IVABRADINE 5 mg AND 7.5 mg FILM-COATED TABLETS

Package leaflet: Information for the patient

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 is and what it is used for

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. It usually appears between 40 and 50 years of age. The most common symptom of angina is chest pain or discomfort. Angina is more likely to happen when the heart beats faster in situations such as exercise, emotion, exposure to the cold or after eating. This increase in heart rate can cause the chest pain in people who suffer from angina.

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 work?
Ivabradine mainly works by reducing the heart rate by a few beats per minute. This lowers the heart's need for oxygen especially in the situations when an angina attack is more likely to happen. In this way Ivabradine helps to control and reduce the number of angina attacks.

Furthermore as elevated heart rate adversely affects the heart functioning and vital prognosis in patients with chronic heart failure, the specific heart rate lowering action of ivabradine helps to improve the heart functioning and vital prognosis in these patients.

2 What you need to know before you take Ivabradine

Do not take Ivabradine if:
- you are allergic to ivabradine or any of the other ingredients of this medicine (listed in section 6)
- your resting heart rate before treatment is too slow (below 70 beats per minute)
- you are suffering from cardiogenic shock (a heart condition treated in hospital)
- you suffer from a heart rhythm disorder
- you are having a heart attack
- you suffer from very low blood pressure
- you suffer from unstable angina (a severe form in which chest pain occurs very frequently and with or without exertion)
- you have heart failure which has recently become worse
- your heartbeat is exclusively imposed by your pacemaker
- you suffer from severe liver problems
- 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)
- you are a woman able to have children and not using reliable contraception
- you are pregnant or trying to become pregnant
- you are breast-feeding.

Warnings and precautions
Talk to your doctor or pharmacist before taking Ivabradine 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'
- have symptoms such as tiredness, dizziness or shortness of breath (this could mean that your heart is slowing down too much)
- 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)
- have had a recent stroke (cerebral attack)
- suffer from mild to moderate low blood pressure
- suffer from uncontrolled blood pressure, especially after a change in your antihypertensive treatment
- suffer from severe heart failure or heart failure with abnormality of ECG called 'bundle branch block'
- suffer from chronic eye retinal disease
- suffer from moderate liver problems
- suffer from severe renal problems.

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

Children and adolescents
Ivabradine is not intended for use in children and adolescents younger than 18 years.

Other medicines and Ivabradine
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 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 with food and drink
Avoid grapefruit juice during treatment with Ivabradine.

Pregnancy and breast-feeding
Do **not** take Ivabradine if you are pregnant or are planning to have a baby (see "Do not take Ivabradine").
If you are pregnant and have taken Ivabradine, talk to your doctor.
Do **not** take Ivabradine if you are able to become pregnant unless you use reliable contraceptive measures (see "Do not take Ivabradine").

Do **not** take Ivabradine if you are breast-feeding (see "Do not take Ivabradine").
Talk to your doctor if you are breast-feeding or intending to breast-feed as breast-feeding should be discontinued if you take Ivabradine.

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.

Driving and using machines
Ivabradine 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 contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3 How to take Ivabradine

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 should be taken during meals.

If you are being treated for stable angina pectoris
The starting dose should not exceed one tablet of Ivabradine 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 elderly), your doctor may prescribe half the dose i.e., one half 5 mg tablet of Ivabradine 5 mg (corresponding to 2.5 mg ivabradine) in the morning and one half 5 mg tablet in the evening.

If you are being treated for chronic heart failure
The usual recommended starting dose is one tablet of Ivabradine 5 mg twice daily increasing if necessary to one tablet of Ivabradine 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 elderly), your doctor may prescribe half the dose i.e., one half 5 mg tablet of Ivabradine 5 mg (corresponding to 2.5 mg ivabradine) in the morning and one half 5 mg tablet in the evening.

The 5 mg tablet can be divided into equal doses.

If you take more Ivabradine than you should
A large dose of Ivabradine 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
If you forget to take a dose of Ivabradine, take the next dose at the usual time. Do **not** take a double dose to make up for the forgotten dose.

If you stop taking Ivabradine
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 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, abnormal perception of heartbeat, 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 spasms, 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 heartbeats.

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 the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

5 How to store Ivabradine

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 and 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 contains
- The active substance is ivabradine (as adipate).
  Each 5 mg film-coated tablet contains 5 mg ivabradine (equivalent to 6.56 mg ivabradine adipate).
  Each 7.5 mg film-coated tablet contains 7.5 mg ivabradine (equivalent to 9.84 mg ivabradine adipate).
- The other ingredients in the tablet core are microcrystalline cellulose, croscarmellose sodium, colloidal anhydrous silica, magnesium stearate.
  Film-coating contains hypromellose, macrogol 4000, titanium dioxide (E171), red iron oxide (E172) and yellow iron oxide (E172).

What Ivabradine looks like and contents of the pack
Ivabradine 5 mg tablets are beige to pale-orange oval, biconvex film-coated tablets with breaking score on one side and embossing "5" on other side and are approx. 9 mm x 4.5 mm in size.
Ivabradine 7.5 mg tablets are beige to pale-orange round, biconvex film-coated tablets with embossing "7.5" on one side and are approx. 8 mm in size.

Ivabradine 5 mg tablets are available in PVC/PVdC/Al blister packs of 14, 28, 30, 56, 60, 84, 98, 100, 112 and 120 tablets, perforated unit dose packs of 56x1 tablets and calendar packs of 56 tablets.
Ivabradine 7.5 mg tablets are available in PVC/PVdC/Al blister packs of 28, 30, 56, 60, 84, 98, 100, 112 and 120 tablets, perforated unit dose packs of 56x1 tablets and calendar packs of 56 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
TEVA UK Limited, Eastbourne, BN22 9AG, UK

Manufacturer
TEVA Gyógyszergyár Zrt., Pallagi út 13, Debrecen, H-4042, Hungary

This leaflet was last revised in September 2020

PL 00289/2038
PL 00289/2039

TEVA UK LIMITED