

APPROVED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

TINSUNEB 12,5 capsules

Sunitinib malate

Contains sugar alcohol: mannitol 57,669 per capsule

TINSUNEB 25 capsules

Sunitinib malate

Contains sugar alcohol mannitol 115,338 per capsule

TINSUNEB 50 capsules

Sunitinib malate

Contains sugar alcohol: mannitol 230,675 per capsule

Read all of this leaflet carefully before you start taking TINSUNEB

- 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.
- TINSUNEB 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 TINSUNEB is and what it is used for
2. What you need to know before you take TINSUNEB
3. How to take TINSUNEB

4. Possible side effects
5. How to store TINSUNEB
6. Contents of the pack and other information

1. What TINSUNEB is and what it is used for

The active substance is sunitinib.

Sunitinib belongs to a group of medicines called Cytostatic Agents. They are used for treatment of cancer by preventing the activity of a special group of proteins which are known to be involved in the growth and spread of cancer cells.

TINSUNEB is used to treat adults with the following types of cancer:

- Gastrointestinal stromal tumour (GIST), a type of cancer of the stomach and bowel, where imatinib (another anticancer medicine) no longer works or you cannot take imatinib.
- Metastatic renal cell carcinoma (MRCC), a type of kidney cancer that has spread to other parts of the body.
- Pancreatic neuroendocrine tumours (pNET) (tumours of the hormone-producing cells in the pancreas) that have progressed or cannot be removed with surgery.

2. What you need to know before you take TINSUNEB:

TINSUNEB should not be administered you:

- if you are hypersensitive (allergic) to sunitinib or to any other ingredient of TINSUNEB (listed in section 6).

- if you are pregnant or breastfeeding your baby (see **Pregnancy and Breastfeeding**).

Warnings and precautions

Special care should be taken with TINSUNEB:

- as you may experience skin discolouration while taking TINSUNEB, other skin effects may include dryness, thickness or cracking of the skin, blisters or occasional rash on the palms of the hands and soles of the feet
- you may experience mouth pain or/and taste disturbance when taking TINSUNEB
- if you develop skin or mouth lesions that have a pink-red centre surrounded by a pale ring border and an outer pink-red ring [erythema multiforme (EM)] and Stevens-Johnson syndrome (SJS) as sunitinib should be discontinued
- if you have a history of internal bleeding or develop internal bleeding such as bleeding in the stomach, respiratory or urinary track
- if you are taking blood thinning medicine such as warfarin or acenocoumarole
- if you have solid tumours as you may develop nose bleeding
- if you experience nausea, diarrhoea, stomatitis, dyspepsia and vomiting as it may indicate gastrointestinal complications
- if you experience stomach pains, fever, rapid pulse accompanied by nausea and vomiting as it may indicate the inflammation of your pancreas
- if you have or have had liver problems, usual signs are itching, yellow eyes or skin, dark urine, and pain or discomfort in the right upper

stomach area, your doctor will do blood tests to check this before and during treatment

- if you have blood cell disorders, symptoms of which may be feeling fatigued, shortness of breath, trouble concentrating muscle weakness and fast heartbeat, your doctor will do a blood test before and during treatment
- if you have a history of heart attacks or develop symptoms such as you tiredness, shortness of breath, or swollen feet and ankles. These may be symptoms of heart problems that may include heart failure and heart muscle problems
- if you have high blood pressure as TINSUNEB may aggravate the condition
- if you have aneurysms (enlargement and weakening of a blood vessel wall), symptoms of which are feeling or being sick, a stiff neck or neck pain, sensitivity to light, blurred or double vision, sudden confusion, loss of consciousness, fits (seizures), weakness on 1 side of the body or on any limbs.
- if you have been diagnosed with thyroid disease (growth or swelling in your neck) or develop symptoms such as anxiety, irritability, nervousness, weight loss, having weak muscles and tremors. Your thyroid function should be checked before you take TINSUNEB and regularly while you are taking it.
- if you have or have had seizures and reversible posterior leukoencephalopathy syndrome (abnormal changes in the brain that can cause a collection of symptoms including headache, confusion,

seizures, and vision loss). Tell your doctor as soon as possible if you have high blood pressure, headache, or loss of sight

- if you have recently had surgery as TINSUNEB may slow down the process of wound healing
- if you have or have had pain in the mouth, teeth and/or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or loosening of a tooth, tell your doctor and dentist, should you need to undergo an invasive dental treatment or dental surgery, tell your dentist that you are being treated with especially if you are taking medicines used to prevent bone complications called intravenous bisphosphonates, that may have been given for another medical condition
- if you have or have had tumours as taking TINSUNEB as may cause a condition called Tumour Lysis syndrome (when a large number of cancer cells die within a short period, releasing their contents in to the blood)
- if you develop a severe bacterial infection on your skin accompanied by blisters, fever, fatigue and pain
- if you have or have had damage to the smallest blood vessels known as thrombotic microangiopathy (TMA). Tell your doctor if you develop fever, fatigue, tiredness, bruising, bleeding, swelling, confusion, vision loss, and seizures
- if you have diabetes, tell your doctor as soon as possible if you experience any signs and symptoms of low blood sugar (fatigue, palpitations, sweating, hunger and loss of consciousness)

- if you have renal dysfunction, where you pass too little or too much urine than normal or diagnosed with proteinuria
- if you develop sores or ulcers in your stomach (Fistula), inform your doctor if you experience pain in your stomach
- if you develop swelling underneath the skin (angioedema) and serious infections
- if you have or have had Hepatitis B (symptoms such as fever, chills, weakness, confusion, vomiting and jaundice), as TINSUNEB may reactivate the virus infection
- if you are taking other anti-cancer medicines such as TINSUNEB.

Children and adolescents

The efficacy and safety has not been studied in children under 18 years of age has not been established.

Other medicines and TINSUNEB

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

TINSUNEB may interact with:

- ketoconazole, itraconazole – used to treat fungal infections, as it increases the blood concentration of TINSUNEB
- ritonavir –used to treat HIV, as they may decrease the blood concentration of TINSUNEB
- erythromycin, clarithromycin, rifampicin –used to treat infections, as they may change the concentration of TINSUNEB of your blood

- dexamethasone – a corticosteroid used for various conditions (such as allergic/breathing disorders or skin diseases), as they may decrease the blood concentration of TINSUNEB
- phenytoin, carbamazepine, phenobarbital – used to treat epilepsy and other neurological conditions, as they may decrease the blood concentration of TINSUNEB
- herbal preparations containing St. John's Wort (*Hypericum perforatum*) – used to treat depression and anxiety, they may decrease the blood concentration of TINSUNEB

Pregnancy and breastfeeding:

If you are pregnant or breastfeeding, think that you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before you are given this medicine. This medicine may harm a baby developing in the womb. If you are sexually active, women are advised to use effective birth control to prevent pregnancy during treatment and for 6 months after treatment discontinuation. Men are advised not to father a child during and up to 3 months following treatment with TINSUNEB-sunitinib. Sexually active men who take TINSUNEB- sunitinib, are advised to use a condom to avoid pregnancy in their partner

If you would like to father a child during the treatment or in the 3 months following treatment, seek advice from your doctor or pharmacist. You may want to seek counselling on sperm storage before starting your therapy.

Do not take TINSUNEB if you are breast feeding your baby.

Driving and using machines:

It is not always possible to predict to what extent TINSUNEB 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 TINSUNEB affects them.

3. How to take TINSUNEB

Do not share medicines prescribed for you with any other person.

Dosage:

Always take this medicine exactly as your doctor or pharmacist has told you.

Check with your doctor if you are not sure.

Your doctor will prescribe a dose that is right for you, depending on the type of cancer to be treated.

If you are being treated for:

- GIST or MRCC: the usual dose is 50 mg once daily taken for 28 days (4 weeks), followed by 14 days (2 weeks) of rest (no medicine), in 6-week cycles.
- pNET: the usual dose is 37,5 mg once daily without a rest period.

Your doctor will determine the appropriate dose you need to take, as well as if and when you need to stop treatment with TINSUNEB.

TINSUNEB is for oral use and can be taken with or without food.

If you take more TINSUNEB than you should:

In the event of over dosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take TINSUNEB

Do not take a double dose to make up for forgotten individual doses

4. Possible side effects

TINSUNEB can have side effects.

Not all side effects reported for TINSUNEB are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving TINSUNEB, please consult your doctor, pharmacist or any other healthcare professional for advice.

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

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

These are very serious side effects. If you have them, you may have had a serious allergic reaction to TINSUNEB. 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:

- tiredness, shortness of breath, or swollen feet and ankles. These may be symptoms of heart problems that may include heart failure and heart muscle problems (cardiomyopathy).

- cough, chest pain, sudden onset of shortness of breath, or coughing up blood. These may be symptoms of a condition called pulmonary embolism that occurs when blood clots travel to your lungs.
- altered frequency or absence of urination which may be symptoms of kidney failure.
- intestinal bleeding problem, painful, swollen stomach (abdomen); vomiting blood; black, sticky stools
- blood in your urine

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

Tell your doctor if you notice any of the following:

Frequent:

- infection, chills, fever above 100,4 degrees Celsius and sweating which may be an indication of reduction in the number of platelets, red blood cells and/or white blood cells (leukopenia)
- Respiratory infections, such as infections in the breathing passages and lungs
- a collection of pus in any part of the body
- development of diseases caused by a fungus (yeast or mold)
- shortness of breath
- high blood pressure
- extreme tiredness, loss of strength
- irritation or mouth pain, mouth sores, mouth dryness, taste disturbances, upset stomach, nausea, vomiting, diarrhoea, constipation, abdominal pain/swelling, loss/decrease of appetite
- decreased activity of thyroid gland (hypothyroidism)

- headache
- dizziness
- nose bleeding
- back pain, joint pain, pain in arms and legs
- yellow skin/skin discoloration, excess pigmentation of the skin, hair colour change, rash on the palms of the hands and soles of the feet, rash, dryness of the skin
- cough
- fever, chills, weakness, confusion
- difficulty in falling asleep
- blood clots in the blood vessels
- deficiency of blood supply to the heart muscle, due to obstruction or constriction of the coronary arteries (heart attack)
- chest pain
- decrease in the amount of blood pumped by the heart
- fluid retention including around the lungs
- infections
- complication of severe infection (infection is present in the bloodstream) that can lead to tissue damage, organ failure, and death
- decreased blood sugar level
- loss of protein in the urine sometimes resulting in swelling
- influenza-like illness
- abnormal blood tests including pancreatic and liver enzymes
- haemorrhoids, pain in the rectum, gingival bleeding, difficulty in swallowing or inability to swallow

- burning or painful sensation in the tongue, inflammation of the digestive tract lining, excessive gas in the stomach or intestine
- Weight loss
- Musculoskeletal pain (pain in muscles and bones), muscular weakness, muscular fatigue, muscle pain, muscle spasms
- Nasal dryness, congested nose
- Excessive tear flow
- Abnormal sensation of the skin, itching, flaking and inflammation of the skin, blisters, acne, nail discolouration, hair loss
- Abnormal sensations in extremities
- Abnormally decreased/increased sensitivity, particularly to touch
- Acid heartburn
- Dehydration
- Abnormally coloured urine
- Depression
- Chills.

Less frequent:

- Life-threatening infection of the soft tissue including the ano-genital region
- Stroke
- Heart attack caused by an interrupted or decreased blood supply to the heart
- Changes in the electrical activity or abnormal rhythm of the heart
- Liver failure
- Pain in the stomach (abdomen) caused by inflammation of the pancreas
- Tumour destruction leading to hole in the intestine (perforation).

- Inflammation (swelling and redness) of the gallbladder with or without associated gallstones
- Abnormal tube like passage from one normal body cavity to another body cavity or the skin
- Pain in the mouth, teeth and/or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or loosening of a tooth. These could be signs and symptoms of bone damage in the jaw (osteonecrosis)
- Overproduction of thyroid hormones which increases the amount of energy the body uses at rest
- Increased blood level of enzyme (creatine phosphokinase) from muscle.
- Excessive reaction to an allergen including hay fever, skin rash, itchy skin, hives, swelling of body parts, and trouble breathing
- Inflammation of the colon (colitis, colitis ischaemic)
- Severe reaction of the skin and/or mucous membranes (Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme)
- Tumour lysis syndrome (TLS) – TLS consists of a group of metabolic complications that can occur during treatment of cancer. These complications are caused by the break-down products of dying cancer cells and may include the following: nausea, shortness of breath, irregular heartbeat, muscular cramps, seizure, clouding of urine and tiredness associated with abnormal laboratory test results (high potassium, uric acid and phosphorous levels and low calcium levels in the blood) that can lead to changes in kidney function and acute renal failure.

- Abnormal muscle breakdown which can lead to kidney problems (rhabdomyolysis)
- Painful skin ulceration (pyoderma gangrenosum)
- Inflammation of the liver (hepatitis)
- Inflammation of the thyroid gland
- Damage to the smallest blood vessels known as thrombotic microangiopathy (TMA)
- An enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections).

If any of the side effects become serious, or if you notice any side-effects not listed 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 TINSUNEB.

5. How to store TINSUNEB

Store all medicines out of reach of children.

Store at or below 25 °C in the original container.

Do not refrigerate.

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

6. Contents of the pack and other information

The active substance is sunitinib.

TINSUNEB 12,5:

Each capsule contains sunitinib malate equivalent to sunitinib 12,5 mg

Contains sugar alcohol: mannitol 57,669 per capsule

TINSUNEB 25: Each capsule contains sunitinib malate equivalent to sunitinib

25 mg

Contains sugar alcohol: mannitol 115,338 per capsule

TINSUNEB 50: Each capsule contains sunitinib malate equivalent to sunitinib

50 mg

Contains sugar alcohol: mannitol 230,675 per capsule

What TINSUNEB looks like and contents of the pack

Hard gelatin capsules

TINSUNEB 12,5:

Hard gelatin capsule with opaque reddish brown cap and opaque reddish brown body, self lock capsule, imprinted with 'RM53' on cap and 'RM53' on body in white ink, containing yellow to orange coloured powder.

TINSUNEB 25:

Hard gelatin capsule with opaque caramel cap and opaque reddish brown body, self lock capsule, imprinted with 'RM54' on cap and 'RM54' on body in white ink, containing yellow to orange coloured powder.

TINSUNEB 50:

Hard gelatin capsule with opaque caramel cap and opaque caramel body, self lock capsule, imprinted with 'RM56' on cap and 'RM56' on body in white ink, containing yellow to orange coloured powder.

Holder of Certificate of Registration

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South Africa

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