

Applicant/PHRC: **Hetero Drugs South Africa (Pty) Ltd**

Product proprietary name: **TILOMIA 150 and 200**

Dosage form and strength: **Capsules and 150 mg & 200 mg**

Patient information Leaflet for TILOMIA 150 and 200 capsules

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

TILOMIA 150 capsules

TILOMIA 200 capsules

Nilotinib

Sugar free.

Read all of this leaflet carefully before you start taking TILOMIA.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor, pharmacist, nurse or healthcare provider.
- TILOMIA 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 TILOMIA is and what it is used for
2. What you need to know before you take TILOMIA
3. How to take TILOMIA
4. Possible side effects
5. How to store TILOMIA
6. Contents of the pack and other information.

1. What TILOMIA is and what it is used for

TILOMIA is a medicine containing an active substance called nilotinib. TILOMIA is used to treat a type of leukaemia called Philadelphia chromosome positive chronic myelogenous leukaemia (Ph+ CML). CML is a cancer of the blood which makes the body produce too many abnormal white blood cells. TILOMIA is used in adult patients with newly diagnosed CML or in patients with CML who are no longer benefiting from previous treatment including imatinib. It is also used in adult 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 TILOMIA

Do not take TILOMIA:

- if you are hypersensitive (allergic) to nilotinib or any of the other ingredients of TILOMIA (see section 6 for other ingredients).

Warnings and precautions

Take special care with TILOMIA:

TILOMIA may cause disturbances in your ECG. Your potassium or magnesium levels should be monitored regularly by your health care provider. While taking TILOMIA you should avoid medicines known to cause disturbances in ECG. Special care to be taken in patients with loss of liver function. Obtain ECGs at baseline, seven days after initiation, and periodically thereafter, as well as following any dose adjustments.

- if you have symptoms such as easy bruising, feeling tired or short of breath or have experienced repeated infections.

- if you have a heart disorder, such as an abnormal electrical signal called “prolongation of the QT interval”.
- if you suffer from lack of potassium or magnesium.
- if you are being treated with medicines that affect the heart beat (anti-dysrhythmics) (see Other medicines and TILOMIA).
- 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 TILOMIA.
- if you experience an unexpected, rapid increase in body mass.
- 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 ever had or might now have a hepatitis B infection. This is because TILOMIA could cause hepatitis B to become active again, which can be fatal in some cases. You will be carefully checked by your doctor for signs of this infection before treatment with TILOMIA is started.
- if you have diabetes. Your doctor should assess the level of sugar in your blood before initiating treatment with TILOMIA and during treatment.
- if you have a liver or pancreas disorder.
- if you have had a surgical procedure involving the removal of your entire stomach (total gastrectomy).
- 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 nilotinib, as in TILOMIA.

Other medicines and TILOMIA:

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes in particular:

- ketoconazole, itraconazole, voriconazole (used to treat certain fungal infections)
- ritonavir (used to treat HIV infection (AIDS))
- clarithromycin, telithromycin, moxifloxacin (used to treat certain bacterial infections)
- rifampicin (used to treat tuberculosis (TB))
- phenytoin, carbamazepine, phenobarbital (used to treat epilepsy)
- St John's wort (a herbal remedy, used to treat depression and other conditions (also known as *Hypericum perforatum*))
- amiodarone, dysopyramide, procainamide, quinidine, sotalol (antidysrhythmics, used to treat irregular heart beat)
- chloroquine, halofantrine (used to prevent and treat malaria)
- haloperidol (used to treat psychotic disorders like schizophrenia)
- methadone (used to treat addiction to opioids)

If you are taking any of these, your doctor might prescribe other alternative medicines.

PRODUCT NAME] with food, drink and alcohol:

- Do not take TILOMIA with food.

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- Take TILOMIA 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 TILOMIA. It may increase the amount of nilotinib in your 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, please consult your doctor, pharmacist or other health care provider for advice before taking TILOMIA.

TILOMIA is not recommended during pregnancy unless clearly necessary. If you are a woman of childbearing potential, you are advised to use highly effective contraception during TILOMIA treatment and for up to two weeks after ending treatment.

Breastfeeding is not recommended during treatment with TILOMIA and for two weeks after the last dose. Tell your doctor if you are breastfeeding.

Sexually active male or female patients taking TILOMIA should use adequate contraception.

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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 TILOMIA, you should refrain from these activities until the effect has disappeared.

3. How to take TILOMIA

Do not share medicines prescribed for you with any other person. Always take TILOMIA exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

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

How much TILOMIA to take:

The starting dose is 2 capsules twice a day, either 300 mg (2 x 150 mg capsules) or 400 mg (2 x 200 mg capsules) twice a day, depending on your exact condition.

Always take TILOMIA exactly as your doctor has told you.

When to take TILOMIA:

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.

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

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

How to take TILOMIA:

- 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 TILOMIA than you should:

In the event of overdose, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre. Always take the labelled medicine package with you, whether there are any TILOMIA capsules left or not.

If you forget to take TILOMIA:

If you forget to take a dose, take it as soon as you remember. Do not take a double dose to make up for forgotten individual doses.

If you stop taking TILOMIA:

Do not stop taking TILOMIA unless your doctor tells you to. Should you need to stop taking TILOMIA, your doctor will decide which is the best method for you.

If you have any further questions on the use of TILOMIA, ask your doctor or pharmacist.

4. Possible side effects

TILOMIA can have side effects.

Not all side effects reported for TILOMIA are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking TILOMIA, please consult your doctor, pharmacist or other health care provider for advice.

If any of the following happens, stop taking TILOMIA and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

These are all very serious side effects. If you have them, you may have had a serious reaction to TILOMIA. You may need urgent medical attention or hospitalisation.

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 (signs of water retention)
- chest pain or discomfort, high or low 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 breathing 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, severe or 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, changes in eyesight, loss of consciousness, confusion, disorientation, trembling, sensation of tingling, pain or numbness in fingers and toes (signs of nervous system disorders)
- thirst, dry skin, irritability, dark urine, decreased urine output, difficulty and pain when urinating, exaggerated sense of needing to urinate, blood in urine, abnormal urine colour (signs of kidney or urinary tract disorders)
- visual disturbances including blurred vision, double-vision or perceived flashes of light, decreased sharpness or loss of vision, blood in eye, increased sensitivity of the eyes to light, eye pain, redness, itching or irritation, dry eye, swelling or itching of the eyelids (signs of eye disorders)
- swelling and pain in one part of the body (signs of clotting within a vein)
- abdominal pain, nausea, vomiting of blood, black or 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)
- fast heartbeat, bulging eyes, weight loss, swelling at the front of the neck (signs of overactive thyroid gland)
- weight gain, tiredness, hair loss, muscle weakness, feeling cold (signs of underactive thyroid gland)
- 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).

These are all serious side effects. You may need urgent medical attention.

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Tell your doctor if you notice any of the following:

Frequent side effects:

- diarrhoea
- headache
- tiredness, lack of energy
- muscle pain
- itching, rash
- nausea (feeling sick)
- stomach pain
- constipation
- vomiting (being sick)
- hair loss (temporary)
- musculoskeletal pain, muscle pain, pain in extremity, pain in joints, bone pain and spinal pain upon discontinuing treatment with TILOMIA
- upper respiratory tract infections
- stomach discomfort after meals, flatulence, swelling or bloating of the abdomen
- bone pain, pain in joints, muscle spasms, muscle weakness
- pain including back pain, neck pain and pain in extremity, pain or discomfort in the side of the body
- dry skin, acne, wart, decreased skin sensitivity, hives
- loss of appetite, disturbed sense of taste, weight decrease or increase
- insomnia, depression, anxiety
- night sweats, excessive sweating
- generally feeling unwell
- voice disorder

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- nose bleed
- frequent urine output

Less frequent side effects:

- increased skin sensitivity (hyperaesthesia)
- dry mouth, sore throat, mouth sores
- breast pain
- painful and swollen joints (gout)
- increased appetite
- attention disorder
- inability to achieve or maintain an erection
- breast enlargement in men
- flu-like symptoms
- pneumonia, bronchitis
- urinary tract infection
- herpes virus infection
- oral or vaginal thrush
- muscle and joint stiffness, joint swelling
- feeling body temperature change (including feeling hot, feeling cold)
- sensitive teeth

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Side effects with an unknown frequency:

- memory loss, disturbed mood
- skin cyst, thinning or thickening of the skin, thickening of the outermost layer of the skin, skin discolouration, fungal infection of the feet, thickened patches of red/silver skin (signs of psoriasis)
- bleeding, tender or enlarged gums
- oral warts
- reddening and/or swelling and possibly peeling on the palms and soles (so called hand-foot syndrome)
- increased sensitivity of the skin to light
- difficulty hearing, ear pain, noises (ringing) in the ears
- joint inflammation
- urinary incontinence
- enterocolitis (inflammation of the bowel)
- haemorrhoids, anal abscess
- feeling of hardening in the breasts, heavy periods, nipple swelling
- symptoms of restless legs syndrome (an irresistible urge to move a part of the body, usually the leg, accompanied by uncomfortable sensations).

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 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 TILOMIA.

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5. How to store TILOMIA

- Store at or below 25 °C. Protect from light and moisture.
- Keep capsules in original container until required for use.
- STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
- Do not use after the expiry date printed on the carton.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What TILOMIA contains:

The active substance is nilotinib.

Other ingredients are dibasic calcium phosphate dihydrate, povidone, colloidal silicon dioxide, magnesium stearate, iron oxide red (E172) (only for TILOMIA 150), iron oxide yellow (E172), sodium laurilsulfate, titanium dioxide (E171), gelatine.

What TILOMIA looks like and contents of the pack:

TILOMIA 150: Opaque red cap and opaque red body size '1' hard gelatine capsules imprinted with 'H' on cap and '23' on body, filled with slightly yellow to yellowish granular powder.

TILOMIA 200: Opaque yellow cap and yellow body size '0' hard gelatine capsules imprinted with 'H' on cap and '24' on body, filled with slightly yellow to yellowish granular powder.

Round, white opaque HDPE 60 mL container, closed with a child resistant plastic cap with a pulp liner, containing a 2 gram silica gel desiccant.

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Pack size: 28 capsules.

Aluminium/aluminium blister strips of cold PVC/aluminium/OPA forming foil and plain aluminium lidding foil, containing 6 or 10 capsules per blister strip.

Pack sizes: 36 (6 blister strips containing 6 capsules) or 60 (6 blister strips containing 10 capsules).

Holder of Certificate of Registration:

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This leaflet was last revised in

Registration number

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