Package leaflet: Information for the patient

Bisoprolol Krka 2.5 mg film-coated tablets
Bisoprolol Krka 5 mg film-coated tablets
Bisoprolol Krka 10 mg film-coated tablets
bisoprolol fumarate

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 Bisoprolol Krka is and what it is used for

The active substance in Bisoprolol Krka is bisoprolol. Bisoprolol belongs to a group of medicines called beta-blockers. These medicines work by affecting the body`s response to some nerve impulses, especially in the heart. As a result, bisoprolol slows down the heart rate and makes the heart more efficient at pumping blood around the body. At the same time bisoprolol reduces the oxygen demand and blood supply of the heart. Heart failure occurs when the heart muscle is weak and unable to pump enough blood to supply the body’s needs.

Bisoprolol Krka is used to
- treat high blood pressure (hypertension).
- treat angina pectoris.
- treat stable chronic heart failure. It is used in combination with other medicines suitable for this condition (such as ACE-inhibitors, diuretics, and heart glycosides).

2. What you need to know before you take Bisoprolol Krka

Do not take Bisoprolol Krka
Do not take Bisoprolol Krka if you have one of the following conditions:
- allergy to the active substance or any of the other ingredients of this medicine (listed in section 6).
- severe asthma.
- severe blood circulation problems in your limbs (such as Raynaud’s syndrome), which may cause your fingers and toes to tingle or turn pale or blue.
- untreated phaeochromocytoma, which is a rare tumour of the adrenal gland.
- metabolic acidosis, which is a condition when there is too much acid in the blood.

Do not take Bisoprolol Krka if you have one of the following heart problems:
- acute heart failure.
- worsening heart failure requiring an injection of medicines into a vein, that increase the force of

contraction of the heart.
- low blood pressure.
- certain heart conditions causing a very slow heart rate or irregular heartbeat.
- cardiogenic shock, which is an acute serious heart condition causing low blood pressure and circulatory failure.

Warnings and precautions
Talk to your doctor or pharmacist before taking Bisoprolol Krka. If you have any of the following conditions tell your doctor before taking Bisoprolol Krka tablets; he or she may want to take special care (for example give additional treatment or perform more frequent checks):
- diabetes.
- strict fasting.
- certain heart diseases such as disturbances in heart rhythm, or severe chest pain at rest (Prinzmetal's angina).
- kidney or liver problems.
- less severe blood circulation problems in your limbs.
- less severe asthma or chronic lung disease.
- history of a scaly skin rash (psoriasis).
- tumour of the adrenal gland (phaeochromocytoma).
- thyroid disorder.
- first degree heart block (a condition in which nerve signals to the heart are disturbed, possibly causing it occasionally to skip a beat, or beat irregularly).

In addition, tell your doctor if you are going to have:
- desensitisation therapy (for example for the prevention of hay fever), because Bisoprolol Krka tablets may make it more likely that you experience an allergic reaction, or such a reaction may be more severe.
- anaesthesia (for example for surgery), because Bisoprolol Krka tablets may influence how your body reacts to this situation.

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

<u>Do not take the following medicines with Bisoprolol Krka tablets without special advice from your doctor:</u>
- certain medicines used to treat irregular or abnormal heartbeat (Class I antiarrhythmic medicines such as quinidine, disopyramide, lidocaine, phenytoin; flecainide, propafenone).
- certain medicines used to treat high blood pressure, angina pectoris or irregular heartbeat (calcium antagonists such as verapamil and diltiazem).
- certain medicines used to treat high blood pressure such as clonidine, methyldopa, moxonodine, rilmenidine. However, **do not stop taking these medicines** without checking with your doctor first.

<u>Check with your doctor before taking the following medicines with Bisoprolol Krka tablets; your doctor may need to check your condition more frequently:</u>
- certain medicines used to treat high blood pressure or angina pectoris or abnormal heart beat (dihydropyridine-type calcium antagonists, such as nifedipine, felodipine and amlodipine).
- certain medicines used to treat irregular or abnormal heartbeat (Class III antiarrhythmic medicines such as amiodarone).
- beta-blockers applied locally (such as timolol eye drops for glaucoma treatment).
- certain medicines used to treat for example Alzheimer's disease or glaucoma (parasympathomimetics, such as tacrine or carbachol) or medicines that are used to treat acute heart problems (sympathomimetics such as isoprenaline and dobutamine).
- antidiabetic medicines including insulin.
- anaesthetic agents (for example during surgery).

- digitalis, used to treat heart failure.
- non-steroidal anti-inflammatory medicines (NSAIDs) used to treat arthritis, pain or inflammation (for example ibuprofen or diclofenac).
- any medicine, which can lower blood pressure as a desired or undesired effect such as antihypertensives, certain medicines for depression (tricyclic antidepressants such as imipramine or amitriptyline), certain medicines used to treat epilepsy or during anaesthesia (barbiturates such as phenobarbital), or certain medicines to treat mental illness characterised by a loss of contact with reality (phenothiazines such as levomepromazine).
- mefloquine, used for prevention or treatment of malaria.
- depression treatment medicines called monoamine oxidase inhibitors (except MAO-B inhibitors) such as moclobemide.
- moxisylyte, which is used to treat circulatory problems like Raynaud's syndrome.

Pregnancy and breast-feeding
There is a risk that use of Bisoprolol Krka during pregnancy may harm the baby. 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. He or she will decide whether you can take Bisoprolol Krka during pregnancy.
It is not known whether bisoprolol passes into human breast milk. Therefore, breast-feeding is not recommended during therapy with Bisoprolol Krka.

Children and adolescents
Bisoprolol Krka is not recommended for use in children or adolescents.

Driving and using machines
Your ability to drive or use machinery may be affected depending on how well you tolerate the medicine. Please be especially cautious at the start of treatment, when the dose is increased or the medication is changed, as well as in combination with alcohol.

Bisoprolol Krka contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

3. How to take Bisoprolol Krka

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.
Take the tablet with some water in the morning, with or without food. Do not crush or chew the tablet.
Treatment with Bisoprolol Krka requires regular monitoring by your doctor. This is particularly necessary at the start of treatment and during dose increase, and when you stop treatment.
Treatment with Bisoprolol Krka is usually long-term.

Hypertension and angina pectoris
Adults including the elderly
The dose should be adjusted individually. The usual daily dose is 10 mg bisoprolol.
Depending on how well you respond to the medicine, your doctor may decide to decrease the dose to 5 mg or he may decide to increase it to 20 mg. The dose should not exceed 20 mg in one day.

Stable chronic heart failure
Adults including the elderly
Treatment with bisoprolol must be started at a low dose and increased gradually.
Your doctor will decide how to increase the dose, and this will normally be done in the following way:
- 1.25 mg bisoprolol once daily for one week
- 2.5 mg bisoprolol once daily for one week
- 3.75 mg bisoprolol once daily for one week

- 5 mg bisoprolol once daily for four weeks
- 7.5 mg bisoprolol once daily for four weeks
- 10 mg bisoprolol once daily for maintenance (on-going) therapy.

The maximum recommended daily dose is 10 mg bisoprolol.
Depending on how well you tolerate the medicine, your doctor may also decide to lengthen the time between dose increases. If your condition gets worse or you no longer tolerate the drug, it may be necessary to reduce the dose again or to interrupt treatment. In some patients a maintenance dose lower than 10 mg bisoprolol may be sufficient. Your doctor will tell you what to do. If you have to stop treatment entirely, your doctor will usually advise you to reduce the dose gradually, as otherwise your condition may become worse.

Use in patients with hepatic and /or renal impairment
In patients with mild to moderate impairment of renal or hepatic function no dosage adjustment is normally required.
In patients with severe renal impairment (creatinine clearance < 20 ml/min) and in patients with severe hepatic impairment it is recommended not to exceed a daily dose of 10 mg bisoprolol.

Use in children and adolescents
Bisoprolol Krka is not recommended for use in children.

If you take more Bisoprolol Krka than you should
If you have taken more Bisoprolol Krka than you should, tell your doctor immediately. Your doctor will decide what measures are necessary.
Symptoms of an overdose may include slowed heart rate, severe difficulty in breathing, feeling dizzy, or trembling (due to decreased blood sugar).

If you forget to take Bisoprolol Krka
Do not take a double dose to make up for a forgotten tablet dose. Take your usual dose the next morning.

If you stop taking Bisoprolol Krka
Never stop taking Bisoprolol Krka unless on your doctor's advice. Otherwise your condition could become much worse. Especially in patients with ischemic heart disease treatment should not be stopped abruptly. If you are considering stopping treatment, your doctor will normally advise you to reduce your dose gradually.

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.
To prevent serious reactions, speak to a doctor immediately if a side effect is severe, occurred suddenly or gets worse rapidly. The most serious side effects are related to the heart function:
- slowing of heart rate (may affect up to 1 in 10 people)
- worsening of heart failure (may affect up to 1 in 10 people)
- slow or irregular heartbeat (may affect up to 1 in 100 people)
  If you feel dizzy or weak, or have breathing difficulties please contact your doctor as soon as possible.

Further side effects are listed below according to how frequently they may occur:

Common (may affect up to 1 in 10 people):
- tiredness, feeling weak, dizziness, headache
- feeling of coldness or numbness in hands or feet
- low blood pressure

- stomach or intestine problems such as nausea, vomiting, diarrhoea, or constipation.

Uncommon (may affect up to 1 in 100 people):
- sleep disturbances
- depression
- dizziness when standing up
- breathing problems in patients with asthma or chronic lung disease
- muscle weakness, muscle cramps.

Rare (may affect up to 1 in 1 000 people):
- hearing problems
- allergic runny nose
- reduced tear flow (dry eyes)
- inflammation of the liver which can cause yellowing of the skin or whites of the eyes
- certain blood test results for liver function or fat levels differing from normal
- allergy-like reactions such as itching, flush, rash. You should see your doctor straight away if you experience more severe allergic reactions, which may involve face, neck, tongue, mouth or throat swelling, or difficulty breathing.
- impaired erection
- nightmares, hallucinations
- fainting.

Very rare (may affect up to 1 in 10 000 people):
- irritation and redness of the eye (conjunctivitis)
- hair loss
- appearance or worsening of scaly skin rash (psoriasis); psoriasis-like rash.

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:
HPRA Pharmacovigilance
Website: www.hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Bisoprolol Krka

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 packaging after EXP. The expiry date refers to the last day of that month.

Store in the original package in order to protect from light and moisture.
This medicine does not require any special temperature storage conditions.

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 Bisoprolol Krka contains
- The active substance is bisoprolol fumarate.
  Each film-coated tablet contains 2.5 mg bisoprolol fumarate.
  Each film-coated tablet contains 5 mg bisoprolol fumarate.
  Each film-coated tablet contains 10 mg bisoprolol fumarate.

- The other ingredients are microcrystalline cellulose, sodium starch glycolate type A, povidone K30, colloidal anhydrous silica and magnesium stearate (E470b) in the tablet core and hypromellose 2910, macrogol 400, titanium dioxide (E171), talc, yellow iron oxide (E172) – only for 5 mg and 10 mg film-coated tablets and red iron oxide (E172) – only for 5 mg and 10 mg film-coated tablets in the film coating.
  See section 2 "Bisoprolol Krka contains sodium".

What Bisoprolol Krka looks like and contents of the pack
2.5 mg: White to almost white, oval, slightly biconvex film-coated tablets (tablets), scored on one side (length: 8.3–8.7 mm, width: 5.5 mm, thickness: 2.8–3.6 mm). The tablet can be divided into equal doses.
5 mg: Pale brownish yellow, oval, slightly biconvex film-coated tablets (tablets), scored on one side (length: 8.3–8.7 mm, width: 5.5 mm, thickness: 2.8–3.6 mm). The tablet can be divided into equal doses.
10 mg: Pale brownish yellow, round, slightly biconvex film-coated tablets (tablets) with bevelled edges, scored on one side (diameter: 10.0–10.3 mm, thickness: 2.8–3.6 mm). The tablet can be divided into equal doses.

Blisters (Alu/Alu foil): 10, 20, 28, 30, 50, 56, 60, 84, 90 and 100 tablets in a box.
Not all pack sizes may be marketed.

Marketing Authorisation Holder
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

Manufacturer
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia
TAD Pharma GmbH, Heinz-Lohmann-Straße 5, 27472 Cuxhaven, Germany

This medicine is authorised in the Member States of the European Economic Area under the following names:

Czech Republic, Bulgaria, Estonia, Hungary, Poland, Latvia, Slovenia, Slovakia	Sobycor
Austria, Denmark, Spain, Finland, Ireland, Portugal, Sweden	Bisoprolol Krka
France	BISOPROLOL KRKA
Germany	Bisoprolol TAD
Italy	Bisoprololo Krka
Romania	Sobyc

This leaflet was last revised in