PACKAGE LEAFLET: Information for the patient

DILAPRO

Tablets – 12.5 mg

Tablets – 25 mg

(Carvedilol)

Read all of this leaflet carefully before you start using 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 becomes worse or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT DILAPRO IS AND WHAT IT IS USED FOR?

Dilapro contains carvedilol as active substance, which causes unselective blockade of beta-1 and beta-2 receptors and selective blockade of alpha-1 receptors in heart and vascular system.

Dilapro is used in:

- the treatment of essential high blood pressure
- the treatment of chronic stable angina pectoris
- supplementary treatment in chronic stable heart failure.

2. BEFORE YOU TAKE DILAPRO

Do not take Dilapro in:

- hypersensitivity (allergy) to carvedilol or to any of the excipients of Dilapro;
- cardiogenic shock;
- decompensated heart failure;
- acute pulmonary embolism;
- Prinzmetal's angina;
- severe hypotension (systolic blood pressure < 90 mm Hg);
- very low pulse (patients which are treated with Dilapro in heart failure, should have at least a pulse of 65 beats / minute);
- disturbances in the conduction system of the heart**:** AV-block of II and III degree, sick sinus syndrome, sinoatrial block (pacemaker therapy is excluded);
- cardiac failure because of pulmonary airway diseases (cor pulmonale);
- asthma and chronic obstructive pulmonary disease;
- untreated phaeochromocytoma;
- clinically severe manifest of liver dysfunction;
- metabolic acidosis;
- case of taking at the same time monoaminooxidase inhibitors (MAOIs) (except MAOIs-B);
- concomitant intravenous treatment with verapamil, diltiazem or other antiarrythmic drugs;
- breastfeeding.

Take special care with Dilapro

Ask your doctor before taking Dilapro:

- if you have heart failure accompanied by:
  - low blood pressure;
  - compromised blood and oxygen supply to the heart (ischaemic heart disease) and narrowing of the arteries (atherosclerosis);
  - and/or kidney problems (your renal function should be monitored then; it may be necessary to reduce your dose);
- if you have left ventricular dysfunction after an acute myocardial infarction;
- if you have diabetes; treatment with Dilapro may mask the signs of low blood sugar; your blood sugar should therefore be monitored regularly;
- if you have severe breathing problems for which you are not receiving medication; Dilapro

may worsen these breathing difficulties;

- if you use contact lenses; carvedilol may reduce tear production;
- if you have Raynaud's phenomenon (fingers or toes turn first bluish, then whitish and then reddish together with pain), or any other peripheral vascular disease; Dilapro may worsen the symptoms;
- if you have overfunction of thyroid gland, with elevated production of thyroid hormone; Dilapro may mask the symptoms;
- if you are using Dilapro and are to undergo an operation involving an anaesthetic; you should discuss this with the doctor responsible for the anaesthesia well in advance;
- if you have a very low pulse (less than 55 beats per minute);
- if you have had a serious allergic reaction (e.g. to an insect bite or food) or if you are undergoing or are due to undergo allergic desensitisation therapy because Dilapro may weaken the efficacy of medicines used to treat such allergic reactions;
- if you have psoriasis;
- in children and adolescents (below 18 years of age) due to insufficient data on the efficacy and harm that it may cause; it is not recommended to use carvedilol in these patients;
- in elderly, because they may be sensitive to carvedilol and should be monitored carefully. As with other beta-blockers, carvedilol must not be discontinued suddenly, but gradually, especially in patients with coronary circulatory disorders.

Effects of misuse as doping agent

Use of Dilapro may cause positive doping results.

Health consequences may not be predicted. Health hazard may not be excluded.

Taking other medicines

Other concomitant drug treatment may affect or be affected by Dilapro.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. Remember to tell your doctor about the treatment with Dilapro if you are prescribed another drug during treatment.

It is especially important that your doctor be aware if you are already being treated with:

- digoxin (to treat heart failure);
- rifampicin (antibiotic used in treating tuberculosis);
- cimetidine (medicine to treat stomach ulcers, heartburn and acid reflux);
- ketoconazole (medicine to treat mycosis);

- fluoxetine (medicine to treat depression);
- haloperidol (medicine to treat particular mental/psychic disorders);
- erythromycin (antibiotic);
- cyclosporin (medicine to suppress the immune system, to prevent ejective reactions after organ transplantation, also used for e.g., certain rheumatic or dermatological problems);
- clonidine (medicine to reduce blood pressure or to treat migraine);
- verapamil, diltiazem, amiodarone (medicines to treat irregular heartbeat);
- quinidine, disopyramide, mexiletin, propafenone, flecainide (drugs to treat irregular heartbeat);
- other blood pressure reducing drugs; carvedilol can enhance the effects of other blood pressure reducing drugs given concurrently (e.g. alpha1-receptor antagonists) and drugs where reduction in blood pressure transpires as a side effect, e.g. barbiturates (in the treatment of epilepsy), phenothiazines (to treat psychoses), tricyclic antidepressants (in the treatment of depression), vasodilating drugs (drugs for widening the blood vessels) and alcohol;
- insulin or oral anti-diabetic medicines (blood sugar reducing agents) as their blood sugar reducing effect can be increased and the symptoms of low blood sugar covered up;
- anaesthetics (drugs used in anaesthesia);
- sympathomimetics (drugs which increase the function of the sympathetic nervous system);
- dihydropyridines (medicines to treat high blood pressure and heart diseases);
- nitrates (medicine to treat heart diseases);
- neuromuscular blocking preparations (drugs which reduce muscle tension);
- ergotamine (migraine medicine);
- certain painkilling tablets (NSAID), oestrogens (hormones) and corticosteroids (adrenal hormone), as these can in some instances reduce the blood pressure reducing effect of carvedilol;
- drugs containing reserpine, guanethidine, methyldopa, guanfacine and monoaminooxidase inhibitors (MAOIs), medicines to treat depression, as these may give rise to further reduction in the heart rate.

Taking Dilapro with food and drinks

Carvedilol may enhance the effects of alcohol.

Pregnancy and breastfeeding

If you are pregnant or breast-feeding, if you think you are pregnant or intend to become pregnant, ask your doctor or pharmacist for advice before using this medicine.

There is a risk of harm to the unborn child. It may only be used during pregnancy if your doctor deems it necessary (in cases where the need for treatment outweighs the potential hazards to the foetus / newborn baby). Always, therefore, consult your doctor before using Dilapro during pregnancy.

Carvedilol passes over in human breastmilk and should therefore not be used during breast-feeding.

Driving and using machines

Treatment with this drug requires regular medical examinations.

Dizziness and tiredness may occur at the beginning of treatment or when the treatment is changed or during interaction with alcohol. If you feel dizzy or weak when taking the tablets, you should avoid driving or work involving high attention.

3. HOW TO TAKE DILAPRO

Always take Dilapro exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. If you feel that the effects of Dilapro are too strong or too weak, talk to your doctor or pharmacist.

You should swallow the tablets with at least half glass of water.

It is recommended to take Dilapro with food, to allow the absorption of the active substance to be slower and the risk of orthostatic hypotension to be reduced.

Treatment duration is determined by the doctor. Usually, carvedilol treatment lasts and must not be discontinued suddenly. Carvedilol must be withdrawn gradually (over 1-2 weeks).

Administration only in adults:

If not otherwise prescribed by the doctor, the usual dose is:

Chronic stable heart failure	**Daily dose**
Initial dose	In the first 14 days: 3.125 mg carvedilol in the morning and 3.125 mg carvedilol in the evening
Maintenance dose	If this dose is tolerated, it is increased in intervals of at least 2 weeks in: 6.25 mg carvedilol in the morning and 6.25 mg carvedilol in the evening, then 12.5 mg carvedilol in the morning and 12.5 mg carvedilol in the evening, then 25 mg carvedilol in the morning and 25 mg carvedilol in the evening. The maximum tolerated dose will be taken by the patient.
Maximum dose in special cases	25 mg carvedilol in the morning and 25 mg carvedilol in the evening.

Only in patients with chronic stable heart failure, mild or moderate, with a body weight over 85 kg, the maximum daily dose may be increased to 50 mg carvedilol twice daily, keeping the patient under supervision and intensive care.

High blood pressure	**Daily Dose**
Initial Dose	In the first 2 days 12.5 mg carvedilol once in the morning.
Maintenance Dose	25 mg carvedilol once daily in the morning.
Maximum dose in special cases	At least after 14 days: 25 mg carvedilol in the morning and 25 mg carvedilol in the evening.

Note! A single dose of 25 mg or a daily dose of 50 mg should not be exceeded.

Chronic Stable Angina Pectoris	**Daily Dose**
Initial Dose	In the first 2 days 12.5 mg carvedilol in the morning and 12.5 mg carvedilol in the evening.
Maintenance Dose	25 mg carvedilol in the morning and 25 mg carvedilol in the evening.
Maximum dose in special cases	After at least 14 days: 50 mg carvedilol in the morning and 50 mg carvedilol in the evening.

Administration in the elderly

In essential hypertension (high blood pressure)

Initial dose	In the first two days: 12.5 mg carvedilol in the morning
Maintenance dose	If the effect is not sufficient, the dose can be increased further at intervals of at least 14 days in: 12.5 mg carvedilol in the morning and 12.5 mg carvedilol in the evening, up to 25 mg carvedilol in the morning and 25 mg carvedilol in the evening.
Maximum dose	At least after 14 days: 25 mg carvedilol in the morning and 25 mg carvedilol in the evening.

At the beginning of treatment, 12.5 mg carvedilol daily is recommended also for elderly. In some patients, this dose can assure sufficient decrease of blood pressure also in the long-term treatment.

In chronic stable angina pectoris

Maximum dose	In the long-term treatment 25 mg carvedilol in the morning and 25 mg carvedilol in the evening.

In the elderly, the daily dose of 2 x 25 mg carvedilol in divided doses, should not be exceeded.
If you stop taking carvedilol for more than two weeks, the therapy should be resumed at the initial dose and then gradually increased according to the reccomendations.

If you have taken more Dilapro than you should
If you have taken more Dilapro than you should, or if the children have been taking the medicine by accident, please contact your doctor, the hospital or call the emergency to get an opinion of the risk and advice on the actions to be taken.
Symptoms of overdose can include: feelings of faintness due to excessively low blood pressure, slow heart rate and in serious instances occasional missed heartbeats. Also breathing difficulties, constricted airways, malaise, vomiting, lowered level of consciousness and seizures may occur.

If you forget to take Dilapro
If you forget a dose (or more doses), take the next dose when it is the normal time to take it. Do not take a double (or higher) dose to make up for a forgotten dose(s).

If you stop the treatment with Dilapro
The dose of this drug should not be changed without medical advice. Also, the treatment should not be stopped without medical advice. The treatment with Dilapro should not be discontinued suddenly, but should be reduced gradually.
If you have any further questions on the use of this medicinal product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

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

The frequency of possible side effects is shown in the table below:

Very common:	Occur in more than 1 in 10 users
Common:	Occur in 1 to 10 users from 100
Uncommon:	Occur in 1 to 10 users from 1.000
Rare:	Occur in 1 to 10 users from 10.000
Very rare:	Occur in less than 1 in 10.000 users
Unknown	Frequency cannot be determined from the available data.

The table below summarizes the side effects reported during carvedilol studies.

Body system	**Side effect**	**Frequency**
Infections and infestations	Bronchitis	Common
	Pulmonary inflammation	Common
	Upper respiratory tract infection	Common
	Urinary tract infection	Common
Blood and lymphatic system disorders	Anaemia	Common
	Thrombocytopenia	Rare
	Leukopenia	Very rare
Immune system disorders	Hypersensitivity (allergic reactions)	Very rare
Metabolism and nutrition disorders	Weight increase	Common
	Hypercholesterolaemia	Common
	Impaired glucose control (increased blood sugar values, very low blood sugar values) in patients with diabetes mellitus	Common
Psychiatric disorders	Depression, depressive state	Common
	Sleep disorders	Uncommon
	Nightmares	Uncommon
	Hallucinations	Uncommon
	Confusion	Uncommon
	Psychosis	Very rare
Nervous system disorders	Dizziness	Very common
	Headache	Very common

Body system	Side effect	Frequency
	Short-term loss of consciousness (syncope [including presyncope])	Common
	Paresthesia	Uncommon
Eye disorders	Visual impairment	Common
	Lacrimation decreased (dry eye)	Common
	Eye irritation	Common
Cardiac disorders	Cardiac failure	Very commmon
	Bradycardia (slow heart beats)	Common
	Increased amount of circulating blood (hypervolaemia)	Common
	Improper liquid elimination	Common
	Atrioventricular block	Uncommon
	Angina pectoris attack	Uncommon
Vascular disorders	Hypotension	Very common
	Orthostatic hypotension, disturbances of peripheral circulation (cold extremities), peripheral occlusive disease, worsening of symptoms in patients with *Claudicatio intermitens*, vascular pain in fingers or toes (Raynaud's disease)	Common
	Hypertension	Common
Respiratory, thoracic and mediastinal disorders	Shortness of breath	Common
	Water accumulation in the lungs (pulmonary oedema)	Common
	Asthma and shortness of breath in patients with tendency for narrowed airways	Common
	Nasal congestion	Rare
Gastrointestinal disorders	Nausea	Common
	Diarrhoea	Common
	Vomiting	Common
	Difficulty in digestion	Common
	Abdominal pain	Common
	Constipation	Uncommon
	Dry mouth	Rare
Hepatobiliary disorders	Increased serum transaminases	Very rare

Body system	Side effect	Frequency
Skin and subcutaneous tissue disorders	Skin reactions such as allergic exanthema, dermatitis, urticaria, pruritus, psoriasis, rash similar to psoriasis.	Uncommon
	Severe cutaneous reactions (e.g. erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis).	Unknown
	Hair loss	Unknown
Musculoskeletal and connective tissue disorders	Body pain	Common
Renal and urinary disorders	Renal failure, or renal function disorders in patients with diffuse vascular disease and / or reduced kidney function.	Common
	Urination disorders	Common
	Urinary incontinence in women	Very rare
Reproductive system and breast disorders	Impotence	Uncommon
General disorders and administration site conditions	Asthenia	Very common
	Pain	Common
	Oedema	Common

Description of some side effects:

Dizziness, syncope, headache and asthenia are generally mild and mostly occur at the beginning of the treatment. In patients with congestive heart failure, its deterioration and the deterioration of fluid retention may occur at the stage of adjusting the dose of carvedilol.

In patients with chronic heart failure with low blood pressure, ischemic heart disease, and diffuse vascular disease and / or existing renal insufficiency, a reversible deterioration of renal function has been observed during carvedilol therapy.

The beta-blockers class can cause the onset of latent diabetes, exacerbation of existing diabetes, and worsening of the mechanism of blood sugar regulation.

Carvedilol can cause urinary incontinence in women, which is resolved by discontinuing treatment.

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

5. HOW TO STORE DILAPRO

Keep out of the reach and sight of children.

Do not use Dilapro after the expiry date which is stated on the label.

Do not store above 25°C.

Store in the original package in order to protect from light and in a dry place.

6. FURTHER INFORMATION

What Dilapro 12.5 mg tablets contain

The active substance is carvedilol.

Each tablet contains 12.5 mg of carvedilol.

The excipients are: silicified microcrystalline cellulose, magnesium stearate.

What Dilapro 25 mg tablets contain

The active substance is carvedilol.

Each tablet contains 25 mg of carvedilol.

The excipients are: silicified microcrystalline cellulose, magnesium stearate.

Contents of the pack

Dilapro 12.5 mg: Box with 30 tablets.

Dilapro 25 mg: Box with 30 tablets.

Marketing Authorisation Holder (MAH) and Manufacturer

PROFARMA Sh.a.,

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Tirana, Albania.

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This leaflet was last revised in August 2023.