1.3.2 Proposed Patient Information Leaflet (clean copy)

SCHEDULING STATUS

S4

EUROSTIB 200 mg Film-coated tablet

Sorafenib (as tosylate)

Sugar free

Read all of this leaflet carefully before you are given EUROSTIB

- 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.
- EUROSTIB 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 EUROSTIB is and what it is used for

EUROSTIB belongs to a group of medicine called Cytostatic Agents.

EUROSTIB is used to treat liver cancer (hepatocellular carcinoma).

EUROSTIB is also used to treat kidney cancer (advanced renal cell carcinoma) at an advanced

stage when standard therapy has not helped to stop your disease or is considered unsuitable.

EUROSTIB is used to treat thyroid cancer (differentiated thyroid carcinoma).

EUROSTIB is a so-called multikinase inhibitor. It works by slowing down the rate of growth of cancer cells and cutting off the blood supply that keeps cancer cells growing.

2. What you need to know before you take EUROSTIB

Do not take EUROSTIB

- if you are hypersensitive (allergic) to sorafenib or to any of the other ingredients of EUROSTIB (listed in section 6).
- if you are pregnant, planning to become pregnant or are breastfeeding.

Warnings and precautions

Talk to your doctor or pharmacist before taking EUROSTIB.

Take special care with EUROSTIB

- if you experience skin problems, as EUROSTIB can cause rashes and skin reactions, especially on the hands and feet. These can usually be treated by your doctor. If not, your doctor may interrupt treatment or stop it altogether.
- if you have high blood pressure. EUROSTIB can raise blood pressure, and your doctor will usually monitor your blood pressure and may give you a medicine to treat your high blood pressure.
- if you have or have had an aneurysm (enlargement and weakening of a blood vessel wall) or a tear in a blood vessel wall.
- if you have diabetes. Blood sugar levels in diabetic patients should be checked regularly in order to assess if anti-diabetic medicine’s dosage needs to be adjusted to minimize the risk of low blood sugar.
- if you get any bleeding problems, or are taking warfarin or phenprocoumon. Treatment with EUROSTIB may lead to a higher risk of bleeding. If you are taking warfarin or phenprocoumon, medicines which thin the blood to prevent blood clots, there may be a greater risk of bleeding.

- if you get chest pain or heart problems. Your doctor may decide to interrupt treatment or stop it altogether.
- if you have a heart disorder, such as an abnormal electrical signal called "prolongation of the QT interval".
- if you are going to have surgery, or if you had an operation recently. EUROSTIB might affect the way your wounds heal. You will usually be taken off EUROSTIB if you are having an operation. Your doctor will decide when to start with EUROSTIB again.
- if you are taking irinotecan or are given docetaxel, which are also medicines for cancer. EUROSTIB may increase the effects and, in particular, the side effects of these medicines.
- if you are taking Neomycin or other antibiotics. The effect of EUROSTIB may be decreased.
- if you have severe liver impairment. You may experience more severe side effects when taking this medicine.
- if you have poor kidney function. Your doctor will monitor your fluid and electrolyte balance.
- EUROSTIB may reduce fertility in both men and women. If you are concerned, talk to a doctor.
- holes in the gut wall (gastrointestinal perforation) may occur during treatment (see section 4: Possible Side Effects). In this case your doctor will interrupt the treatment.
- if you have thyroid cancer. Your doctor will monitor blood calcium and thyroid hormone levels.

Children

The safety and effectiveness of EUROSTIB in children has not been established.

Other medicines and EUROSTIB

Always tell your health care provider if you are taking any other medicine.

(This includes all complementary or traditional medicines.)

Some medicines may affect EUROSTIB, or be affected by it. Tell your doctor or pharmacist if you are taking, have recently taken or might take anything in this list or any other medicines, including medicines obtained without a prescription:

- rifampicin, neomycin or other medicines used to treat infections (called antibiotics).
- St John's wort, a herbal treatment for depression.
- phenytoin, carbamazepine or phenobarbitone, treatments for epilepsy and other conditions.
- dexamethasone, a corticosteroid used for various conditions.
- warfarin or phenprocoumon, anticoagulants used to prevent blood clots.
- doxorubicin, capecitabine, docetaxel, paclitaxel and irinotecan, which are cancer treatments.
- digoxin, a treatment for mild to moderate heart failure.

EUROSTIB with food and drink

EUROSTIB can be taken with or without food.

Pregnancy and breastfeeding

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 this medicine. Avoid becoming pregnant while being treated with EUROSTIB, and use adequate contraception during treatment. If you become pregnant while being treated with EUROSTIB, immediately tell your doctor who will decide if the treatment should be continued.

You should not breastfeed your child during treatment with EUROSTIB, as it may interfere with the growth and development of your baby.

Driving and using machines

The development of damage to the nerves outside of the brain and spinal cord (peripheral nerves), often causes weakness, numbness and pain, usually in your hands and feet (also known as peripheral sensory neuropathy) as a result of treatment with EUROSTIB, may affect your ability to drive and to operate machinery.

There is no evidence that treatment with EUROSTIB will affect your daily activities.

It is not always possible to predict to what extent EUROSTIB may interfere with your daily activities.

You should ensure that you do not engage in activities requiring mental alertness, judgment and/or sound coordination and vision e.g. driving, riding, flying, sailing or operating machines/equipment

until you are aware of the measure to which EUROSTIB affects you.

3. How to take EUROSTIB

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

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

The usual dose is 2 x 200 mg tablets, twice daily.

This is equivalent to a daily dose of 800 mg or four tablets a day.

Swallow the EUROSTIB tablets whole with a glass of water, either without food or with a low-fat or moderate fat meal. Do not take this medicine with high fat meals, as this may make EUROSTIB less effective. If you intend to have a high fat meal, take the tablets at least 1 hour before or 2 hours after the meal.

Your doctor will tell you how long your treatment with EUROSTIB will last. You will usually keep taking this medicine as long as you are getting clinical benefits, and not suffering unacceptable side effects. Your doctor may also lower your dose in certain instances depending on your specific cancer or side effects.

Do not stop treatment early because your condition may worsen.

If you have the impression that the effect of EUROSTIB is too strong or too weak, tell your doctor or pharmacist.

If you take use more EUROSTIB than you should

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

Taking too much EUROSTIB makes side effects more likely or more severe, especially diarrhoea and skin reactions. Your doctor may tell you to stop taking this medicine.

If you missed a dose of EUROSTIB

If you have missed a dose, take it as soon as you remember. If it is nearly time for the next dose, forget about the missed one and carry on as normal. Do not take a double dose to make up for forgotten individual doses.

If you stop taking EUROSTIB

You are being given EUROSTIB for the treatment of cancer. You must not stop your treatment with EUROSTIB without discussing it with your doctor.

4. Possible side effects

EUROSTIB can have side effects.

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

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

- sever rash,
- itching,
- shortness of breath,
- swelling of the swelling of the lower layer of skin and tissue just under the skin or mucous membranes (also known as angioedema).

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

- chest pain, tightness in the chest, difficulty breathing, abnormal heart beats, changes in the way your heart beats, sweating and/or anxiety. These are all signs of a heart attack or a serious heart condition.
- abdominal pain and tenderness, caused by a ruptured bowel (a hole in the wall of the oesophagus, stomach, small- and large intestines (also known as gastrointestinal perforation).
- jaundice.
- excessive bleeding.

- dizziness and headache (caused by high blood pressure).

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

Tell your doctor if you notice any of the following:

Frequent side effects:

- diarrhoea.
- feeling weak or tired (fatigue).
- hair loss (alopecia).
- infections.
- flushed or painful palms or soles (hand foot skin reaction).
- inflammation of hair follicles (folliculitis).
- abnormally high levels of protein in the urine (proteinuria), decrease in the number of white blood cells (leucopoenia and neutropenia), decrease in the number of red blood cells (anaemia), low number of platelets in the blood (thrombocytopenia).
- underactive thyroid gland (hypothyroidism).
- loss of appetite (anorexia).
- low calcium levels in the blood (hypocalcaemia).
- low potassium levels in the blood (hypokalaemia).
- low blood sugar level (hypoglycaemia).
- low sodium levels in the blood (hyponatraemia).
- low phosphate levels in the blood (hypophosphataemia).
- depression.
- distortion of the sense of taste (dysgeusia).
- disturbed sensations in fingers and toes, including tingling or numbness (peripheral sensory neuropathy).
- ringing sound in the ears (tinnitus).
- heart attack (myocardial infarction) or chest pain related to heart failure.

- redness in the face and often other areas of the skin (flushing).
- bleeding (including bleeding in the brain, gut wall and respiratory tract; haemorrhage).
- high blood pressure, or increases in blood pressure (hypertension).
- altered voice (dysphonia).
- runny nose (rhinorrhoea).
- constipation.
- diarrhoea.
- indigestion (dyspepsia).
- difficulty swallowing (dysphagia)
- heartburn (gastro oesophageal reflux disease).
- nausea and vomiting.
- inflamed or dry mouth, tongue pain (stomatitis and mucosal inflammation).
- acne.
- inflamed, dry or scaly skin that sheds (dermatitis, skin desquamation).
- a thickening of the outer layer of the skin (hyperkeratosis).
- joint pain (arthralgia), muscle pain (myalgia) and muscle spasms.
- abnormally high levels of protein in the urine (proteinuria).
- kidney failure (renal failure).
- erection problems (erectile dysfunction).
- general weakness or loss of strength (asthenia).
- fever.
- pain (including mouth pain, abdominal pain, headache, bone pain, tumour pain).
- flu-like illness.
- weight loss.

Less frequent side effects:

- a sudden, severe allergic reaction (anaphylactic reaction).
- allergic reaction with swelling of the skin (e. g. face, tongue) that may cause difficulty in breathing or swallowing (angioedema).
- allergic like reactions (including skin reactions and hives).
- overactive thyroid gland (hyperthyroidism).
- dehydration.
- reversible swelling in the rear part of the brain that can be associated with headache, altered consciousness, fits and visual symptoms including visual loss (reversible posterior leukoencephalopathy).
- abnormal heart rhythm (QT prolongation).
- sudden (life threatening) increased in blood pressure (hypertensive crisis).
- breathing difficulty (lung disease).
- inflamed stomach lining (gastritis).
- holes in the gut wall (gastrointestinal perforation).
- pain in the tummy (abdomen) caused by pancreatitis, inflammation of the gall bladder and/or bile ducts.
- inflammation of the liver, which may lead to nausea, vomiting, abdominal pain, and jaundice (medicine induced hepatitis).
- eczema (patches of inflamed, itchy, red, cracked, and rough skin).
- multiple skin eruptions (erythema multiforme).
- inflammation of the vessels in the skin which may result in rash (leucocytoclastic vasculitis).
- a sunburn-like rash that may occur on skin that has previously been exposed to radiotherapy and can be severe (radiation recall dermatitis).
- serious reactions of the skin and/or mucous membranes which may include painful blisters and fever, including extensive detachment of the skin (Stevens-Johnson syndrome and

toxic epidermal necrolysis).

- abnormal muscle breakdown which can lead to kidney problems (rhabdomyolysis).
- damage of the kidney causing them to leak large amounts of protein (nephrotic syndrome).
- enlarged breasts (gynaecomastia).
- changes in the clotting time and clotting factors in your blood.

Side effects of unknown frequency:

- impaired brain function that can be associated with e.g. drowsiness, behavioural changes, or confusion (encephalopathy).
- an enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections).

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 or nurse. This includes any possible side effects not listed in this leaflet. 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 EUROSTIB.

5. How to store EUROSTIB

Store all medicines out of reach of children.

- Store at or below 25 °C.
- 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 EUROSTIB contains

The active substance is sorafenib (as tosylate).

The other ingredients are croscarmellose sodium, hypromellose HPMC 2910, macrogol (E1521), magnesium stearate (E470b), microcrystalline cellulose (E460), sodium laurilsulfate, red iron oxide (E172), titanium dioxide (E171).

What EUROSTIB looks like and contents of the pack

Film-coated tablet.

Red-brown, round, biconvex film-coated tablets, debossed with “200” on one side and plain on the other side.

Holder of Certificate of Registration

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2144

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