**Composition**

*Active ingredient:* carvedilol.

Tablets 6.25 mg. Round scored tablets with the imprint BM F1.
Tablets 12.5 mg. Round scored tablets with the imprint BM H3.
Tablets 25 mg. Round scored tablets with the imprint BM D5.

*Excipients:* lactose monohydrate, magnesium stearate, povidone, crospovidone, sucrose, colloidal silicon dioxide, hydrated iron oxide (E172), and iron (III) oxide (E172).

**Indications**

*Essential hypertension:* Dilatrend 25 mg is indicated for the treatment of essential (non-organically determined) hypertension.

*Chronic stable angina pectoris:* Dilatrend 25 mg is indicated for the treatment of chronic stable angina pectoris.

*Chronic heart failure:* Dilatrend 6.25 mg, 12.5 mg are indicated for the treatment of chronic heart failure in addition to diuretics, digitalis, ACE inhibitors, and/or other vasodilators.

**Warnings (on use in chronic heart failure)**

Patients to be treated with the drug should have reduced left-ventricular ejection fraction (as a rule ≤35% but at least <45%) and should have been clinically stable (no change in NYHA class or basic therapy and no admission to hospital because of heart failure) for approximately four weeks before the start of treatment with Dilatrend.

As at present insufficient data are available on treatment with Dilatrend in patients with severe heart failure (NYHA class IV), Dilatrend should not be used in such patients.

**Contraindications**

Dilatrend should not be used in any of the following cases: in patients hypersensitive to the active ingredient carvedilol or to other ingredients of the product; in cardiogenic shock; in pronounced myocardial insufficiency (decompensated heart failure); in acute pulmonary embolism; in acute myocardial infarction (within the last four weeks); in Prinzmetal's angina; in the presence of pronounced low blood pressure (systolic pressure <90 mmHg); in bradycardia (patients who are receiving Dilatrend for heart failure should have a resting heart rate of at least 65 beats/mm); in certain disturbances of stimulus formation/conduction in the heart (2nd and 3rd-degree atrioventricular block); in cases of sick sinus syndrome or sinoatrial block (exception: pacemaker therapy); in cor pulmonale (heart failure due to respiratory disease); in bronchial asthma or other respiratory diseases with a bronchospastic component (e.g. chronic obstructive lung disease); in the presence of an untreated pheochromocytoma (tumour of adrenal medulla); in the presence of severely impaired liver function; in metabolic acidosis; in patients currently receiving MAO inhibitors (exception: MAO-B inhibitors); in patients receiving simultaneous intravenous treatment with verapamil, diltiazem or other antiarrhythmic drugs.

**Side Effects**

*Possible Side Effects of Dilatrend*

**Central nervous system:** Dizziness, headache, and
Skin reactions (e.g. isolated cases of hives (urticaria), itching, lichen planus-like reactions, and rare cases of allergic eruptions) have been reported during treatment with Dilatrend.

Special Warning
In isolated cases drugs with β-blocking properties (e.g. Dilatrend) can cause psoriasis, aggravate the signs and symptoms of psoriasis, or lead to psoriasis-like (psoriasiform) skin eruptions.

Blood: In rare instances there have been changes in certain liver function values in the blood (serum transaminases) and decreases in platelet and white blood cell counts (thrombocytopenia and leukopenia).

Metabolism: In view of the β-blocking properties of the product it is impossible to rule out the possibility of latent diabetes becoming manifest, of existing diabetes becoming worse, or of blood-glucose counterregulation being inhibited. Signs of a low blood glucose level or of an overactive thyroid gland (such as a rapid heart rate) may be masked. Abnormally high blood glucose levels (hyperglycemia), weight gain, and elevated cholesterol levels can occasionally occur in patients with heart failure (with regard to diabetic patients, see also Warnings and Precautions).

Other Side Effects
There have been occasional reports of limb pains and rare reports of sensory disturbances (paresthesias), disturbed vision, eye irritation, dryness of the mouth, disturbance of urination, and erectile dysfunction.

Contact lens wearers in particular should note that tear flow may be reduced during treatment with Dilatrend.

The following side effects have been found to be dose-dependent: dizziness, visual disturbances, excessively slow heart rate, and exacerbation of heart failure.

Should any other side effects be experienced, the patient should inform the physician or pharmacist. The doctor will decide what to do if any side effects occur.
Should you experience any of the side effects referred to above, please inform your physician. Depending on the severity of the side effect, he will decide what action needs to be taken.

Precautions
Under any of the circumstances described below, Dilatrend may only be taken under certain conditions and only with particular care. These restrictions also apply if any of the circumstances described below applied previously. As only limited clinical experience is available on use of Dilatrend in patients with unstable angina pectoris, its use in this condition calls for particular care.

Caution is required when Dilatrend is used in patients with peripheral vascular disease, as β-blockers can trigger or exacerbate the signs and symptoms of arterial blood flow disturbances. Patients with angiospasm in the fingers or toes (Raynaud's disease) may experience a worsening of symptoms. In patients with a history of severe hypersensitivity reactions and in those receiving desensitisation therapy, the use of β-blockers calls for particular care of the possibility that such hypersensitivity reactions may be intensified.

In patients with a personal or family history of psoriasis, drugs with β-blocking properties (such as Dilatrend) should be used only after a careful consideration of risks and benefits.

Pregnancy and Lactation
As insufficient data is available on use in pregnancy, Dilatrend should be used in pregnancy only after a careful consideration of risks and benefits.

Carvedilol and/or its metabolites pass into breast milk. Women should therefore refrain from breast-feeding during treatment with Dilatrend.

Children, Adolescents, and the Elderly
Dilatrend should not be used in children or juveniles under 18 years of age, as insufficient clinical data are available on its use in this group. In the elderly (persons over 70 years) an exaggerated fall in blood pressure may occur after the first dose of Dilatrend or after dose increments. Elderly patients should therefore remain under medical supervision for about 2 hours after the first dose of Dilatrend and after any dose increments.

Effects on Ability Drive and Operate Machinery
No studies have been performed on the effects of Dilatrend on patients' fitness to drive or to operate machinery.

Patients treated with this drug should have regular medical checkups. Because of individually variable reactions (e.g., dizziness, tiredness), the ability to drive, operate machinery, or work without firm support may be impaired. This applies particularly at the start of treatment, after dose increments, on changing products, and in combination with alcohol.

Overdosage
Overdosage can lead to a pronounced fall in blood pressure, slowing down of heart rate, heart failure, cardiogenic shock, and even cardiac arrest. Respiratory problems, bronchospasm, vomiting, impairment of consciousness, and generalised convulsions can also occur.

If overdosage of Dilatrend is suspected, the physician should be informed and he will decide on the appropriate action depending on the severity of the intoxication. If too little Dilatrend was taken or a dose was forgotten, the number of tablets on the next occasion should not be increased. The drug should be continued as described.

The dosage of Dilatrend should be changed only on the physician’s instructions. This applies also to discontinuation of treatment. Dilatrend must never be broken off abruptly, but should be withdrawn gradually (see also Warnings and Precautions)

Storage Conditions
The expiry date of this pack is printed on the folding box and the blister strip. Do not use tablets from this pack after the expiry date.

Warnings
Patients with a tumour of the adrenal medulla (pheochromocytoma) may be treated with β-blockers only after effective alpha-receptor blockade. As no data are available on treatment with Dilatrend in such sit-
particular increased fluid retention. In order to combat this, an increase in the dose of diuretic may be tried initially.

Occasionally, however, it may be necessary to reduce the dose of Dilatrend or to suspend treatment temporarily.

In patients with heart failure and low blood pressure (systolic pressure <100 mmHg) who also suffer from myocardial blood flow disturbances (ischemic heart disease), generalized vascular diseases, or impaired renal function, a deterioration of renal function may occur during treatment with Dilatrend, though this is usually reversible. The renal function of patients with these risk factors must therefore be checked at frequent intervals during the dose titration phase of Dilatrend therapy. Should renal function deteriorate, the dose of Dilatrend should be reduced or treatment stopped altogether.

Dilatrend can cause an appreciable decrease in heart rate. As a rule the dose of Dilatrend should be reduced if the heart rate falls below 55 beats/min. Dilatrend should be used with caution in patients with first-degree atrioventricular block because of the adverse effect on stimulus conduction from the atrium to the ventricle (AV conduction).

Administration of Dilatrend simultaneously with calcium antagonists or antiarrhythmics calls for careful monitoring of blood pressure, heart rate and cardiac rhythm (ECG required, especially in the case of verapamil or diltiazem), as it can lead to a greater decrease in blood pressure, a slow heart rate, and/or heart rhythm disturbances.

In connection with anesthesia it should be noted that the effects on heart function (negative inotropism) and the blood-pressure-lowering action of Dilatrend and of some anesthetics and narcotics may undergo mutual potentiation.

Particularly careful medical monitoring is required in diabetics with large fluctuations in blood glucose level, as the early warning signs and symptoms of an acute fall in blood glucose level (hypoglycemia) may be masked or delayed. In patients who have both heart failure and diabetes mel-
the verapamil and diltiazem type, or other antiarhythmic drugs, the cardiodepressive action may be increased. Careful monitoring of the blood pressure, heart rate, and heart rhythm (ECG) is therefore required under these conditions (see also Warnings and Precautions).

- On simultaneous administration of Dilatrend and certain narcotics and anesthetics the effects on heart function (negative inotropism) and the blood-pressure-lowering action of the two drugs may potentiate each other. Therefore, before undergoing anesthesia, the physician should be informed that the patient is taking Dilatrend.

- Cyclooxygenase inhibitors (e.g. acetylsalicylic acid, corticosteroids) can weaken the antihypertensive effect of Dilatrend.

- The action of insulin or of oral antihyperglycemic drugs may be potentiated. Signs of low blood glucose (hypoglycemia) may be masked or weakened (particularly the increased heart rate). Regular checks of blood glucose are therefore necessary in diabetics.

- Cimetidine, hydralazine, and alcohol can increase the systemic availability of Dilatrend, as via enzyme inhibition they inhibit the breakdown of the active ingredient in the liver. Careful monitoring is therefore recommended in patients who are also taking these drugs.

- Rifampicin increases the metabolic degradation of carvedilol via enzyme induction and may thus reduce the action of Dilatrend.

**Dosage and Administration**

The daily dose will be determined by the physician.

**Hypertension**

Treatment should be started with ½ tablet of Dilatrend 25 mg (12.5 mg carvedilol) per day for the first two days. Treatment can then be continued with 1 tablet of Dilatrend 25 mg (25 mg carvedilol) per day. A daily dose of 1 tablet of Dilatrend 25 mg is generally sufficient. Only the physician can decide whether the dose should be increased. Where the effect is inadequate, the dose can be increased after a minimum of 14 days to 1 tablet of Dilatrend 25 mg.
vals of at least 2 weeks to 6.25 mg carvedilol twice daily and then to 12.5 mg carvedilol twice daily and 25 mg carvedilol twice daily. Dividable tablets with different content of active ingredient (Dilatrend 6.25 mg, Dilatrend 12.5 mg, and Dilatrend 25 mg) are available for the adjustment therapy.

The maintenance dose must be established for each patient individually with strict medical monitoring. Long-term treatment should then proceed with the highest tolerated dose.

The minimal effective dose is 6.25 mg carvedilol twice daily. In patients weighing under 85 kg the maximum dose should not exceed 25 mg carvedilol twice daily. In patients weighing over 85 kg a cautious attempt may be made to increase the dose up to a maximum of 50 mg carvedilol twice daily, provided that the patient is closely monitored. The dose of Dilatrend may be increased only if the patient's clinical condition is satisfactory and stable, i.e. if there are no signs of worsening of the heart failure and no clinically relevant side effects, especially ones caused by vasodilation (e.g. a decrease in blood pressure or dizziness). Patients must therefore be checked for such symptoms, in particular, before each dose increment. Frequent and regular medical checks (e.g. of renal function, body weight, blood pressure, heart rate, and heart rhythm) must also be carried out, particularly during the dose titration period (increase of the dose to the maintenance level). A deterioration in the symptoms of heart failure and side effects due to the vasodilation action of Dilatrend often occur for a short time only and should be treated by temporarily reducing the dose of the product or if necessary by suspending treatment. However, if the symptoms are caused primarily by fluid retention the dose of diuretic can be increased temporarily.

An exaggerated fall in blood pressure may occur after the first dose of Dilatrend or after increments, particularly in patients with severe heart failure (NYHA≥III) and/or on high-dose diuretic therapy. Therefore, in order to prevent an uncontrolled fall in blood pressure, the dose of Dilatrend should be adjusted carefully. The initial dose for chronic heart failure is 3.125 mg carvedilol twice daily for 2 weeks.

Dosage in elderly patients:
A daily dose of ½ tablet of Dilatrend 25 mg (12.5 mg carvedilol) is also recommended for elderly patients at the start of treatment. In some patients this dose has been found to bring about a satisfactory fall in blood pressure even during long-term treatment. Where the effect is inadequate, the dose can be increased at intervals of at least 14 days up to maximum levels (individual dose of 25 mg or daily of 50 mg carvedilol).

Dilatrend should always be used in combination with the standard treatment of heart failure which consists of diuretics, digitalis, ACE inhibitors, and/or vasodilators. Treatment with Dilatrend must not be started until the patient has been stabilized on the conventional basic therapy for heart failure, i.e. the dosage of this standard therapy must have been stable for at least 4 weeks prior to the start of treatment with Dilatrend.

Only physicians with specialist qualifications in internal medicine and/or cardiology may use Dilatrend in patients with chronic heart failure.

The recommended dose at the beginning of treatment is 3.125 mg carvedilol twice daily for 2 weeks. If this dose is tolerated it can be increased at inter-

Chronic Stable Angina Pectoris
Treatment should be started with ½ tablet of Dilatrend 25 mg (12.5 mg carvedilol) twice daily on each of the first two days and then continued with 1 tablet of Dilatrend 25 mg (25 mg carvedilol) twice daily. A dose of 1 tablet of Dilatrend 25 mg (25 mg carvedilol) twice daily is generally sufficient. Where the effect is inadequate, the dose can be increased after a minimum of 14 days to 2 tablets of Dilatrend 25 mg (50 mg carvedilol) twice daily.

Dosage in elderly patients: In elderly patients on long-term therapy a dose of ½ tablet of Dilatrend 25 mg (25 mg carvedilol) twice daily should not be exceeded.
blood pressure, such patients should remain under medical supervision for about 2 hours after the first dose of Dilatrend and after any dose increments. Where treatment with Dilatrend has been interrupted for more than two weeks it should be resumed with 3.126 mg carvedilol twice daily for two weeks followed by gradual dose titration as described above.

**Dosage in Patients with Impaired Renal Function**

The appropriate dose must be established for each patient individually. On the basis of the pharmacokinetic parameters of carvedilol in heart failure, no dosage adjustment of Dilatrend is required.

*Note on tablet division:* Place the tablet on a hard surface and press down with one thumb on the left of the dividing groove and the other thumb on the right. The tablet can thus be readily split into halves. Dilatrend should be swallowed whole with sufficient liquid.

Unless otherwise prescribed the drug should generally be taken in the morning, or one tablet in the morning and one in the evening. It is recommended that Dilatrend be taken with meals in order to retard the absorption of the active ingredient and thus possibly to reduce circulatory regulation disturbances on change of position (orthostatic effects).

**Duration of Treatment**

The duration of treatment will be determined by the physician. Treatment with Dilatrend is generally long-term therapy and if possible should not be stopped abruptly, but rather tapered off over 1-2 weeks.

In order to prevent any exacerbation of angina pectoris, antianginal therapy can, if necessary, be given during this tapering-off period.