NOVARTIS

Tasigna® (nilotinib hydrochloride)

150 mg and 200 mg, capsule

Patient Information Leaflet

Document status: Final

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SCHEDULING STATUS **S4**

TASIGNA® 200 mg capsule

TASIGNA® 150 mg capsule

Nilotinib

Contains sugar:

156,11 mg of lactose (TASIGNA 200 mg capsule)

117,08 mg of lactose (TASIGNA 150 mg capsule)

Read all of this leaflet carefully before you start using TASIGNA®

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- TASIGNA has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What TASIGNA is and what it is used for

2. What you need to know before you use TASIGNA

3. How to use TASIGNA

4. Possible side effects

5. How to store TASIGNA

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1. WHAT TASIGNA IS AND WHAT IT IS USED FOR

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

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

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 (hypersensitive) to nilotinib or any of the other ingredients of (see "What TASIGNA contains").

If you think you may be allergic, tell your doctor without taking TASIGNA.

Take special care with TASIGNA:

- If you have had prior cardiovascular events such as a heart attack, chest pain (angina), problems with your brain blood supply (stroke), or problems with your leg blood flow (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) or if you are a smoker.

- 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 affect the heartbeat (antidysrhythmics) or the liver (see “Taking other medicines with TASIGNA”)
- if you suffer from a low level of potassium or magnesium in your blood
- if you have been treated with a medicine of the type called anthracyclines (frequently used in leukaemia therapy)
- if you have a liver disorder
- if you have had pancreatitis (inflamed pancreas)
- 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 during treatment with TASIGNA, hepatitis B may become active again. Your doctor will check for signs of this infection before treatment with TASIGNA is started.

During treatment with TASIGNA

TASIGNA should not be used as first line therapy in patients with prior severe peripheral arterial occlusive disease (PAOD). Call your doctor right away or as soon as possible if you faint (loss of consciousness) or have an irregular pulse while taking TASIGNA as these may be due to a serious heart condition.

Call your doctor right away or as soon as possible if you develop chest pain or discomfort, numbness or weakness or problems with gait or speech, or pain, numbness, discoloration or a cool feeling in a limb.

Call your doctor right away or as soon as possible if you develop fever, skin rash, joint pain and inflammation as well as tiredness, loss of appetite, nausea, jaundice (yellowing of the skin), stomach pain, pale stools and dark urine (potential signs of hepatitis B reactivation).

If any of these apply to you, tell your doctor before taking TASIGNA.

Children and adolescents (below the age of 18 years):

There is no experience with the use of TASIGNA in children and adolescents and hence should not be used by these patients.

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.

Other medicines and TASIGNA:

Always tell your healthcare professional if you are taking any other medicine.

(This includes complementary or traditional medicines.)

TASIGNA may interfere with some other medicines.

If you are taking other medicines on a regular basis, including complementary or traditional medicines, the use of TASIGNA with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare profession for advice.

Tell your doctor or pharmacist before taking TASIGNA if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This includes in particular:

- antidysrhythmics - used to treat irregular heartbeat;
- chloroquine, halofantrine, clarithromycin, haloperidol, methadone, moxifloxacin – medicines that may have an unwanted effect on the function of the heart.
- ketoconazole, itraconazole, voriconazole, clarithromycin, telithromycin - used to treat fungal and bacterial infections;
- ritonavir - an anti-HIV medicine from the class protease inhibitors;
- carbamazepine, phenobarbital, phenytoin - used to treat epilepsy;
- rifampicin - used to treat tuberculosis;
- St. John's Wort - a herbal product used to treat depression (also known as *Hypericum perforatum*);
- midazolam - used to relieve anxiety;
- warfarin - used to treat blood coagulation disorders (such as blood clots or thromboses)
- alfentanil and fentanyl - used to treat pain and used as a sedative before or during surgery or medical procedure;
- ciclosporin, sirolimus and tacrolimus - medicines that suppress the "self-defence" ability of the body and fight infections - commonly used to prevent the rejection of transplanted organs such as liver, heart and kidney;
- dihydroergotamine and ergotamine – used to treat migraine;
- lovastatin, simvastatin – used to treat high level of fats in blood.

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

In addition, tell your doctor or pharmacist before taking TASIGNA if you are taking antacids (medicines against heartburn). These medications need to be taken separately from TASIGNA:

- H_2 blockers decrease the production of acids in the stomach – 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 neutralise the high acidity of the stomach – 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 you have not taken previously during TASIGNA treatment.

Taking TASIGNA with food and drink:

Do not take TASIGNA with food.

Take the capsules at least two hours after any food and then wait at least one hour before eating again.

Do not drink grapefruit juice or eat grapefruit while on TASIGNA. It may increase the amount of TASIGNA in the blood, possibly to a harmful level.

Pregnancy, breastfeeding and fertility:

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby while taking TASIGNA, please consult your doctor, pharmacist or other health care professional for advice before taking this medicine.

- TASIGNA should not be used in women in their fertile years unless adequate contraceptive measures are taken.

- Women of child-bearing potential or sexually active men must use effective birth control while taking TASIGNA and for up to two weeks after ending treatment.
- Breastfeeding is not recommended during treatment with TASIGNA. Tell your doctor if you are breastfeeding.

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 TASIGNA, you should refrain from these activities.

It is not always possible to predict to what extent TASIGNA may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which TASIGNA affects them.

TASIGNA contains lactose:

- TASIGNA contains lactose (milk sugar). If you know that you have intolerance to lactose or severe lactase deficiency or galactosaemia, tell your doctor before taking TASIGNA.

3. HOW TO TAKE TASIGNA

Always take TASIGNA exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Do not share medicines prescribed for you with others.

Your doctor will tell you how long your treatment with TASIGNA will last. Do not stop treatment early. If you have the impression that the effect of TASIGNA is too strong or too weak, tell your doctor or pharmacist.

Monitoring your TASIGNA treatment:

You will have regular tests including blood tests during treatment. These will monitor the amount of blood cells (white blood cells, red blood cells and platelets) in your body to see how TASIGNA is tolerated. Blood tests will also monitor the electrolytes in your body (potassium, magnesium); these are important in the functioning of your heart. Your heart will be checked using a machine that measures electrical activity of the heart (a test called “ECG”). Blood test will also monitor the level of sugar and fats (cholesterol) in your blood.

Your doctor may also consider prescribing uric acid lowering medicines for you if necessary.

Your doctor may consider discontinuing your treatment with TASIGNA based on specific criteria.

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

How much TASIGNA to take:

The starting dose is 2 capsules twice a day of either 150 mg or 200 mg depending on your exact condition. Always take TASIGNA exactly as your doctor has told you.

When to take TASIGNA:

Take the capsules twice a day (approximately every 12 hours), at least 2 hours after any food. Then wait for at least 1 hour before eating again.

If you have questions about when to take TASIGNA, talk to your doctor or pharmacist.

Taking TASIGNA at the same time each day will help you remember when to take your capsules.

How to take TASIGNA:

Do not take any food together with the capsules.

Swallow the capsules whole with water.

If you are unable to swallow the capsules, disperse the contents of each capsule in one teaspoon of applesauce (pureed apple) and take immediately. Not more than one teaspoon of applesauce and no food other than applesauce must be used.

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 capsules, contact a doctor or the hospital for advice straight away. Show them the pack of capsules.

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 the forgotten capsules.

If you stop taking TASIGNA:

Do not stop taking TASIGNA unless your doctor tells you to. If you have any further questions on the use of TASIGNA, ask your doctor or pharmacist.

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 TASIGNA. 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.

4. POSSIBLE SIDE EFFECTS

TASIGNA can cause side effects

Not all side-effects reported for TASIGNA are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while taking TASIGNA, please consult your doctor, pharmacist or other health care professional for advice.

Some side effects can be serious:

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- rapid weight gain, swelling of hands, ankles, feet or face;
- chest pain or discomfort, high blood pressure, irregular heart rhythm;
- difficulty breathing, cough, wheezing with or without fever, swelling of the feet or legs;
- fever, sore throat, mouth sores, weakness, bruising, frequent infections;
- weakness or paralysis of limbs or face, difficulty speaking, severe headache, seeing, feeling or hearing things that are not there;
- thirst, dry skin, irritability, dark urine, decreased urine output;

- blurred vision, loss of vision, visible bleeding in white of eye;
- swelling and pain in one part of the body;
- abdominal pain, nausea, vomiting of blood, black stools, constipation, swollen abdomen;
- yellow skin and eyes, nausea, loss of appetite, light-coloured urine;
- rash, painful red lumps, pain in joints and muscles;
- excessive thirst, high urine output, increased appetite with weight loss, tiredness;
- nausea, shortness of breath, irregular heartbeat, clouding of urine, tiredness and/or joint discomfort;
- pain or discomfort, weakness, or cramping in leg muscles which may be due to decreased blood flow, ulcers that heal slowly or not at all, and noticeable changes in colour (blueness or paleness) or in temperature (coolness) as these symptoms could be signs of artery blockage in the affected limb (leg or arm) and digits (toes and fingers);
- numbness, pain, discomfort, coldness in your legs and feet that usually appear during walking or exercise (signs of artery blockage in the legs);
- reactivation of hepatitis B infection when you have had hepatitis B (an infection of the liver) in the past;
- pain resulting from not enough blood flowing to the heart (angina pectoria);
- compression of the heart by an accumulation of fluid in the pericardial sac (cardiac tamponade).

If you get any of these, tell your doctor straight away.

Frequent side effects

- nausea, constipation, diarrhoea;
- headache;
- tiredness;
- itching, rash;
- low level of white blood cells, red blood cells or platelets and high level of lipase in the blood (changes in blood test results);
- vomiting, abdominal pain, stomach discomfort after meals, flatulence bloating of the stomach;
- bone pain, pain in joints, muscle spasms, muscle pain;
- skin reddening, dry skin;
- weight decrease or increase;
- hair loss;
- insomnia (sleeplessness);
- night sweats, excessive sweating, hot flushes;
- dizziness, generally feeling unwell, spinning sensation;
- tingling or numbness;
- voice disorder (weak or hoarse voice);
- abnormal liver function test and other changes in blood test results such as high level of potassium or low level of magnesium;
- palpitations (sensation of rapid heartbeat);
- anxiety;
- disturbed sense of taste.

If any of these affect you severely, tell your doctor.

Less frequent side effects

- decreased or increased skin sensitivity;
- eye irritation, swelling, discharge, itching or redness, dry eye (signs of eye disorders);
- dry mouth;
- heartburn, swelling or bloating of the abdomen;
- breast pain;
- nose bleed;
- decrease or increase appetite;
- difficulty and pain when passing urine, exaggerated sense of needing to urinate;
- inability to achieve or maintain an erection;
- breast enlargement in men;
- flu-like symptoms;
- trembling;
- decreased sharpness of vision;
- frequent urine output;
- abnormal kidney function test results;
- sensitivity to light;
- fast heartbeat, bulging eyes, swelling at front of the neck;
- depression;
- feeling body temperature change (including feeling hot, feeling cold;)
- sensitivity of teeth.

During TASIGNA treatment, you may also have some abnormal blood test results such as low level of blood cells (white cells, red cells, platelets), high blood level of lipase or amylase

(pancreas function), high blood level of bilirubin (liver function), high blood level of creatinine (kidney function), high level of potassium or low level of magnesium, low or high level of sugar, high level of fats in the blood.

If any of these affect you tell your doctor.

The following other side effects have also been reported

- confusion, disorientation;
- sensation of numbness or tingling in fingers and toes;
- increased sensitivity of the eyes or the skin to light;
- eye pain or redness, pain, swelling, and itching of the eyelids;
- thickened patches of red/silver skin (signs of psoriasis);
- difficulty hearing, ear pain;
- joint stiffness, muscle weakness;
- unconsciousness;
- blood in urine;
- weight gain, tiredness, hair loss, muscle weakness, feeling cold.

If any of these affect you tell your doctor.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under

SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of TASIGNA.

5. HOW TO STORE TASIGNA

Keep out of the reach and sight of children.

Do not use TASIGNA after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

Store at or below 30 °C.

Store in the original package in order to protect from moisture.

Do not use any pack that is damaged or shows signs of tampering.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What TASIGNA contains:

The active substance is nilotinib.

Each capsule contains either 200 mg or 150 mg nilotinib.

The other ingredients are lactose, crospovidone, poloxamer 188, colloidal silicon dioxide and magnesium stearate. The capsule shell is composed of gelatin, titanium dioxide, iron oxide yellow and iron oxide red as well as a printing ink.

What TASIGNA looks like and contents of the pack:

TASIGNA® 200 mg capsule: White to yellowish powder, in light yellow capsules with red imprint "NVR/TKI" on each capsule.

TASIGNA® 150 mg capsule: White to yellowish powder, in red capsules with a black imprint "NVR/BCR" on each capsule.

TASIGNA comes in packs of 28 or 112 capsules in colourless, transparent PVC/PVDC (polyvinylchloride/polyvinylidene chloride) blisters with an aluminium foil backing. The blisters are packed into cardboard cartons.

Not all pack sizes may be available.

Holder of Certificate of Registration:

NOVARTIS SOUTH AFRICA (PTY) LTD

Magwa Crescent West

Jukskei View

Waterfall City

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Registration numbers:

TASIGNA® 200 mg capsule: 41/26/0973

TASIGNA® 150 mg capsule: 45/26/0410

Tasigna® 150 mg	
Namibia: 14/26/0068	NS2
Botswana: BOT 1502708	S2
Tasigna® 200 mg	
Namibia: 12/26/0030	NS2
Botswana: BOT 1502707	S2