Package leaflet: Information for the user

Tasigna® 150 mg hard capsules
nilotinib

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 Tasigna is and what it is used for

What Tasigna is
Tasigna is a medicine containing an active substance called nilotinib.

What Tasigna is used for
Tasigna is used to treat a type of leukaemia called Philadelphia chromosome positive chronic myeloid leukaemia (Ph-positive CML). CML is a cancer of the blood which makes the body produce too many abnormal white blood cells.

Tasigna is used in adult and paediatric patients with newly diagnosed CML. It is also used in paediatric patients with CML who are no longer benefiting from previous treatment including imatinib or who experienced serious side effects with previous treatment and are not able to continue taking it.

How Tasigna works
In patients with CML, a change in DNA (genetic material) triggers a signal that tells the body to produce abnormal white blood cells. Tasigna blocks this signal, and thus stops the production of these cells.

Monitoring during Tasigna treatment
Regular tests, including blood tests, will be performed during treatment. These tests will monitor:
- the amount of blood cells (white blood cells, red blood cells and platelets) in the body to see how Tasigna is tolerated.
- pancreas and liver function in the body to see how Tasigna is tolerated.
- the electrolytes in the body (potassium, magnesium). These are important in the functioning of the heart.
- the level of sugar and fats in the blood.

The heart rate will also be checked using a machine that measures electrical activity of the heart (a test called an “ECG”).

Your doctor will regularly evaluate your treatment and decide whether you should continue to take Tasigna. If you are told to discontinue this medicine, your doctor will continue to monitor your CML and may tell you to re-start Tasigna if your condition indicates that this is necessary.

If you have any questions about how Tasigna works or why it has been prescribed for you or your child, ask your doctor.

2. What you need to know before you take Tasigna

Follow all the doctor's instructions carefully. They may differ from the general information contained in this leaflet.

Do not take Tasigna
- if you are allergic to nilotinib or any of the other ingredients of this medicine (listed in section 6).

If you think you may be allergic, tell your doctor **before taking Tasigna**.

Warnings and precautions
Talk to your doctor or pharmacist before taking Tasigna:
- if you have suffered prior cardiovascular events such as a heart attack, chest pain (angina), problems with the blood supply to your brain (stroke) or problems with the blood flow to your leg (claudication) or if you have risk factors for cardiovascular disease such as high blood pressure (hypertension), diabetes or problems with the level of fats in your blood (lipid disorders).
- if you have a **heart disorder**, such as an abnormal electrical signal called "prolongation of the QT interval".
- if you are being **treated with medicines** that lower your blood cholesterol (statins), or affect the heart beat (anti-arrhythmics) or the liver (see **Other medicines and Tasigna**).
- if you suffer from lack of potassium or magnesium.
- if you have a liver or pancreas disorder.
- if you have symptoms such as easy bruising, feeling tired or short of breath or have experienced repeated infections.
- if you have had a surgical procedure involving the removal of the entire stomach (total gastrectomy).
- if you have ever had or might now have a hepatitis B infection. This is because Tasigna could cause hepatitis B to become active again, which can be fatal in some cases. Patients will be carefully checked by their doctor for signs of this infection before treatment is started.

If any of these apply to you or your child, tell your doctor.

<u>During treatment with Tasigna</u>
- if you faint (loss of consciousness) or have an irregular heart beat while taking this medicine, **tell your doctor immediately** as this may be a sign of a serious heart condition. Prolongation of the QT interval or an irregular heart beat may lead to sudden death. Uncommon cases of sudden death have been reported in patients taking Tasigna.
- if you have sudden heart palpitations, severe muscle weakness or paralysis, seizures or sudden changes in your thinking or level of alertness, **tell your doctor immediately** as this may be a sign of a fast breakdown of cancer cells called tumour lysis syndrome. Rare cases of tumour lysis syndrome have been reported in patients treated with Tasigna.
- if you develop chest pain or discomfort, numbness or weakness, problems with walking or with your speech, pain, discolouration or a cool feeling in a limb, **tell your doctor immediately** as this may be a sign of a cardiovascular event. Serious cardiovascular events including problems with the blood flow to the leg (peripheral arterial occlusive disease), ischaemic heart disease and problems with the blood supply to the brain (ischaemic cerebrovascular disease) have been reported in patients taking Tasigna. Your doctor should assess the level of fats (lipids) and sugar in your blood before initiating treatment with Tasigna and during treatment.
- if you develop swelling of the feet or hands, generalised swelling or rapid weight gain tell your doctor as these may be signs of severe fluid retention. Uncommon cases of severe fluid retention have been reported in patients treated with Tasigna.

If you are the parent of a child who is being treated with Tasigna, tell the doctor if any of the above

conditions apply to your child.

Children and adolescents
Tasigna is a treatment for children and adolescents with CML. There is no experience with the use of this medicine in children below 2 years of age. There is no experience with the use of Tasigna in newly diagnosed children below 10 years of age and limited experience in patients below 6 years of age who are no longer benefiting from previous treatment for CML. The long-term effects of treating children with Tasigna for long periods of time are not known.

Some children and adolescents taking Tasigna may have slower than normal growth. The doctor will monitor growth at regular visits.

Other medicines and Tasigna
Tasigna may interfere with some other medicines.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes in particular:
- anti-arrhythmics – used to treat irregular heart beat;
- chloroquine, halofantrine, clarithromycin, haloperidol, methadone, moxifloxacin - medicines that may have an unwanted effect on the electrical activity of the heart;
- ketoconazole, itraconazole, voriconazole, clarithromycin, telithromycin – used to treat infections;
- ritonavir – a medicine from the class " antiproteases" used to treat HIV;
- carbamazepine, phenobarbital, phenytoin – used to treat epilepsy;
- rifampicin – used to treat tuberculosis;
- St. John's Wort – a herbal product used to treat depression and other conditions (also known as *Hypericum perforatum*);
- midazolam – used to relieve anxiety before surgery;
- alfentanil and fentanyl – used to treat pain and as a sedative before or during surgery or medical procedures;
- cyclosporine, sirolimus and tacrolimus – medicines that suppress the "self-defence" ability of the body and fight infections and are commonly used to prevent the rejection of transplanted organs such as the liver, heart and kidney;
- dihydroergotamine and ergotamine – used to treat dementia;
- lovastatin, simvastatin – used to treat high level of fats in blood;
- warfarin – used to treat blood coagulation disorders (such as blood clots or thromboses);
- astemizole, terfenadine, cisapride, pimozide, quinidine, bepridil or ergot alkaloids (ergotamine, dihydroergotamine).

These medicines should be avoided during your treatment with Tasigna. If you are taking any of these, your doctor might prescribe other alternative medicines.

If you are taking a statin (a type of medicine to lower your blood cholesterol), talk to your doctor or pharmacist. If used with certain statins, Tasigna may increase the risk of statin-related muscle problems, which on rare occasions can lead to serious muscle breakdown (rhabdomyolysis) resulting in kidney damage.

In addition, tell your doctor or pharmacist before taking Tasigna if you are taking any antacids, which are medicines against heartburn. These medicines need to be taken separately from Tasigna:
- H2 blockers, which decrease the production of acid in the stomach. H2 blockers should be taken approximately 10 hours before and approximately 2 hours after you take Tasigna;
- antacids such as those containing aluminium hydroxide, magnesium hydroxide and simethicone, which neutralise high acidity in the stomach. These antacids should be taken approximately 2 hours before or approximately 2 hours after you take Tasigna.

You should also tell your doctor **if you are already taking Tasigna** and you are prescribed a new medicine that you have not taken previously during Tasigna treatment.

Tasigna with food and drink
Do not take Tasigna with food. Food may enhance the absorption of Tasigna and therefore increase the amount of Tasigna in the blood, possibly to a harmful level. Do not drink grapefruit juice or eat grapefruit. It may increase the amount of Tasigna in the blood, possibly to a harmful level.

Pregnancy and breast-feeding
- **Tasigna is not recommended during pregnancy** unless clearly necessary. If you are pregnant or think that you may be, tell your doctor who will discuss with you whether you can take this medicine during your pregnancy.
- **Women who might get pregnant** are advised to use highly effective contraception during treatment and for up to two weeks after ending treatment.
- **Breast-feeding is not recommended** during treatment with Tasigna and for two weeks after the last dose. Tell your doctor if you are 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.

Driving and using machines
If you experience side effects (such as dizziness or visual disorders) with a potential impact on the ability to safely drive or use any tools or machines after taking this medicine, you should refrain from these activities until the effect has disappeared.

Tasigna contains lactose
This medicine contains lactose (also known as milk sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Tasigna

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much Tasigna to take

Use in adults
- The recommended dose is 600 mg per day. This dose is achieved by taking two hard capsules of 150 mg twice a day.

Use in children and adolescents
- The dose given to your child will depend on your child's body weight and height. The doctor will calculate the correct dose to use and tell you which and how many capsules of Tasigna to give to your child. The total daily dose you give to your child must not exceed 800 mg.

Your doctor may prescribe a lower dose depending on how you respond to treatment.

Older people (age 65 years and over)
Tasigna can be used by people aged 65 years and over at the same dose as for other adults.

When to take Tasigna
Take the hard capsules:
- twice a day (approximately every 12 hours);
- at least 2 hours after any food;
- then wait 1 hour before eating again.

If you have questions about when to take this medicine, talk to your doctor or pharmacist. Taking Tasigna at the same time each day will help you remember when to take your hard capsules.

How to take Tasigna
- Swallow the hard capsules whole with water.
- Do not take any food together with the hard capsules.
- Do not open the hard capsules unless you are unable to swallow them. If so, you may sprinkle the content of each hard capsule in **one** teaspoon of apple sauce and take it immediately. Do not use more than one teaspoon of apple sauce for each hard capsule and do not use any food other than apple sauce.

How long to take Tasigna
Continue taking Tasigna every day for as long as your doctor tells you. This is a long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.
Your doctor may consider discontinuing your treatment with Tasigna based on specific criteria.
If you have questions about how long to take Tasigna, talk to your doctor.

If you take more Tasigna than you should
If you have taken more Tasigna than you should have, or if someone else accidentally takes your hard capsules, contact a doctor or hospital for advice straight away. Show them the pack of hard capsules and this package leaflet. Medical treatment may be necessary.

If you forget to take Tasigna
If you miss a dose, take your next dose as scheduled. Do not take a double dose to make up for a forgotten hard capsule.

If you stop taking Tasigna
Do not stop taking this medicine unless your doctor tells you to do so. Stopping Tasigna without your doctor's recommendation places you at risk for worsening of your disease which could have life-threatening consequences. Be sure to discuss with your doctor, nurse, and/or pharmacist if you are considering stopping Tasigna.

If your doctor recommends that you discontinue treatment with Tasigna
Your doctor will regularly evaluate your treatment with a specific diagnostic test and decide whether you should continue to take this medicine. If you are told to discontinue Tasigna, your doctor will continue to carefully monitor your CML before, during and after you have discontinued Tasigna and may tell you to re-start Tasigna if your condition indicates that this is necessary.

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. Most of the side effects are mild to moderate and will generally disappear after a few days to a few weeks of treatment.

Some side effects could be serious.
These side effects are very common (may affect more than 1 in 10 people), common (may affect up to 1 in 10 people), uncommon (may affect up to 1 in 100 people) or have been reported with frequency not known (cannot be estimated from the available data).
- rapid weight gain, swelling of hands, ankles, feet or face (signs of water retention)
- chest pain or discomfort, high blood pressure, irregular heart rhythm (fast or slow), palpitations (sensation of rapid heartbeat), fainting, blue discolouration of the lips, tongue or skin (signs of heart disorders)
- difficulty or painful breathing, cough, wheezing with or without fever, swelling of the feet or legs (signs of lung disorders)
- fever, easy bruising or unexplained bleeding, frequent infections, unexplained weakness (signs of blood disorders)

- weakness or paralysis of the limbs or face, difficulty speaking, severe headache, seeing, feeling or hearing things that are not there, loss of consciousness, confusion, disorientation, trembling, sensation of tingling, pain or numbness in fingers and toes (signs of nervous system disorders)
- difficulty and pain when passing urine, abnormal urine colour (signs of kidney or urinary tract disorders)
- visual disturbances including blurred vision, perceived flashes of light, loss of vision, blood in eye, eye pain, redness, itching or irritation, dry eye, swelling or itching of the eyelids (signs of eye disorders)
- abdominal pain, nausea, vomiting of blood, bloody stools, constipation, heartburn, stomach acid reflux, swollen abdomen (signs of gastrointestinal disorders)
- severe upper (middle or left) abdominal pain (sign of pancreatitis)
- yellow skin and eyes, nausea, loss of appetite, dark-coloured urine (signs of liver disorders)
- painful red lumps, skin pain, skin reddening, peeling or blisters (signs of skin disorders)
- pain in joints and muscles (signs of musculoskeletal pain)
- excessive thirst, high urine output, increased appetite with weight loss, tiredness (signs of high level of sugar in the blood)
- severe headache often accompanied by nausea, vomiting and sensitivity to light (signs of migraine)
- dizziness or spinning sensation (signs of vertigo)
- nausea, shortness of breath, irregular heartbeat, clouding of urine, tiredness and/or joint discomfort associated with abnormal results of blood tests (such as high levels of potassium, uric acid and phosphorous and low levels of calcium)
- pain, discomfort, weakness or cramping in the leg muscles, which may be due to decreased blood flow, ulcers on the legs or arms that heal slowly or not at all and noticeable changes in colour (blueness or paleness) or temperature (coolness) of the legs or arms, as these symptoms could be signs of artery blockage in the affected limb (leg or arm) and digits (toes or fingers)
- recurrence (reactivation) of hepatitis B infection when you have had hepatitis B in the past (a liver infection).

Some side effects are very common (may affect more than 1 in 10 people)
- headache
- tiredness
- muscle pain
- itching, rash
- nausea
- hair loss
- musculoskeletal pain, muscle pain, pain in extremity, pain in joints, bone pain and spinal pain upon discontinuing treatment with Tasigna
- slowing of growth in children and adolescents

Some side effects are common (may affect up to 1 in 10 people)
- diarrhoea, vomiting, abdominal pain, stomach discomfort after meals, flatulence, swelling or bloating of the abdomen, constipation
- bone pain, pain in joints, muscle spasms, muscle weakness, pain in extremity, back pain, pain or discomfort in the side of the body
- upper respiratory tract infections
- dry skin, acne, wart, decreased skin sensitivity
- loss of appetite, disturbed sense of taste, weight increase
- insomnia, anxiety, depression
- night sweats, excessive sweating

Some side effects are uncommon (may affect up to 1 in 100 people)
- generally feeling unwell
- painful and swollen joints (gout)
- inability to achieve or maintain an erection
- feeling body temperature change (including feeling hot, feeling cold)

- sensitive teeth

The following other side effects have been reported with frequency not known (cannot be estimated from the available data):
- allergy (hypersensitivity to Tasigna)
- memory loss, disturbed or depressed mood, lack of energy
- oral thrush
- skin cyst, thinning or thickening of the skin, thickening of the outermost layer of the skin, skin discolouration, hives, fungal infection of the feet
- thickened patches of red/silver skin (signs of psoriasis)
- increased skin sensitivity
- bleeding, tender or enlarged gums
- nose bleed
- dry mouth, sore throat, mouth sores
- frequent urine output
- haemorrhoids, anal abscess
- enterocolitis (inflammation of the bowel)
- herpes virus infection
- feeling of hardening in the breasts, heavy periods, nipple swelling
- appetite disorder, weight decreased
- breast enlargement in men
- symptoms of restless legs syndrome (an irresistable urge to move a part of the body, usually the leg, accompanied by uncomfortable sensations)
- paralysis of any muscle of the face

During Tasigna treatment, you may also have some **abnormal blood test results** such as:
- low level of blood cells (white cells, red cells, platelets) or haemoglobin
- increase in the number of platelets or white cells, or specific types of white cells (eosinophils) in the blood
- high blood level of lipase or amylase (pancreas function)
- high blood level of bilirubin or liver enzymes (liver function)
- low or high blood level of insulin (a hormone regulating blood sugar level)
- low or high level of sugar, or high level of fats (including cholesterol) in the blood
- high blood level of parathyroid hormone (a hormone regulating calcium and phosphorus level)
- change in blood proteins (low level of globulins or presence of paraprotein)
- high blood level of alkaline phosphatase
- high blood level of potassium, calcium, phosphorus or uric acid
- low blood level of potassium or calcium

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 at 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 Tasigna

- 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. The expiry date refers to the last day of that month.
- Do not store above 30°C.
- Store in the original package in order to protect from moisture.
- Do not use this medicine if you notice that the pack is damaged or shows signs of tampering.
- 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 Tasigna contains
- The active substance is nilotinib. Each hard capsule contains 150 mg nilotinib (as hydrochloride monohydrate).
- The other ingredients are lactose monohydrate, crospovidone type A, poloxamer 188, colloidal anhydrous silica, magnesium stearate. The hard capsule shell is composed of gelatin, titanium dioxide (E171), red and yellow iron oxide (E172) and, shellac, black iron oxide (E172), n-butyl alcohol, propylene glycol, dehydrated ethanol, isopropylalcohol and ammoniumhydroxide for stamping of the imprint.

What Tasigna looks like and contents of the pack
Tasigna is supplied as hard capsules. The hard capsules are red. A black imprint is stamped on each hard capsule ("NVR/BCR").

Tasigna is available in packs containing 28 or 40 hard capsules and in multipacks of 112 hard capsules (comprising 4 cartons, each containing 28 hard capsules), 120 hard capsules (comprising 3 cartons, each containing 40 hard capsules) or 392 hard capsules (comprising 14 cartons, each containing 28 hard capsules).

Not all packs may be marketed in your country.

Marketing Authorisation Holder
Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

Manufacturer
Lek d.d., PE PROIZVODNJA LENDAVA
Trimlini 2D
Lendava, 9220
Slovenia

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

United Kingdom
Novartis Pharmaceuticals UK Ltd.
Tel: +44 1276 698370

This leaflet was last revised in November 2020.

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/. There are also links to other websites about rare diseases and treatments.