Package leaflet: Information for the patient

Ivabradine Krka 5 mg film-coated tablets
Ivabradine Krka 7.5 mg film-coated tablets
ivabradine

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 Ivabradine Krka is and what it is used for

Ivabradine Krka (ivabradine) is a heart medicine used to treat:
- Symptomatic stable angina pectoris (which causes chest pain) in adult patients whose heart rate is over or equal to 70 beats per minute. It is used in adult patients who do not tolerate or cannot take heart medicines called beta-blockers. It is also used in combination with beta-blockers in adult patients whose condition is not fully controlled with a beta-blocker.
- Chronic heart failure in adult patients whose heart rate is over or equal to 75 beats per minute. It is used in combination with standard therapy, including beta-blocker therapy or when beta-blockers are contraindicated or not tolerated.

About stable angina pectoris (usually referred to as “angina”):
Stable angina is a heart disease which happens when the heart does not receive enough oxygen. The most common symptom of angina is chest pain or discomfort.

About chronic heart failure:
Chronic heart failure is a heart disease which happens when your heart cannot pump enough blood to the rest of your body. The most common symptoms of heart failure are breathlessness, fatigue, tiredness and ankle swelling.

How does Ivabradine Krka work?
The specific heart rate lowering action of ivabradine helps:
- to control and reduce the number of angina attacks by lowering heart’s need for oxygen.
- to improve the heart functioning and vital prognosis in patients with chronic heart failure.

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

Do not take Ivabradine Krka
- if you are allergic to ivabradine or any of the other ingredients of this medicine (listed in section 6);

- if your resting heart rate before treatment is too slow (below 70 beats per minute);
- if you are suffering from cardiogenic shock (a heart condition treated in hospital);
- if you suffer from a heart rhythm disorder (sick sinus syndrome, sino-atrial block, AV-block of 3rd degree);
- if you are having a heart attack;
- if you suffer from very low blood pressure;
- if you suffer from unstable angina (a severe form in which chest pain occurs very frequently and with or without exertion);
- if you have heart failure which has recently become worse;
- if your heart beat is exclusively imposed by your pacemaker;
- if you suffer from severe liver problems;
- if you are already taking medicines for the treatment of fungal infections (such as ketoconazole, itraconazole), macrolide antibiotics (such as josamycin, clarithromycin, telithromycin or erythromycin given orally), medicines to treat HIV infections (such as nelfinavir, ritonavir) or nefazodone (medicine to treat depression) or diltiazem, verapamil (used for high blood pressure or angina pectoris);
- if you are a woman able to have children and not using reliable contraception;
- if you are pregnant or trying to become pregnant;
- if you are breast-feeding.

Warnings and precautions
Talk to your doctor or pharmacist before taking Ivabradine Krka.
- if you suffer from heart rhythm disorders (such as irregular heartbeat, palpitation, increase in chest pain) or sustained atrial fibrillation (a type of irregular heartbeat), or an abnormality of electrocardiogram (ECG) called 'long QT syndrome',
- if you have symptoms such as tiredness, dizziness or shortness of breath (this could mean that your heart is slowing down too much),
- if you suffer from symptoms of atrial fibrillation (pulse rate at rest unusually high (over 110 beats per minute) or irregular, without any apparent reason, making it difficult to measure),
- if you have had a recent stroke (cerebral attack),
- if you suffer from mild to moderate low blood pressure,
- if you suffer from uncontrolled blood pressure, especially after a change in your antihypertensive treatment,
- if you suffer from severe heart failure or heart failure with abnormality of ECG called 'bundle branch block',
- if you suffer from chronic eye retinal disease,
- if you suffer from moderate liver problems,
- if you suffer from severe renal problems.

If any of the above applies to you, talk straight away to your doctor before or while taking Ivabradine Krka.

Children and adolescents
Do not give this medicine to children and adolescents younger than 18 years. Available data are insufficient in this age group.

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

Make sure to tell your doctor if you are taking any of the following medicines, as a dose adjustment of Ivabradine Krka or monitoring should be required:
- fluconazole (an antifungal medicine)
- rifampicin (an antibiotic)
- barbiturates (for difficult sleeping or epilepsy)
- phenytoin (for epilepsy)
- *Hypericum perforatum* or St John's Wort (herbal treatment for depression)

- QT prolonging medicines to treat either heart rhythm disorders or other conditions:
  - quinidine, disopyramide, ibutilide, sotalol, amiodarone (to treat heart rhythm disorders)
  - bepridil (to treat angina pectoris)
  - certain types of medicines to treat anxiety, schizophrenia or other psychoses (such as pimozide, ziprasidone, sertindole)
  - anti-malarial medicines (such as mefloquine or halofantrine)
  - intravenous erythromycin (an antibiotic)
  - pentamidine (an antiparasitic medicine)
  - cisapride (against the gastro-oesophageal reflux)
- Some types of diuretics which may cause decrease in blood potassium level, such as furosemide, hydrochlorothiazide, indapamide (used to treat oedema, high blood pressure).

Ivabradine Krka with food and drink
Avoid grapefruit juice during treatment with Ivabradine Krka.

Pregnancy and breast-feeding
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.
Do not take Ivabradine Krka if you are pregnant or are planning to have a baby (see "Do not take Ivabradine Krka").
If you are pregnant and have taken Ivabradine Krka, talk to your doctor.
Do not take Ivabradine Krka if you are able to become pregnant unless you use reliable contraceptive measures (see "Do not take Ivabradine Krka").
Do not take Ivabradine Krka if you are breast-feeding (see "Do not take Ivabradine Krka"). Talk to your doctor if you are breast-feeding or intending to breast-feed as breastfeeding should be discontinued if you take Ivabradine Krka.

Driving and using machines
Ivabradine Krka may cause temporary luminous visual phenomena (a temporary brightness in the field of vision, see "Possible side effects"). If this happens to you, be careful when driving or using machines at times when there could be sudden changes in light intensity, especially when driving at night.

Ivabradine Krka 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 Ivabradine 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.
Ivabradine Krka should be taken during meals.
Ivabradine Krka 5 mg tablet can be divided into equal doses.

<u>If you are being treated for stable angina pectoris</u>
The starting dose should not exceed one tablet of Ivabradine Krka 5 mg twice daily. If you still have angina symptoms and if you have tolerated the 5 mg twice daily dose well, the dose may be increased. The maintenance dose should not exceed 7.5 mg twice daily. Your doctor will prescribe the right dose for you. The usual dose is one tablet in the morning and one tablet in the evening. In some cases (e.g. if you are aged 75 years or more), your doctor may prescribe half the dose i.e., one half 5 mg tablet of Ivabradine Krka 5 mg (corresponding to 2.5 mg ivabradine) in the morning and one half 5 mg tablet in the evening.

<u>If you are being treated for chronic heart failure</u>

The usual recommended starting dose is one tablet of Ivabradine Krka 5 mg twice daily increasing if necessary to one tablet of Ivabradine Krka 7.5 mg twice daily. Your doctor will decide the right dose for you. The usual dose is one tablet in the morning and one tablet in the evening. In some cases (e.g. if you are aged 75 years or more), your doctor may prescribe half the dose i.e., one half 5 mg tablet of Ivabradine Krka 5 mg (corresponding to 2.5 mg ivabradine) in the morning and one half 5 mg tablet in the evening.

If you take more Ivabradine Krka than you should
A large dose of Ivabradine Krka could make you feel breathless or tired because your heart slows down too much. If this happens, contact your doctor immediately.

If you forget to take Ivabradine Krka
If you forget to take a dose of Ivabradine Krka, take the next dose at the usual time. Do not take a double dose to make up for a forgotten tablet.

If you stop taking Ivabradine Krka
As the treatment for angina or chronic heart failure is usually life-long, you should discuss with your doctor before stopping this medicinal product.
If you think that the effect of Ivabradine Krka is too strong or too weak, talk to your doctor or pharmacist.

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.

The most common adverse reactions with this medicine are dose dependent and related to its mode of action:

Very common (may affect more than 1 in 10 people):
Luminous visual phenomena (brief moments of increased brightness, most often caused by sudden changes in light intensity). They can also be described as a halo, coloured flashes, image decomposition or multiple images. They generally occur within the first two months of treatment after which they may occur repeatedly and resolve during or after treatment.

Common (may affect up to 1 in 10 people):
Modification in the heart functioning (the symptoms are a slowing down of the heart rate). They particularly occur within the first 2 to 3 months of treatment initiation.

Other side effects have also been reported:

Common (may affect up to 1 in 10 people):
Irregular rapid contraction of the heart (atrial fibrillation), abnormal perception of heartbeat (bradycardia, ventricular extrasystoles, AV 1st degree block (ECG prolonged PQ interval), uncontrolled blood pressure, headache, dizziness and blurred vision (cloudy vision).

Uncommon (may affect up to 1 in 100 people):
Palpitations and cardiac extra beats, feeling sick (nausea), constipation, diarrhoea, abdominal pain, spinning sensation (vertigo), difficulty breathing (dyspnoea), muscle spasm, changes in laboratory parameters : high blood levels of uric acid, an excess of eosinophils (a type of white blood cell) and elevated creatinine in blood (a breakdown product of muscle), skin rash, angioedema (such as swollen face, tongue or throat, difficulty in breathing or swallowing), low blood pressure, fainting, feeling of tiredness, feeling of weakness, abnormal ECG heart tracing, double vision, impaired vision.

Rare (may affect up to 1 in 1 000 people):
Urticaria, itching, skin reddening, feeling unwell.

Very rare (may affect up to 1 in 10 000 people):
Irregular heart beats (AV 2nd degree block, AV 3rd degree block, sick sinus syndrome).

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 Ivabradine 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 carton or blister after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special 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 Ivabradine Krka contains
- The active substance is ivabradine.
  Ivabradine Krka 5 mg film-coated tablets:
  Each film-coated tablet contains 5 mg ivabradine (as ivabradine hydrochloride).
  Ivabradine Krka 7.5 mg film-coated tablets:
  Each film-coated tablet contains 7.5 mg ivabradine (as ivabradine hydrochloride).
- The other ingredients (excipients) are maltodextrin, lactose monohydrate, maize starch, colloidal anhydrous silica, magnesium stearate (E470b) and hypromellose 3 cP in the tablet core and hypromellose 6 cP, titanium dioxide (E171), talc, propylene glycol, yellow iron oxide (E172) and red iron oxide (E172) in the film coating. See section 2 "Ivabradine Krka contains lactose".

What Ivabradine Krka looks like and contents of the pack
Ivabradine Krka 5 mg film-coated tablets: Film-coated tablets (tablets) are pale pinkish orange, rectangular, slightly biconvex, with a score line on one side, dimensions 8 mm x 4.5 mm. The tablet can be divided into equal doses.
Ivabradine Krka 7.5 mg film-coated tablets: Film-coated tablets (tablets) are pale pinkish orange, round, slightly biconvex, with bevelled edges, 7 mm in diameter.

Ivabradine Krka is available in boxes containing:
- 14, 28, 56, 98, 112 and 180 film-coated tablets in blisters,
- 14 x 1, 28 x 1, 56 x 1, 98 x 1, 112 x 1 and 180 x 1 film-coated tablet in perforated unit dose blisters.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Belgium, France, Ireland	Ivabradine Krka
Denmark, Sweden	Ivabradin Krka
Spain, Portugal, Italy	Ivabradina Krka
United Kingdom (Northern Ireland)	Ivabradine

This leaflet was last revised in