PACKAGE LEAFLET: Information for the patient

PRONIPIN

Sustained release film-coated tablets – 20 mg

(Nifedipine)

Read 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 only. 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 gets worse or if you notice any side effect not listed in this leaflet, please inform your doctor or pharmacist.

In this leaflet:

1. WHAT PRONIPIN IS AND WHAT IT IS USED FOR

Pronipin contains the active substance nifedipine, which is a calcium-channel blocker that improves oxygen supply in the myocardium by reducing at the same time the demand for oxygen. Nifedipine has a vasodilator effect on the peripheral arterial surfaces causing a reduction of the peripheral vascular resistance and a decrease of the peripheral blood flow. Ca^{2+} channel blockers are very useful in reducing hypertension. Pronipin dilates coronary arteries, thus protects the heart against coronary spasms and relieves myocardial ischemia.

Pronipin is used in:

- chronic angina pectoris;
- hypertension.

Please do not use Pronipin for the relief of an acute attack of angina.

Your doctor may have prescribed Pronipin to you for another purpose. Ask your doctor why this drug has been given to you.

2. BEFORE YOU TAKE PRONIPIN

Do not take Pronipin and ask your doctor if you:

- are hypersensitive to the active substance nifedipine or to any of the excipients of Pronipin tablets (see the excipients at the end of this leaflet);
- are hypersensitive to the active substances similar to nifedipine like: amlodipine, felodipine and isradipine;
- are in cardiovascular shock condition;
- have advanced stenosis of aorta;
- suffer of unstable angina;
- have passed a myocardial infarction within 4 weeks;
- are pregnant or breast - feeding the baby;
- are being treated with rifampicin.

Its use is not recommended in children and adolescents under 18 years old.

Take special care with Pronipin

Care should be taken when a low blood pressure is clearly identified (severe systolic hypotension, less than 90 mm Hg) accompanied with congestive heart failure.

Care should be taken in dialysis patients with a severe hypertension and in patients with renal damages with hypovolemia which indicates a drop of the blood pressure which may be repeated.

Nifedipine should not replace nitroglycerine in an acute attack of angina pectoris.

Care should be taken in patients with angina and which are accompanied by hypotension.

Care should be taken in patients with diabetes mellitus, because a transitory blood glucose increase may happen.

Pronipin should be carefully taken in patients with a poor cardiac reserve.

In patients with liver damage the complete monitoring of the recommended dosage should be made and in the most common cases a reduced dosage is given if it is necessary.
The tablet should be taken exactly as your doctor has told you. If you do not follow the instructions of the doctor, you may not control your blood pressure or calm the angina.
Tell your doctor if you continue to have an attack of angina or if it is more common when you take Pronipin.
Tell your doctor, dentist and pharmacist if you are being treated with Pronipin.
Be careful during driving and using machinery if you do not yet know the effects that will appear to you during Pronipin use.

Taking other medicines

Pronipin interacts with a large number of drugs. You should tell your doctor if you take one of the following drugs because you may need to change your treatment.
The blood pressure lowering effect may be stimulated by the coadministration of nifedipine with other antihypertensives.
When nifedipine is taken concomitantly with β-receptor blockers the patient should be carefully monitored because an immediate hypotension may occur. In isolated cases a cardiac failure may initiate.
Digoxin: concomitant administration of nifedipine with digoxin may decrease the clearance of digoxin and thus its plasmatic concentration is increased. Patients should be monitored for digoxin overdosage symptoms and if necessary, the dosage of the glycosides should be reduced considering the plasmatic concentration of digoxin.
Phenytoin: phenytoin stimulates the cytochrome P450 3A4 system. During coadministration with phenytoin the biodisponibility of nifedipine is reduced thus the efficiency is decreased. When the two drugs are coadministered, the clinical response of nifedipine should be monitored and if it is necessary, the dose of nifedipine may be increased. If the dose of nifedipine is increased during coadministration of the two drugs, a reduction of its dose is necessary when the treatment with phenytoin is interrupted.
Quinidine: co-administration of nifedipine with quinidine may lower plasma quinidine levels and after discontinuation of nifedipine, a distinct increase in plasma quinidine levels have been observed in a few patients. For these cases, when nifedipine is added or stopped during

the administration, the plasmatic concentration of quinidine should be monitored and if necessary, the regulation of the recommended dose of quinidine be done. However, blood pressure should be carefully monitored if quinidine is a subsidiary of an existing therapy with nifedipine. If it is necessary, the dose of nifedipine should be reduced.

Cimetidine: because it is a cytochrome P450 3A4 inhibitor, cimetidine increases the plasmatic concentration of nifedipine and may potentiate the antihypertensive effect.

Rifampicin: rifampicin significantly stimulates cytochrome P450 3A4 system. During the simultaneous administration with rifampicin, the bioavailability of nifedipine is markedly reduced and thereby the efficacy is reduced. The use of nifedipine in combination with rifampicin is contraindicated.

Diltiazem: diltiazem decreases nifedipine clearance. Nifedipine increases the biodisponibility and decreases the clearance of diltiazem. The combination of both these drugs should be carefully administered and a reduction of both doses may be kept in mind.

Grapefruit juice: this juice inhibits nifedipine metabolism. Nifedipine administration with grapefruit juice results with the increase of the plasmatic concentration of nifedipine and with the increase of the biodisponibility of the drug. As a consequence, the antihypertensive effect may increase.

Erythromycin: both drugs, nifedipine and erythromycin are metabolisable by the cytochrome P450 3A4 system, thus the possibility to interact may not be excluded. Erythromycin is known as a cytochrome P450 3A4 inhibitor that interferes in the metabolism of the other drugs.

Ketoconazole, itraconazole, fluconazole: the drugs of this group are inhibitors of the cytochrome P450 3A4 system. When orally administered together with nifedipine, an increase in the nifedipine biodisponibility is noted where it is not excluded its absorption increase. During concomitant administration, blood pressure should be monitored and if necessary a reduction of nifedipine dosage may be made.

Tacrolimus: this drug is metabolised by the cytochrome P450 3A4 system. In the coadministration of tacrolimus with nifedipine, the plasmatic concentration of tacrolimus should be monitored and if necessary the dose of tacrolimus may be reduced.

Carbamazepine: this drug is known as a reducer of the plasmatic concentration of the calcium - channel blockers structurally related to nimodipine through the enzyme induction. A decrease of the plasmatic concentration of nifedipine and a decrease of its efficacy should not be excluded.

Valproic acid: this drug is known to increase the plasmatic concentration of the calcium-channel blockers structurally related to nimodipine through enzyme inhibition; an increase of the plasmatic concentration of nifedipine and an increase of its effect should not be excluded.

Taking Pronipin with food and drinks

Pronipin is not advised to be taken concomitantly with grapefruit juice.

Pregnancy and breastfeeding

Pronipin is not recommended during pregnancy or breastfeeding.
Ask your doctor or pharmacist before taking this drug.

Driving and using machinery

The side effects of Pronipin tablets, which may change in intensity from person to person, may worse the ability to drive and use machinery. This happens especially at the beginning of the treatment, when changing the drug and in combination with alcohol.
Driving and using machinery during Pronipin administration is not advisable.

Important information about some of the excipients of Pronipin

This drug contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. HOW TO TAKE PRONIPIN

Always take Pronipin exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.
The doctor will tell you how much Pronipin you should take and when you should take it. The dose that has been prescribed to you depends on your conditions and how much serious are them. Take the tablets for as long as you are told if you don’t have any problem. In these cases, visit your doctor.
Instructions for dose administration:
The treatment should be individual in accordance with the gravity of the disease and the patients response to the drug.

- For coronary diseases, the recommended dose is 20 mg twice daily.
  The dose may be increased to 40 mg twice daily.
- For high blood pressure (hypertension) the recommended dose is 20 mg twice daily.
  The dose may be increased to 40 mg twice daily.

Pronipin tablets are commonly swallowed as whole after meal with a little water.
The interval of administration between two individual doses of 20 mg nifedipine should not be less than 4 hours. The doctor should attend the patient during treatment.

If you take more Pronipin than you should

If you have taken more Pronipin than you should, or if the children have taken this medicine incorrectly, please contact your doctor, the hospital or call the emergency to get an opinion for the risk and an advice for the actions to be taken.
Take the carton box with you to see what you have taken.

If you forget to take Pronipin

If you forget a dose (or more doses), take the following dose when it is time to take it usually.
Do not take a double dose (or higher) to make up for a forgotten dose (s).
If you have further questions on the use of this medicinal product, ask your doctor or pharmacist.

If you stop the treatment with Pronipin

Please consult your doctor before you stop the treatment with Pronipin.
Discontinuation of the treatment with Pronipin, especially at high doses, should be made gradually.

4. POSSIBLE SIDE EFFECTS

Like all other medicines, Pronipin may cause side effects, although not everybody manifests them. Sometimes they are serious, sometimes not. Do not get alarmed by this list of possible side effects. None of them may appear to you.

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

Very common	Occur in more than 1 in 10 users
Common	Occur in less than 1 in 10, but more than 1 in 100 users
Uncommon	Occur in less than 1 in 100, but more than 1 in 1,000 users
Rare	Occur in less than 1 in 1,000, but more than 1 in 10,000 users
Very rare	Occur in less than 1 in 10,000 users, including isolated cases

Common:

General:	asthenia, oedema, headache
Cardiovascular system:	palpitation, peripheral oedema, vasodilatation
Digestive system:	nausea
Nervous system:	dizziness

Rare:

General:	abdominal pain, chest pain, tiredness, pain
Cardiovascular system:	angina pectoris, postural hypotension, syncope, tachycardia
Digestive system:	constipation, diarrhea, dry mouth, dyspepsia, vomiting
Musculo-skeletal system:	arthralgia, myalgia
Nervous system:	sleep disturbances, anxiety, migraine, nervosity, paraesthesia, somnolence, tremor, vertigo
Respiratory system:	dyspnea, nasal congestion
Skin and other:	pruritus, itching, skin disorders, sweating
Urogenital system:	nocturia, polyuria, pain during urination erectile dysfunction

Disorders of the metabolism:	hyperglycaemia
Blood disorders:	anemia, leucopenia, thrombocytopenia

Very rare:

General:	allergic reactions, photosensibility
Cardiovascular system:	hypotension
Digestive system:	flatulence, abdominal disorders, increase of GGTP, abnormal liver function test, jaundice
Hemic and lymphatic system:	purpura
Nervous system:	hypoaesthesia
Skin and other:	urticaria
Eye:	visual disturbances, ambliopia

Other undesiderable effects:

Digestive system:	gingival hyperplasia, intestinal obstruction
Hemic and lymphatic system	agranulocytosis
Skin and other:	erythromyalgia, exfoliative dermatitis, anaphylactic reaction, scaled skin, toxic epidermal necrolysis.

If any of these symptoms begins and becomes troubling, or if you notice anything else that is not mentioned above, please consult your doctor. They can give you a different drug.
If you notice other side effects not mentioned in this list, please tell your doctor or pharmacist.

5. HOW TO STORE PRONIPIN

Keep out of the reach and sight of children.
Do not use Pronipin after the expiry date which is stated on the packaging.
Store below 25°C.
Store in the original packaging to protect it from light and humidity.

6. FURTHER INFORMATION

What Pronipin sustained release film-coated tablets contain

The active substance is nifedipine.

Each sustained release film - coated tablet contains 20 mg nifedipine.

The excipients are: lactose monohydrate, maize starch, magnesium stearate, microcrystalline cellulose, polysorbate, hypromellose, povidone, talc, polyvinyl alcohol, macrogol, titanium dioxide, red iron oxide and yellow iron oxide.

Content of the pack:

Carton box with 30 sustained release film-coated tablets.

Marketing Authorisation Holder (MAH) and Manufacturer:

PROFARMA sh.a.,

St. “Skënder Vila”,

Tirana, Albania.

Tel.: +355 4 23 89 602

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