Applicant: Aurogen SA (Pty) Ltd
Product Name: CANCALID 2,5 mg/5 mg/7,5 mg/10 mg/15 mg/20 mg/ 25 mg
Dosage form and strength: Each capsule contains 2,5 mg/ 5 mg/ 7,5 mg/10 mg/ 15 mg/20 mg/25 mg

MODULE 1
1.3.2

1.32 Approved Patient Information Leaflet

SCHEDULING STATUS

S4

CANCALID 2,5 mg capsules

CANCALID 5 mg capsules

CANCALID 7,5 mg capsules

CANCALID 10 mg capsules

CANCALID 15 mg capsules

CANCALID 20 mg capsules

CANCALID 25 mg capsules

(Lenalidomide)

(Contains Sugar: lactose anhydrous)

Read all of this leaflet carefully before you take CANCALID

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist, nurse or other health care provider.
- CANCALID 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.

WARNING: SEVERE LIFE-THREATENING HUMAN BIRTH DEFECTS.

Lenalidomide, the active ingredient contained in CANCALID, is structurally related to thalidomide, a substance that causes severe life-threatening birth defects. Lenalidomide showed malformations in monkeys, similar to those described with thalidomide. If CANCALID is taken during pregnancy, the same effect can be expected in humans.

BECAUSE OF THIS TOXIC EFFECT AND IN AN EFFORT TO MAKE THE CHANCE OF EXPOSURE DURING PREGNANCY TO CANCALID AS SMALL AS POSSIBLE, CANCALID IS APPROVED FOR USE UNDER A SPECIAL RESTRICTED DISTRIBUTION PROGRAMME. THIS PROGRAMME IS CALLED THE KEY ASSIST RISK MANAGEMENT PROGRAM.

What is in this leaflet:

1. What CANCALID is and what it is used for

CANCALID belongs to a group of medicines called immunomodulatory medicines, which can modify or regulate the functioning of the immune system.

- CANCALID in combination with dexamethasone is used to treat adult patients who have been diagnosed with multiple myeloma. Multiple myeloma is a type of blood cancer that affects the white blood cells that produce antibodies.
- CANCALID is also used to treat adult patients who have been diagnosed with myelodysplastic syndromes. Patients with myelodysplastic syndromes have an abnormality of their bone marrow, which means they don't make enough healthy blood cells.

2. What you need to know before you take CANCALID

Your doctor will have enrolled you in the KEY ASSIST RISK MANAGEMENT PROGRAM to ensure that CANCALID is used safely.

Do not take CANCALID:

- if you are allergic (hypersensitive) to lenalidomide or any of the other ingredients of CANCALID listed in the following Section: 'What CANCALID contains. If you think you may be allergic, ask your doctor for advice.
- if you are pregnant or think you may be pregnant or are planning to become pregnant, **as CANCALID is harmful to an unborn child.**
- if you are able to become pregnant, unless you follow all the necessary measures to prevent you from becoming pregnant. If you are able to become pregnant, your doctor will record with each prescription that the necessary measures have been taken and will provide you with this

confirmation.

If any of these apply to you, tell your doctor before you take CANCALID.

Warnings and precautions

Take special care/ Special care should be taken with CANCALID:

For women taking CANCALID

Before starting the treatment, you should ask your doctor if you are able to become pregnant, even if you think this is unlikely.

If you are able to become pregnant

- you will have pregnancy tests under the supervision of your doctor (before treatment, every 4 weeks during treatment, and 4 weeks after the treatment has finished) except in the case of confirmed tubal sterilisation.
- and you must use two effective methods of contraception for 4 weeks before starting treatment, during treatment including dose interruptions and until 4 weeks after stopping treatment. Your doctor will advise you on appropriate methods of contraception.

For men taking CANCALID

CANCALID passes into human semen. If your female partner is pregnant or able to become pregnant, and she doesn't use effective methods of contraception, you must use condoms during treatment including dose interruptions and for 4 weeks after the end of treatment (even if you have undergone vasectomy).

Male patients taking CANCALID should not donate sperm or semen during treatment including dose interruptions and for 4 weeks following the end of treatment.

All patients

Before starting the treatment you should tell your doctor if you had blood clots in the past. During the treatment with CANCALID you have an increased risk of developing blood clots in the veins and arteries.

If you have Myelodysplastic syndromes, which are a group of disorders caused by blood cells that are poorly formed or don't work properly, you may be more likely to get a more advanced condition called acute myeloid leukaemia (AML). In addition, it is not known how CANCALID affects the chances of you getting AML. Your doctor may therefore do tests to check for signs which may better predict the likelihood of you getting AML during your treatment with CANCALID.

Before and during the treatment with CANCALID you will have regular blood tests as CANCALID may cause a fall in the blood cells that help fight infection and help the blood to clot. Your doctor may ask you to have a blood test:

- before treatment
- every week for the first 8 weeks of treatment
- at least every month after that.

Your doctor may adjust your dose of CANCALID or stop your treatment based on the results of your blood tests and on your general condition.

Before you start treatment you should tell your doctor if you

- have kidney disease. Your doctor may adjust your dose of CANCALID based on this information.

- have any signs of an infection, such as a cough or fever.
- have or have ever had previous viral infection, particularly hepatitis B infection, varicella zona, HIV. If you are in doubt, talk to your doctor. Treatment with CANCALID may cause the virus to become active again, in patients who carry the virus, resulting in a recurrence of the infection. Your doctor should check whether you have ever had hepatitis B infection.
- have had a heart attack, have ever had a blood clot, or if you smoke, have high blood pressure or high cholesterol levels.
- have heart or lung disease, as treatment with CANCALID may cause life threatening high blood pressure of the arteries in your lungs and heart. Your doctor will evaluate you before and during treatment for any signs and symptoms of heart or lung disease.
- have had an allergic reaction whilst taking thalidomide (another medicine used to treat multiple myeloma) such as rash, itching, swelling, dizziness or trouble breathing.
- have experienced in the past a combination of any of the following symptoms: rash on face or extended rash, red skin, high fever, flu-like symptoms, enlarged lymph nodes (signs of severe skin reaction called drug reaction with eosinophilia and Systemic Symptoms (DRESS) (see “Possible side effects”).

Your doctor may check if you have a high total amount of tumours throughout the body, including your bone marrow. This could lead to a condition where the tumours break down and cause unusual levels of chemicals in the blood which can lead to kidney failure (this condition is called ‘Tumour Lysis Syndrome’).

Your doctor may check you for changes to your skin such as red spots or rashes.

Your doctor may adjust your dose of CANCALID or stop your treatment based on the results of your blood tests and on your general condition. If you are newly diagnosed, your doctor may also assess your treatment based on your age and other conditions you already have.
You should not donate blood during treatment including dose interruptions and for 4 weeks after the end of treatment.

Your doctor may check your thyroid and it's functioning as CANCALID can have an effect on this.

CANCALID affects the nerves, which can cause numb, tingling or painful hands or feet. You may find it hard to fasten buttons or do other fiddly tasks.

Tell your doctor if you have these symptoms. They sometimes need to lower the dose of the drug. CANCALID may cause clouding of the vision (cataract), it is important to tell your doctor is you have any visual disturbances.

You should never give CANCALID to another person. Return any unused capsules to your pharmacist at the end of treatment.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before being given this medicine.

Children and adolescents

CANCALID has not been studied in children or adolescents and therefore should not be used in this patient population.

Other medicine and CANCALID:

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

The use of CANCALID with these medicines may cause undesirable interactions.

In particular tell your doctor if you are using medicines containing the following active substances:

- Warfarin (medicine to prevent blood clotting);
- Digoxin (medicine used to treat heart problems);
- Medicines that stimulate the production of red blood cells, or other agents that may increase the risk of blood clots (thrombosis), such as hormone replacement therapy;
- Statins (medicines used to treat high cholesterol).

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 healthcare provider for advice before taking this medicine.

Pregnancy:

You must not take CANCALID if you are pregnant, as it is expected to be harmful for an unborn baby. In addition, you must not become pregnant while taking CANCALID. Therefore you must use two effective methods of contraception if you are a woman of

childbearing potential.

If you do become pregnant during the treatment with CANCALID, you must stop the treatment and inform your doctor immediately.

For men taking CANCALID, please see section: 'Warnings and precautions'. If your partner becomes pregnant whilst you are taking CANCALID, you should inform your doctor immediately. It is recommended that your partner seeks medical advice.

Breastfeeding:

You should not breastfeed when taking CANCALID.

Driving and using machines

Do not drive or operate machines if you experience side effects, such as dizziness, tiredness, sleepiness or blurred vision.

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

CANCALID contains sugar

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking CANCALID.

3. How to take CANCALID

Do not share medicines prescribed for you with any other person. Always take CANCALID exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

CANCALID is taken alone or in combination with dexamethasone. Always take CANCALID alone or CANCALID and dexamethasone in combination exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. You should refer to the package leaflet for dexamethasone for further information on its use and effects.

The usual dose for Myelodysplastic Syndromes is: 10 mg given orally once a day on days 1-21 of repeating 28-day treatment cycles.

The usual dose for Multiple Myeloma is: 25 mg/day orally on Days 1-21 of repeated 28-day cycles for multiple myeloma. The recommended dose of dexamethasone is 40 mg/day on Days 1-4, 9-12, and 17-20 of each 28-day cycle for the first 4 cycles of therapy and then 40 mg/day orally on Days 1-4 every 28 days.

Your doctor will prescribe the correct dose for your condition.

Your doctor may adjust your dose of CANCALID or stop your treatment based on the results of your blood tests and on your general condition.

You should swallow the CANCALID capsules whole, preferably with water, once a day. Do not break, open or chew the capsules. The CANCALID capsules can be taken either with or without food.

You should take CANCALID at about the same time each day.

Your doctor will tell you how long your treatment with CANCALID will last. Do not stop any treatment unless your doctor tells you to do so.

CANCALID is taken in treatment cycles, each cycle lasting 28 days. You should continue the cycles of treatment until your doctor tells you to stop.

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

If you take more CANCALID than you should

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

If you forget to take CANCALID

If less than 12 hours has elapsed since missing a dose, you can take the dose. If more than 12 hours has elapsed since missing a dose at the normal time, you should not take the dose, but take the next dose at the normal time on the following day.

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

4. Possible side effects

CANCALID can have side effects.

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

CANCALID may reduce the number of white blood cells that fight infection and also the blood cells which help the blood to clot (platelets). CANCALID may also cause blood clots in the veins (thrombosis).

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

- Swelling around the eyes or face or tongue, (which may rarely be a serious allergic reaction)
- Rash which spreads with loss of skin
- Swelling in the ankles, wrists, arms and legs
- Any fever, chills, sore throat, cough, mouth ulcers or any other symptoms of infection;
- Any bleeding or bruising in the absence of injury;
- Any chest or leg pain;
- Wheezing, any shortness of breath, dry cough

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

It is important to note that patients with multiple myeloma may develop additional types of cancer, and it is possible that this risk may be increased with CANCALID treatment, therefore your doctor should carefully evaluate the benefit and risk when you are prescribed CANCALID.

Tell your doctor if you notice any of the following:

Frequent side effects:

- A fall in the number of white blood cells (the cells that fight infection), platelets (the cells that help the blood to clot, which may lead to bleeding disorders) and red blood cells (anaemia leading to tiredness and weakness)
- Constipation, diarrhoea, nausea, redness of skin, rashes, vomiting, muscle cramps, muscle aches, bone pain, joint pain, tiredness, generalised swelling including swelling of the limbs
- Fever and flu like symptoms including fever, muscle ache, headache, and chills
- Numbness, tingling or burning sensation to the skin, pains in hands or feet, dizziness, tremor
- taste disturbance
- Decreased appetite, low levels of potassium in the blood
- Leg pain (which could be a symptom of blood clots (thrombosis)), chest pain, shortness of breath (which may be a symptom of blood clots in the lungs)
- Infection of the lung and the upper respiratory tract, shortness of breath, nosebleed.
- Blurred vision
- Headache
- Chest pain
- Difficulty breathing
- Infections of all types
- Infection of the sinuses that surround the nose
- Bleeding from the gums, stomach, or bowels, bruising
- Increased blood pressure or a fall in blood pressure, slow, fast or irregular heart beat
- Skin eruptions, skin cracking, flaking

- Hives, itching, dry skin, increased sweating, dehydration
- Sore inflamed mouth, dry mouth
- Abdominal pain
- Production of much more or much less urine than usual (which may be a symptom of kidney failure)
- Shortness of breath especially when lying down (which may be a symptoms of heart failure)
- Difficulty in obtaining an erection
- Chest pain spreading to the arms, neck, jaw, back or stomach, feeling sweaty and breathless, feeling sick or vomiting (which may be symptoms of a heart attack/myocardial infarction)
- Stroke, fainting
- Muscle weakness
- Joint swelling
- Low levels of calcium, phosphate or magnesium in the blood
- Depression
- Cataract
- Reduced vision
- Abnormal liver test results
- Iron overload
- Mood change
- Toothache

<u>Less frequent side effects:</u>

- Bleeding in the brain
- Circulatory problems
- Certain types of cancer of the skin
- Hypersensitivity or an allergic reaction (angioedema), a type of allergic reaction that may have symptoms such as hives, rashes, swelling of eyes, mouth or face, difficulty of breathing, or itching
- Tumour lysis syndrome - metabolic complications that can occur during treatment of cancer and sometimes even without treatment

Other side effects where the frequency is not known are sudden, or mild but worsening pain in the upper abdomen and/or back, which remains for a few days, possibly accompanied by nausea, vomiting, fever and a rapid pulse - these symptoms may be due to inflammation of the pancreas.
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. This includes any possible side effects not listed in this leaflet. You can also report side effects via https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of CANCALID.

5. How to store CANCALID

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

CANCALID will be stored in the pharmacy

Store at or below 25 °C.

Keep the container in the outer carton in order to protect from light.

Do not use after the expiry date stated on the vial and the carton.

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

The active substance is lenalidomide

CANCALID 2,5 mg:

Each capsule contains 2,5 mg lenalidomide.

Contains sugar: lactose anhydrous 20,0 mg

CANCALID 5 mg:

Each capsule contains 5 mg lenalidomide.

Contains sugar: lactose anhydrous 40,0 mg

CANCALID 7,5 mg:

Each capsule contains 7,5 mg lenalidomide.

Contains sugar: lactose anhydrous 60,0 mg

CANCALID 10 mg:

Each capsule contains 10 mg lenalidomide.

Contains sugar: lactose anhydrous 80,0 mg

CANCALID 15 mg:

Each capsule contains 15 mg lenalidomide.

Contains sugar: lactose anhydrous 120,0 mg

CANCALID 20 mg:

Each capsule contains 20 mg lenalidomide.

Contains sugar: lactose anhydrous 160,0 mg

CANCALID 25 mg:

Each capsule contains 25 mg lenalidomide.

Contains sugar: lactose anhydrous 200,0 mg.

The other ingredients of CANCALID are lactose anhydrous, microcrystalline cellulose, croscarmellose sodium, magnesium stearate

Capsule shell composition:

CANCALID 2,5 mg: Gelatine, titanium dioxide, iron oxide yellow, FD &C blue 2

CANCALID 5 mg: Gelatine, titanium dioxide

CANCALID 2,5 mg: Gelatine, titanium dioxide, iron oxide yellow, FD &C blue 2

CANCALID 7,5 mg: Gelatine, titanium dioxide

CANCALID 10 mg: Gelatine, titanium dioxide, iron oxide yellow, iron oxide red, FD &C blue 2

CANCALID 15 mg: Gelatine, titanium dioxide, iron oxide red

CANCALID 20 mg: Gelatine, titanium dioxide, iron oxide yellow, Iron oxide red

CANCALID 25 mg: Gelatine, titanium dioxide

Composition of printing ink: Shellac, dehydrated alcohol, isopropyl alcohol, butyl alcohol, strong ammonia solution, black iron oxide, potassium hydroxide

What CANCALID looks like and contents of the pack:

CANCALID 2,5 mg:

Off-white to pale-yellow powder filled in green opaque capsules imprinted "L 2.5" on the cap in black ink and plain body, size 4, hard gelatine capsule.

CANCALID 5 mg:

Off-white to pale-yellow powder filled in white opaque capsules imprinted "L 5" on the cap in black ink and plain body, size 2, hard gelatine capsule.

CANCALID 7,5 mg:

Off-white to pale- yellow powder filled in white opaque capsules imprinted "L 7.5" on the cap in black ink and plain body, size 2, hard gelatine capsule.

CANCALID 10 mg:

Off-white to pale-yellow powder filled in olive green and orange opaque capsules imprinted "L10" on the cap in black ink and plain body, size 0, hard gelatine capsule.

CANCALID 15 mg

Off-white to pale-yellow powder filled in dark orange opaque capsules imprinted "L 15" on the cap in black ink and plain body, size 0, hard gelatin capsule.

CANCALID 20 mg

Off-white to pale-yellow powder filled in orange opaque capsules imprinted "L 20" on the cap in black ink and plain body, size 0, hard gelatin capsule.

CANCALID 25 mg

Off-white to pale-yellow powder filled in white opaque capsules imprinted "L 25" on the cap in black ink and plain body, size 0, hard gelatin capsule.

CANCALID Capsules 2,5 mg, 5 mg, 7,5 mg, 10 mg, 15 mg, 20 mg and 25 mg are packed in clear PVC film - aluminium foil blister pack. The blisters are further packed in pre-printed cartons with package leaflet.

Pack sizes:

3 x blister of 7 capsules

HOLDER OF CERTIFICATE OF REGISTRATION

AUROGEN SA (Pty) Ltd

Woodhill Office Park, Building 1, First Floor

53 Phillip Engelbrecht Avenue

Meyersdal, Ext. 12, 1448

Johannesburg

South Africa

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Registration number

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CANCALID 5 MG: 56/32/0519.512

CANCALID 7,5 MG: 56/32/0520.513

CANCALID 10 MG: 56/32/0521.514

CANCALID 15 MG: 56/32/0522.515

CANCALID 220 MG: 56/32/0523.516

CANCALID 25 MG: 56/32/0524.517