Package leaflet: Information for the patient

CARIVALAN™ 6.25 mg / 5 mg
film-coated tablets carvedilol/ivabradine

CARIVALAN™ 6.25 mg / 7.5 mg
film-coated tablets carvedilol/ivabradine

CARIVALAN™ 12.5 mg / 5 mg
film-coated tablets carvedilol/ivabradine

CARIVALAN™ 12.5 mg / 7.5 mg
film-coated tablets carvedilol/ivabradine

CARIVALAN™ 25 mg / 5 mg
film-coated tablets carvedilol/ivabradine

CARIVALAN™ 25 mg / 7.5 mg
film-coated tablets carvedilol/ivabradine

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 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. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Carivalan is and what it is used for

Carivalan is used in adult patients to treat:
- Symptomatic stable angina pectoris (which causes chest pain).
- Chronic heart failure.

Instead of taking carvedilol and ivabradine as separate tablets, you will receive one tablet of Carivalan which contains both ingredients at the same strength.

Carivalan is a combination of two active ingredients, carvedilol and ivabradine. Carvedilol is a beta-blocker. Beta-blockers slow the heartbeat, lessen the force with which the heart muscle contracts and reduces the blood vessel contraction in the heart, brain and throughout the body. Ivabradine works mainly by reducing the heart rate by a few beats per minute. This lowers the heart's need for oxygen especially in the situations when an angina attack is more likely to happen. In this way, carvedilol and ivabradine help to control and reduce the number of angina attacks.

2. What you need to know before you take Carivalan

Do not take Carivalan:
- if you are allergic to carvedilol, ivabradine or any of the other ingredients of this medicine (listed in section 6), or to other beta blockers,
- if you suffer from severe liver problems,
- if you started to suffer from heart failure, if the heart failure is not stably controlled, or recently became worse,
- if you suffer from unstable angina (a severe form of angina in which chest pain occurs very frequently, with or without exercise),
- if you suffer from Prinzmetal's angina (chest pain that occurs at rest and in cycles),
- if you suffer from a heart rhythm disorder,
- if your heart rate is too low (under 50 beats per minute) or if you feel weak, have decreased level of consciousness, shortness of breath, hypotension or chest pain (due to symptomatic or severe bradycardia),
- if you are having a heart attack,
- if you are suffering from cardiogenic shock (a serious heart condition treated in hospitals and caused by very low blood pressure),
- if your heartbeat is exclusively regulated by your pacemaker,
- if you have a severe blood vessel disorder (for example Raynaud's phenomenon),
- if you have very low blood pressure,
- if you suffer from chronic obstructive pulmonary disease or COPD (lung disease with symptoms such as wheeziness, difficulty in breathing and chronic cough),
- if you have already experienced breathing problems such as asthma or bronchospasm (difficulty in breathing due to the narrowing of the airways),
- if you have too much acid in your blood (metabolic acidosis),
- if you have high blood pressure due to a tumour near the kidney (untreated phaeochromocytoma),
- if you are taking:
  - medicines for treatment of fungal infections (such as ketoconazole, itraconazole),
  - antibiotics used for bacterial infections (such as clarithromycin, erythromycin given orally, josamycin and telithromycin),
  - medicines called protease inhibitors used to treat HIV (such as nelfinavir, ritonavir),
  - nefazodone (medicine to treat depression),
  - diltiazem or verapamil: medicines used to treat high blood pressure or angina pectoris,
- if you are a woman able to have children and not using reliable contraception,
- if you are pregnant or trying to become pregnant,
- if you are breast-feeding.

Warnings and precautions
Talk to your doctor or pharmacist before taking Carivalan.

You should inform your doctor if you have or have had any of the following conditions:
- if you suffer from heart rhythm disorders (such as irregular heartbeat, palpitations, increase in chest pain), sustained atrial fibrillation (a type of irregular heartbeat) or an abnormality of electrocardiogram (ECG) called 'long QT syndrome',
- if you suffer from severe heart failure or heart failure with abnormality of ECG called 'bundle branch block',
- if you are suffering from heart failure with an inability to carry on any physical activity without discomfort (symptoms may be present even at rest and physical activity increases discomfort),
- if you suffer from symptoms of atrial fibrillation (pulse rate at rest unusually high (over 110 beats per minute) or irregular, without any apparent reason, making it difficult to measure),
- if you suffer from uncontrolled blood pressure, especially after a change in your antihypertensive treatment,
- if you suffer from long-standing heart failure together with: a low blood pressure (< 100mmHg), or heart disease caused by reduced blood flow in the blood vessels of the heart muscle, or a condition with damage to the large and/or small blood vessels, or kidney problems,
- if you have symptoms such as tiredness, dizziness or shortness of breath (this could mean that your heart rate is slowing down too much for example under 50 beats per minute),
- if you are going to have a cardioversion (a medical procedure that can restore a fast or irregular heartbeat to a normal rhythm),
- if you have had a recent stroke (cerebral attack),
- if you have a low blood pressure,
- if you have a blood pressure that fluctuates abruptly and repeatedly,
- if you have high blood pressure caused by another condition,
- if you experience a drop in blood pressure whilst standing up,
- if you have an inflammation of the heart muscle, narrowing of the heart valves impacting the blood flow, final stage circulatory condition in which narrowed arteries reduce blood flow to your limbs,
- if you are taking already α1-receptor antagonist or α2-receptor agonist,
- if you suffer from chronic eye retinal disease or if your eyesight deteriorates,
- if you have diabetes,
- if you have circulation problems such as Raynaud's syndrome (usually affecting the fingers) or peripheral vascular disease causing cold hands and feet or pins-and-needles,
- if you are going to have a surgery which requires a general anaesthesia,
- if you have an overactive thyroid gland (the symptoms are tremors, a fast heart rate, sweating or weight loss),
- if you wear contact lenses,
- if you have a history of hypersensitive reactions or are undergoing desensitisation therapy,
- if you have psoriasis (severe skin rashes),
- if you have or are suspected to have a tumour on the adrenal glands (phaeochromocytoma).

If any of the above applies to you, talk straight away to your doctor before or while taking Carivalan.

Do not suddenly stop taking Carivalan since this can cause severe changes in the rhythm or rate of the heart and increase the risk of a heart attack.

Children and adolescents
Carivalan is not intended for use in children and adolescents younger than 18.

Other medicines and Carivalan
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Treatment with Carivalan can be affected by other medicines. Make sure to tell your doctor if you are taking any of the following medicines as special care may be required for:
- fluconazole (used to treat fungal infections),
- rifampicin (used to treat infections),
- QT prolonging medicines to treat either heart rhythm disorders or other conditions:
  - quinidine, disopyramide, sotalol, ibutilide, amiodarone (used to treat heart rhythm problems),
  - bepridil (used to treat chest pain associated to angina),
  - pimozide, ziprasidone, sertindole (used to treat anxiety, schizophrenia or other psychoses),
  - mefloquine and halofantrine (used to treat malaria),
  - intravenous erythromycin (an antibiotic),
  - pentamidine (used to treat parasitic infection),
  - cisapride (used to treat digestion problems).
- clonidine (used to treat high blood pressure),
- dihydropyridines (used to treat high blood pressure, chest pain associated with angina or Raynaud's phenomenon),
- some types of diuretics which may cause decrease in blood potassium level, such as furosemide, hydrochlorothiazide, indapamide (often used to treat high blood pressure, oedema and heart failure),
- other medicines used to treat high blood pressure,
- nitrates (used to treat chest pain associated with angina),
- sympathomimetics (for example medicines to increase blood pressure or heart frequency or widen the windpipes such as epinephrine used in the treatment of severe allergic reactions and beta-2-agonists used in the treatment of asthma),
- class IA and IC intravenous antiarrhytmics (used to treat heart rhythm problems),
- barbiturates (used to treat epilepsy or difficult sleeping),
- phenytoin (used for epilepsy),
- cimetidine (used for heartburn or stomach ulcers),
- fluoxetine (used to treat depression),
- *hypericum perforatum* or St John's Wort (herbal treatment used for depression),
- reserpine, guanethidine, methyldopa, guanfacine and monoamine oxidase inhibitors (used to treat conditions such as depression and Parkinson's disease),
- digoxin and digitoxin (used to treat heart diseases),
- cyclosporin (used following an organ transplant),
- insulin and antidiabetic agents (used to treat diabetes),
- muscle relaxants used in anaesthesia or anaesthetics (you should tell your doctor before surgery),
- beta-agonist bronchodilators (used to treat asthma),
- non-steroidal anti-inflammatory/antirheumatic agents (NSAID's) (used to reduce inflammation, fever and pain),
- oestrogens (female hormones used for contraception or hormone replacement therapy),
- corticosteroids (used to treat different types of diseases such as asthma, skin dermatitis, etc.),
- ergotamine (used to treat migraine),
- other beta-blockers (in the form of eye drops).

Inform your doctor you are taking Carivalan if you are going to have an operation needing an anaesthetic.

Carivalan with food, drink and alcohol
Avoid grapefruit juice during treatment with Carivalan. You should minimise your alcohol intake when taking this medicine as it may increase the effect of ivabradine.

Pregnancy, 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.
If you are pregnant and have taken Carivalan, talk to your doctor.
Do not take Carivalan if you are able to become pregnant unless you use reliable contraceptive measures (see "Do not take Carivalan").
Do not take Carivalan if you are breast-feeding (see "Do not take Carivalan"). Talk to your doctor if you are breast-feeding or intending to breast-feed as breast-feeding should be stopped if you take Carivalan.

Driving and using machines
Carivalan may cause temporary luminous visual phenomena (a temporary brightness in the field of vision), (see "Possible side effects"). If this happens to you, be careful when driving or using machines at times when there could be sudden changes in light intensity, especially when driving at night.
You should also be careful when taking Carivalan together with alcohol or changing to another medicine since this may affect your ability to drive or use machines.
If the tablets make you feel dizzy or tired or give you a headache, do not drive or use machinery.

Carivalan contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine. If you suffer from hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption, you should not take this medicine.

3. How to take Carivalan

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 tablet must be taken twice daily, once in the morning and once in the evening during meals.

If you take more Carivalan than you should
If you take more tablets than prescribed, contact your nearest accident and emergency department or tell your doctor immediately. The most likely effects are dizziness, feeling faint, tired and difficulty in breathing due to your heart rate slowing down.

If you forget to take Carivalan
If you forget to take a dose of Carivalan, take the next dose at the usual time. Do not take a double dose to make up for the forgotten dose.

If you stop taking Carivalan
As the treatment for angina or chronic heart failure is usually life-long, you should discuss with your doctor before stopping your treatment with this medicine.

Do not suddenly stop taking Carivalan tablets since this can cause severe changes in the rhythm or rate of your heart and increase the risk of a heart attack. Only change the dose or stop the treatment in consultation with your doctor.

If you think that the effect of Carivalan is too strong or too weak, talk to your doctor or pharmacist.

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

4. Possible side effects

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

Very common (may affect more than 1 in 10 people):
- luminous visual phenomena (brief moment of increased brightness, most often caused by sudden changes in light intensity). They can also be described as a halo, coloured flashes, image decomposition or multiple images. They generally occur within the first two months of treatment after which they may occur repeatedly and resolve during or after treatment,
- headache,
- dizziness,
- heart problem which can cause shortness of breath or swelling of the feet or legs due to fluid build-up (heart failure),
- low blood pressure (the signs include feeling dizzy or light-headed), generalised weakness, feeling of tiredness.

Common (may affect up to 1 in 10 people):
- lung or chest infections such as bronchitis or pneumonia and upper respiratory track infection,
- infections of the urinary tract,
- decreased number of red blood cells (the signs include feeling tired, pale skin, a fluttering sensation in your heart (palpitations) and being short of breath when exercising),
- increased levels of cholesterol in the blood,
- increased levels of blood sugar (diabetes), loss of control of blood sugar in people with diabetes,
- weight gain,
- being or feeling depressed,
- lacrimation decreased (dry eyes), impaired vision, eye irritation, blurred vision (cloudy vision),
- fluid retention (the signs include overall swelling of your body, swelling of parts of your body for example your hands, feet, ankles and legs and an increase in the volume of blood you have in your body),
- build-up of fluid in the lungs,
- modification in the heart functioning (the symptoms are a slowing down of the heart rate),
- heart block (irregular heartbeats),

- irregular rapid contraction of the heart,
- feeling dizzy, light-headed or faint when you stand or sit up quickly,
- problems with blood circulation such as cold hands and feet, obstruction of the large arteries in the arms of legs, worsening of symptoms in patients with Raynaud's disease (tingling and colour change (white, blue then red) in fingers and toes when exposed to the cold) or claudication (pain in the leg which gets worse when you walk),
- uncontrolled blood pressure,
- shortness of breath, asthma,
- feeling sick (nausea), stomach pain, indigestion, diarrhoea, vomiting,
- pain in the extremities,
- disease with painful, swollen joints caused by uric acid crystals (gout),
- problems with your kidneys including problems starting, passing and stopping urination or altered frequency of urination,
- pain.

Uncommon (may affect up to 1 in 100 people):
- increased level of some white blood cells,
- increased level of uric acid in the blood,
- sleep disturbance including nightmares, confusion,
- fainting (syncope), light-headedness, muscular weakness, blurred vision and feeling faint (pre-syncope), tingling or numbness of the hands or feet,
- double vision, spinning sensation (vertigo),
- a pain or uncomfortable feeling in the chest, palpitations, changes in heart rate (fast, slow or irregular),
- low blood pressure (possibly related to slow heart rate),
- constipation,
- certain skin reactions (such as skin rash, hives, itching, increased sweating, psoriatic or lichen planus like skin lesions),
- hair loss,
- swelling of the face, lips, tongue or throat which may cause difficulty in breathing or swallowing (angioedema), rash,
- muscle cramps,
- elevated creatinine in blood (a breakdown product of muscles), abnormal ECG heart traces,
- sexual dysfunction, impotence (inability to get or maintain an erection).

Rare (may affect up to 1 in 1,000 people):
- bleeding or bruising more easily than normal (low blood platelets count),
- stuffy nose, wheezing,
- dry mouth,
- redness of the skin,
- feeling unwell.

Very rare (may affect up to 1 in 10,000 people):
- low number of white blood cells,
- abnormal liver tests,
- an allergic reaction (swelling of the lips, face or neck leading to severe difficulty in breathing, skin rash or hives),
- problems with your heart rythm (second or third degree AtrioVentricular block, sick sinus syndrome),
- severe skin reactions:
  - circular, irregular red patches on the skin of the hands and arms (erythema multiforme), severe form of skin rash with flushing, fever, blisters or ulcers (Stevens Johnson syndrome), severe rash involving reddening, peeling and swelling of the skin that resembles severe burns (toxic epidermal necrolysis),
- inability to control the flow of urine in women.

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 the national reporting system. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Carivalan

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.

Store below 30°C.

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 Carivalan contains

- **The active substances are** carvedilol and ivabradine (as hydrochloride):
  - Carivalan 6.25mg/5 mg: each film-coated tablet contains 6.25 mg of carvedilol and 5 mg of ivabradine equivalent to 5.390 mg ivabradine as hydrochloride.
  - Carivalan 6.25 mg/7.5 mg: each film-coated tablet contains 6.25 mg of carvedilol and 7.5 mg of ivabradine equivalent to 8.085 mg ivabradine as hydrochloride.
  - Carivalan 12.5 mg/5 mg: each film-coated tablet contains 12.5 mg of carvedilol and 5 mg of ivabradine equivalent to 5.390 mg ivabradine as hydrochloride.
  - Carivalan 12.5 mg/7.5 mg: each film-coated tablet contains 12.5 mg of carvedilol and 7.5 mg of ivabradine equivalent to 8.085 mg ivabradine as hydrochloride.
  - Carivalan 25 mg/5 mg: each film-coated tablet contains 25 mg of carvedilol and 5 mg of ivabradine equivalent to 5.390 mg ivabradine as hydrochloride.
  - Carivalan 25 mg/7.5 mg: each film-coated tablet contains 25 mg of carvedilol and 7.5 mg of ivabradine equivalent to 8.085 mg ivabradine as hydrochloride.
- **The other ingredients are:**
  - In the tablet core: pregelatinised starch (maize), lactose monohydrate, microcrystalline cellulose (E460), sodium croscarmellose (E468), maltodextrin, colloidal anhydrous silica (E551) and magnesium stearate (E470b).
  - In the tablet film-coating: glycerol (E422), hypromellose (E464), magnesium stearate (E470b), titanium dioxide (E171), iron oxide yellow (E172) *(for 6,25/7,5 mg, 12,5/7,5 mg and 25/7,5 mg)* and macrogol 6000 (E1521).

What Carivalan looks like and contents of the pack
White, hexagonal, film-coated tablet (6.25/5 mg), longest diagonal 7.3 mm, engraved with C|2 on one face and on the other face.
[Yellow, hexagonal, film-coated tablet (6.25/7.5 mg), longest diagonal 7.3 mm, engraved with C|3 on one face and on the other face.]
[White, elliptic, film-coated tablet (12.5/5 mg), 10.6 mm x 5.3 mm, engraved with C|4 on one face and on the other face.]
[Yellow, elliptic, film-coated tablet (12.5/7.5 mg), 10.6 mm x 5.3 mm, engraved with C|5 on one face and on the other face.]
[White, octagonal, film-coated tablet (25/5 mg), diameter 7.8 mm, engraved with C|6 on one face and on the other face.]
[Yellow, octagonal, film-coated tablet (25/7.5 mg), diameter 7.8 mm, engraved with C|7 on one face and on the other face.]

The tablets are available in calendar packs (Aluminium/PVC blisters) of 14, 28, 56, 98 or 112 tablets.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

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