurements
- Treatment will then be continued for a further six weeks, or longer, if symptoms of heart failure persist.

If you take more Bifril than you should
If you accidentally take too many tablets, contact your doctor or nearest Accident & Emergency department immediately (taking any remaining tablets, the carton or this leaflet with you if possible).
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) and kidney dysfunction.

If you forget to take Bifril
If you miss a dose, take the next dose as soon as you remember. However if a long delay has occurred (e.g. several hours) so that the next due dose is near, 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 a forgotten tablet.

If you stop taking Bifril

Always consult your doctor before stopping Bifril treatment, whether you are taking it for high blood pressure or following a heart attack.

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

4. Possible side effects

Like all medicines, Bifril can cause side effects, although not everybody gets them.
Most side effects associated with ACE inhibitors are reversible and disappear after treatment is finished.

Common side effects (may affect up to 1 in 10 people):
- fatigue (tiredness)
- nausea and/or vomiting
- dizziness
- headache
- cough.

Uncommon side effects (may affect up to 1 in 100 people):
- general weakness
- muscle cramps
- skin rash.

Rare side effects (may affect up to 1 in 1,000 people):
- rapid swelling and itching, especially around the face, mouth and throat, with possible difficulty in breathing.

In addition to the side effects reported with Bifril, the following have generally been reported with **ACE inhibitors**:
- Severe low blood pressure at the start of treatment or when the dosage is increased, with dizziness, impaired vision, fainting (syncope)
- Increased or irregular heartbeat, palpitations and chest pain (heart attack or angina pectoris)
- 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)
- Peripheral oedema (accumulation of water in the limbs), low blood pressure on standing, chest pain, muscle aches and/or cramps
- Reduced kidney function, changes in the amount of daily urine, presence of proteins in the urine (proteinuria), impotence
- Abdominal pain, diarrhoea, constipation, dry mouth
- Allergic reactions like skin rash, hives (urticaria), itching, peeling, redness, loosening and blistering of the skin (toxic epidermal necrolysis), worsening of psoriasis (a skin disease characterised by scaly pink patches), hair loss (alopecia)
- Increased sweating and flushing
- 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), bronchitis
- 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 liver enzymes (transaminases) and bilirubin, increased blood urea and creatinine
- Anaemia due to rupture of red blood cells (haemolytic anaemia), which may occur if you suffer from G6PD (glucose-6-phosphate dehydrogenase) deficiency.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Bifril

Keep this medicine out of the sight and reach of children.

This medicinal product does not require any special storage conditions.

Do not use this medicine after the expiry date which is stated on the box and blister pack after 'EXP'. The expiry date refers to the last day of that month.
Do not throw away any medicines via wastewater. 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 Bifril contains
The **active substance** is zofenopril calcium 30mg 7.5mg 15mg 60 mg. The **other ingredients** are microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, magnesium stearate, colloidal anhydrous silica, hypromellose, titanium dioxide (E171), macrogol 400, and macrogol 6000 (see section 2 Bifril contains lactose').

What Bifril looks like and contents of the pack
Bifril 30 is available as white, oblong film-coated tablets in packs of 7, 14, 15, 28, 30, 50, 56, 90 or 100 film-coated tablets and in packs with perforated unit dose blisters of 50 and 56 film-coated tablets.

Bifril 7.5 is available as white, round film-coated tablets with convex faces in packs of 12, 14, 15, 28, 30, 48, 50, 56, 90 or 100 film-coated tablets and in packs with perforated unit dose blisters of 50 and 56 film-coated tablets.

Bifril 15 is available as white, oblong film-coated tablets in packs of 12, 14, 15, 28, 30, 50, 56, 90 or 100 film-coated tablets and in packs with perforated unit dose blisters of 50 and 56 film-coated tablets.

Bifril 60 is available as white, oblong film-coated tablets in packs of 14, 15, 28, 30, 50, 56, 90 or 100 film-coated tablets and in packs with perforated unit dose blisters of 50 and 56 film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Menarini International Operations Luxembourg S.A.
1, Avenue de la Gare L-1611, Luxembourg.

Manufacturer
A. MENARINI Manufacturing Logistics and Services Srl
Campo di Pile, L'Aquila, Italy.

Menarini –Von Heyden GmbH
Leipziger Strasse 7-13,

01097 – Dresden (Germany).

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

Austria: Bifril
Belgium: Zopranol
France: Teoula
Greece: Zofepril
Ireland: Bifril
Italy: Zofepril
Iceland: Bifril
Luxembourg: Zopranol
Portugal: Zopranol
The Netherlands: Zopranol
United Kingdom: Bifril

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