Read all of this leaflet carefully before you start taking this medicine.
- 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 symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Carvetrend® is and what it is used for
2. Before you take Carvetrend®
3. How to take Carvetrend®
4. Possible side effects
5. How to store Carvetrend®
6. Further information

1. WHAT CARVETREND® IS AND WHAT IT IS USED FOR

The active substance of Carvetrend® is carvedilol. Carvedilol is a vasodilating non-selective beta-blocking agent with antioxidant properties. Vasodilation is predominantly mediated through alpha-receptor antagonism. Carvedilol reduces the peripheral vascular resistance through vasodilation and suppresses the renin-angiotensin-aldosterone system through beta blockade. The activity of plasma renin is reduced.

Carvetrend® is indicated for the treatment of:
- **Symptomatic chronic heart failure (CHF)**
  Carvedilol is indicated for the treatment of symptomatic CHF (New York Heart Association (NYHA) Classes II and III) as adjunct to standard therapies e.g. diuretics, digoxin, ACE inhibitors. In these patients, addition of Carvetrend® has been shown to delay the progression of disease. Patients with NYHA Class II CHF are characterised by slight limitation of physical activity. They are comfortable at rest but ordinary physical activity results in fatigue, palpitation or dyspnoea. Patients with NYHA Class III CHF are characterised by marked limitation of physical activity. They are comfortable at rest but even less than ordinary activity causes fatigue, palpitation or dyspnoea.
- **Hypertension**
  Carvedilol is indicated for the treatment of hypertension.
- **Angina**
  Carvedilol is indicated for the prophylactic treatment of stable angina.

2. BEFORE YOU TAKE CARVETREND®

Do not use Carvetrend®
- If you are allergic (hypersensitive) to carvedilol, or to any of the other ingredients of Carvetrend®.
In patients with severe CHF (NYHA Class IV). These patients are characterised by inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency may be present even at rest. If any physical activity is undertaken, discomfort is increased. In patients with obstructive airways disease. In patients with liver dysfunction. In patients with history of bronchospasm or asthma. In patients with 2nd and 3rd degree A-V heart block. In patients with severe bradycardia (<50 bpm). In patients with cardiogenic shock, sick sinus syndrome (including sino-atrial block). In patients with severe hypotension (systolic blood pressure <85mmHg). In patients with metabolic acidosis. In patients with phaeochromocytoma (unless adequately controlled by alpha blockade).

Take special care with Carvetrend®
In chronic heart failure patients, worsening cardiac failure or fluid retention may occur during uptitration of Carvetrend®. If such symptoms occur, the dose of diuretic should be adjusted and the Carvetrend® dose should not be advanced until clinical stability resumes. Occasionally it may be necessary to lower the Carvetrend® dose or temporarily discontinue it. Such episodes do not preclude subsequent successful titration of Carvetrend®.

Patients who progress to severe (NYHA Class IV) heart failure whilst on therapy should, as with all therapies, have their therapeutic regime reassessed at regular intervals according to the discretion of the physician.

In hypertensive patients who have chronic heart failure controlled with digoxin, diuretics and/or an ACE inhibitor, Carvetrend® should be used with caution since both digoxin and Carvetrend® may slow A-V conduction.

As with other drugs with beta-blocking activity, Carvetrend® may mask the early signs of acute hypoglycaemia in patients with diabetes mellitus. Alternatives to beta-blocking agents are generally preferred in insulin-dependent patients. In patients with diabetes, the use of Carvetrend® may be associated with worsening control of blood glucose. Therefore, regular monitoring of blood glucose is required in diabetics when Carvetrend® is initiated or up-titrated and hypoglycaemic therapy adjusted accordingly.

Reversible deterioration of renal function has been observed with Carvetrend® therapy in chronic heart failure patients with low blood pressure (systolic BP <100mmHg), ischaemic heart disease and diffuse vascular disease, and/or underlying renal insufficiency. In CHF patients with these risk factors, renal function should be monitored during up-titration of Carvetrend® and the drug discontinued or dosage reduced if worsening of renal failure occurs.

Wearers of contact lenses should be advised of the possibility of reduced lacrimation.

Although angina has not been reported on stopping treatment, discontinuation should be gradual (1-2 weeks) particularly in patients with ischaemic heart disease, as Carvetrend® has beta-blocking activity.

Carvetrend® may be used in patients with peripheral vascular disease. Pure beta-blockers can precipitate or aggravate symptoms of arterial insufficiency. However, as Carvetrend® also has alphablocking properties this effect is largely counterbalanced.

Carvetrend®, as with other agents with beta-blocking activity, may mask the symptoms of thyrotoxicosis.

If Carvetrend® induces bradycardia, with a decrease in pulse rate to less than 55 beats per minute, the dosage of Carvetrend® should be reduced.
Care should be taken in administering Carvetrend® to patients with a history of serious hypersensitivity reactions and in those undergoing desensitisation therapy as beta-blockers may increase both the sensitivity towards allergens and the seriousness of anaphylactic reactions.

In patients suffering from the peripheral circulatory disorder Raynaud's phenomenon, there may be exacerbation of symptoms.

Patients with a history of psoriasis associated with beta-blocker therapy should be given Carvetrend® only after consideration of the risk-benefit ratio.

In patients with phaeochromocytoma, an alpha-blocking agent should be initiated prior to the use of any beta-blocking agent. There is no experience of the use of Carvetrend® in this condition. Therefore, caution should be taken in the administration of Carvetrend® to patients suspected of having phaeochromocytoma.

Agents with non-selective beta-blocking activity may provoke chest pain in patients with Prinzmetal's variant angina. There is no clinical experience with Carvetrend® in these patients, although the alpha-blocking activity of Carvetrend® may prevent such symptoms. However, caution should be taken in the administration of Carvetrend® to patients suspected of having Prinzmetal's variant angina.

In patients with a tendency to bronchospastic reactions, respiratory distress can occur as a result of a possible increase in airway resistance.

**Do not take this medicine if you have a history of wheezing due to asthma or other lung diseases. Consult your doctor or pharmacist first.**

**Taking other medicines**

As with other agents with beta-blocking activity, Carvetrend® may potentiate the effect of other concomitantly administered drugs that are anti-hypertensive in action (e.g. alpha₁-receptor antagonists) or have hypotension as part of their adverse effect profile.

Patients taking an agent with beta-blocking properties and a drug that can deplete catecholamines (e.g. reserpine and monoamine oxidase inhibitors) should be observed closely for signs of hypotension and/or severe bradycardia.

Isolated cases of conduction disturbance (rarely with haemodynamic disruption) have been observed when Carvetrend® and diltiazem were given concomitantly. Therefore, as with other drugs with beta-blocking activity, careful monitoring of ECG and blood pressure should be undertaken when co-administering calcium channel blockers of the verapamil or diltiazem type, or class I antiarrhythmic drugs. These types of drugs should not be co-administered intravenously in patients receiving Carvetrend®.

The effects of insulin or oral hypoglycaemics may be intensified. Regular monitoring of blood glucose is therefore recommended.

Trough plasma digoxin levels may be increased by approximately 16% in hypertensive patients co-administered Carvetrend® and digoxin. Increased monitoring of digoxin levels is recommended when initiating, adjusting or discontinuing Carvetrend®. Concomitant administration of Carvetrend® and cardiac glycosides may prolong AV-conduction time.

When treatment with Carvetrend® and clonidine together is to be terminated, Carvetrend® should be withdrawn first, several days before gradually decreasing the dosage of clonidine.
Care may be required in those receiving inducers of mixed function oxidases e.g. rifampicin, as serum levels of Carvetrend® may be reduced or inhibitors of mixed function oxidases e.g. cimetidine, as serum levels may be increased.

During general anaesthesia, attention should be paid to the potential synergistic negative inotropic effects of Carvetrend® and anaesthetic drugs.

Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without prescription.

**Pregnancy and lactation**
Carvetrend® should not be used in pregnancy or in breast-feeding mothers unless the anticipated benefits outweigh the potential risks.

**Driving and using machines**
Patients taking Carvetrend® should not drive or operate machinery if they experience dizziness or related symptoms. This applies particularly when starting or changing treatment and in conjunction with alcohol.

**Important information about some of the ingredients of Carvetrend®**
Carvetrend® tablets contain lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this product.

### 3. HOW TO TAKE CARVETREND®

Always take Carvetrend® exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. The usual dose is:

**Chronic heart failure**
The dosage must be titrated to individual requirements.

**Adults:** The recommended dose for the initiation of therapy is 3.125 mg twice a day for two weeks. If this dose is tolerated, the dosage should be increased subsequently, at intervals of not less than two weeks, to 6.25 mg twice daily, followed by 12.5 mg twice daily and thereafter 25 mg twice daily. Dosing should be increased to the highest level tolerated by the patient. The recommended maximum daily dose is 25 mg given twice daily in patients weighing less than 85 kg and 50 mg twice daily in patients weighing more than 85 kg.

During up-titration of the dose in patients with systolic blood pressure <100mmHg, deterioration of renal and/or cardiac functions may occur. Therefore, before each dose increase these patients should be evaluated by the physician for renal function and symptoms of worsening heart failure or vasodilation. Transient worsening of heart failure, vasodilation or fluid retention may be treated by adjusting doses of diuretics or ACE inhibitors or by modifying or temporarily discontinuing Carvetrend® treatment. Under these circumstances, the dose of Carvetrend® should not be increased until symptoms of worsening heart failure or vasodilation have been stabilised.

If Carvetrend® is discontinued for more than two weeks, therapy should be recommenced at 3.125 mg twice daily and up-titrated in line with the above dosing recommendation.

**Elderly:** As for adults.

**Children:** Safety and efficacy in children (under 18 years) has not been established.

**Hypertension**
Once daily dosing is recommended.

**Adults:** The recommended dose for initiation of therapy is 12.5 mg once a day for the first two days.
Thereafter the recommended dosage is 25 mg once a day. Although this is an adequate dose in most patients, if necessary the dose may be titrated up to a recommended daily maximum dose of 50 mg given once a day or in divided doses. Dose titration should occur at intervals of at least two weeks.

**Elderly:** An initial dose of 12.5 mg daily is recommended. This has provided satisfactory control in some cases. If the response is inadequate the dose may be titrated up to the recommended daily maximum dose of 50 mg given once a day or in divided doses.

**Children:** Safety and efficacy in children (under 18 years) has not been established.

**Angina**

**Adults:** The recommended dose for initiation of therapy is 12.5 mg twice a day for the first two days. Thereafter, the recommended dosage is 25 mg twice a day.

**Elderly:** The recommended maximum daily dose is 50 mg given in divided doses.

**Children:** Safety and efficacy in children (under 18 years) has not been established.

**Patients with co-existing hepatic disease**

Carvetrend® is contra-indicated in patients with hepatic dysfunction.

**Patients with co-existing renal dysfunction**

No dose adjustment is anticipated as long as systolic blood pressure is above 100mmHg.

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

### 4. POSSIBLE SIDE EFFECTS

Like all medicines, Carvetrend® can cause side effects, although not everybody gets them. Adverse events are listed separately for each indication, because of differences in the background diseases.

**In chronic heart failure**

The most commonly reported adverse effect is dizziness. Other common effects include bradycardia, postural hypotension, hypotension, gastrointestinal effects (nausea, diarrhoea and vomiting), oedema, hypervolaemia and fluid overload, vision abnormalities, thrombocytopenia, hyperglycaemia (in patients with pre-existing diabetes mellitus), weight increase and hypercholesterolaemia.

Infrequently, syncope, AV-block or cardiac failure during up-titration, acute renal failure and renal abnormalities in patients with diffuse vascular disease and/or impaired renal function have also been reported.

The frequency of adverse experiences is not dose dependent, with the exception of dizziness, abnormal vision and bradycardia.

**In hypertension and angina**

The profile is similar to that observed in chronic heart failure although the incidence of events is generally lower.

Symptomatic postural hypotension, mainly on the initiation of therapy or when increasing the dose, may occur but the incidence is minimised when the drug is used as recommended. Commonly dizziness, headache, fatigue, gastrointestinal upset (nausea, abdominal pain, diarrhoea; infrequently constipation and vomiting), bradycardia and hypotension (infrequently syncope) have been observed. These effects are usually mild, transient and occur early in the course of treatment.

Other common effects have included pain in the extremities and reduced lacrimation and, in predisposed patients, there may be asthma and dyspnoea.

Infrequently there may be depressed mood, sleep disturbance, paraesthesia, wheezing, flu-like symptoms, rare or isolated cases of skin reactions (e.g. allergic exanthema, in isolated cases urticaria, pruritus and lichen planus-like reactions). Psoriatic skin lesions may occur or existing lesions may be exacerbated.
Diminished peripheral circulation (cold extremities) or peripheral oedema may occur infrequently. Rarely there may be AV-block, angina pectoris, exacerbation of symptoms in patients suffering from intermittent claudication, Raynaud's phenomenon, or progression of heart failure. Stuffy nose may occur infrequently. Isolated cases of changes in serum transaminases, thrombocytopenia and leucopenia have been reported. There have also been rare cases of sexual impotence, disturbed vision, eye irritation, dryness of the mouth and disturbances of micturition. Due to the beta-blocking properties it is also possible for latent diabetes mellitus to become manifest, manifest diabetes to be aggravated, and blood glucose counter-regulation to be inhibited.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE CARVETREND®

Store at temperature below 25°C. Keep out of the reach and sight of children! Keep in the original packaging!

Do not use Carvetrend® after the expiry date which is stated on the outer packaging. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Carvetrend® contains
The active substance is carvedilol. Each Carvetrend® 3.125mg tablet contains 3.125 mg carvedilol. Each Carvetrend® 6.25mg tablet contains 6.25 mg carvedilol. Each Carvetrend® 12.5mg tablet contains 12.5 mg carvedilol. Each Carvetrend® 25mg tablet contains 25 mg carvedilol.

What Carvetrend® looks like and contents of the pack
Carvetrend 3.125 mg tablets are white or almost white, round and biconvex with CA3 engraved on one side. Available in packs of 28 or 30 tablets. Carvetrend 6.25 mg tablets are white or almost white, round and biconvex with CA6 engraved on one side. Available in packs of 28 or 30 tablets. Carvetrend 12.5 mg tablets are white or almost white, round and biconvex with CA12 engraved on one side. Available in packs of 28 or 30 tablets. Carvetrend 25 mg tablets are white or almost white, round and biconvex with CA25 engraved on one side. Available in packs of 28 or 30 tablets.

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