Pharmacode position may change as per Supplier's m/c requirement & additional small pharma code may appear on the front / back panel

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CANCALID P1535377

CANCALID P1535377

APPROVED
By Berenice at 1:21 pm, Nov 29, 2023

PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

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 gelatine 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 gelatine 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 gelatine capsule.

WARNING: SEVERE LIFE-THREATENING HUMAN BIRTH DEFECTS. Lenalidomide is structurally related to thalidomide, a known human teratogenic active substance that causes severe life-threatening birth defects. Lenalidomide induced in monkeys malformations similar to those described with thalidomide (see section 4.6). If lenalidomide is taken during pregnancy, a teratogenic effect of lenalidomide in humans is expected. **BECAUSE OF THIS TOXICITY AND IN AN EFFORT TO MAKE THE CHANCE OF FOETAL EXPOSURE TO CANCALID AS NEGLIGIBLE AS POSSIBLE, CANCALID IS APPROVED FOR MARKETING UNDER A SPECIAL RESTRICTED DISTRIBUTION PROGRAMME. THIS PROGRAMME IS CALLED LEN PERM (PROGRAM FOR THE EVALUATION OF RISK AND MANAGEMENT). UNDER THIS RESTRICTED DISTRIBUTION PROGRAMME, ONLY PRECRIBERS REGISTERED WITH THE PROGRAMME ARE ALLOWED TO PRESCRIBE THE PRODUCT AND PHARMACISTS REGISTERED WITH THE PROGRAMME ARE ALLOWED TO DISPENSE THE PRODUCT. IN ADDITION, PATIENTS MUST BE ADVISED OF, AGREE TO, AND COMPLY WITH THE REQUIREMENTS OF LEN PERM (PROGRAM FOR THE EVALUATION OF RISK AND MANAGEMENT).**

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

CANCALID is indicated for:
1. Myelodysplastic Syndromes (MDS): **CANCALID** is indicated for the treatment of patients with transfusion-dependent anaemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality with or without other cytogenetic abnormalities.
2. Multiple myeloma (MM): **CANCALID** in combination with dexamethasone is indicated for the treatment of multiple myeloma patients who have received at least one prior therapy.

4.2. Posology and method of administration

Posology

Myelodysplastic syndromes (MDS):

Recommended dosage:

The recommended starting dose of **CANCALID** is 10 mg given orally once a day on days 1 - 21 of repeating 28 day treatment cycles.

Recommended dose adjustments during treatment and restart of treatment**:**

Platelet counts

Patients who are dosed initially at 10 mg and who experience thrombocytopenia should have their dosage adjusted as follows:

If thrombocytopenia develops WITHIN 4 weeks of starting treatment at 10 mg:

If baseline ≥ 100 x 10^9/L	
When platelets	Recommended course
Fall to < 50 x 10^9/L	Interrupt **CANCALID** treatment
Return to ≥ 50 x 10^9/L	Resume **CANCALID** at 5 mg once a day continuously in repeating 28 day cycles
If baseline < 100 x 10^9/L	
When platelets	Recommended course
Fall to 50 % of the baseline value	Interrupt **CANCALID** treatment
If baseline ≥ 60 x 10^9/Land returns to ≥ 50 x 10^9/L	Resume **CANCALID** at 5 mg once a day continuously in repeating 28 day cycles
If baseline < 60 x 10^9/L and returns to ≥ 30 x 10^9/L	Resume **CANCALID** at 5 mg once a day continuously in repeating 28 day cycles

If thrombocytopenia develops AFTER 4 weeks of starting treatment at 10 mg:

When platelets	Recommended course
< 30 x 10^9/L or < 50 x 10^9/L with platelet transfusions	Interrupt **CANCALID** treatment
Return to ≥ 30 x 10^9/L (without signs of bleeding)	Resume **CANCALID** at 5 mg once a day continuously in repeating 28 day cycles

Patients who experience thrombocytopenia at 5 mg daily should have their dosage adjusted as follows:

If thrombocytopenia develops during treatment at 5 mg daily:

When platelets	Recommended course
< 30 x 10^9/L or < 50 x 10^9/L with platelet transfusions	Interrupt **CANCALID** treatment
Return to ≥ 30 x 10^9/L (without signs of bleeding)	Resume **CANCALID** at 5 mg every other day

Neutrophil counts (ANC)⁺

Patients who are dosed initially at 10 mg and experience neutropenia should have their dosage adjusted as follows:

If neutropenia develops WITHIN 4 weeks of starting treatment at 10 mg:

If baseline ANC ≥ 1 x 10^9/L	
When neutrophils	Recommended course
Fall to < 0,75 x 10^9/L	Interrupt **CANCALID** treatment
Return to ≥ 1 x 10^9/L	Resume **CANCALID** at 5 mg once a day continuously in repeating 28 day cycles
If baseline ANC < 1 x 10^9/L	
When neutrophils	Recommended course
Fall to < 0,5 x 10^9/L	Interrupt **CANCALID** treatment
Return to ≥ 0,5 x 10^9/L	Resume **CANCALID** at 5 mg once a day continuously in repeating 28 day cycles

If neutropenia develops AFTER 4 weeks of starting treatment at 10 mg:

When neutrophils	Recommended course
< 0,5 x 10^9/L for ≥ 7 days or < 0,5 x 10^9/L associated with fever (≥ 38,5 °C)	Interrupt **CANCALID** treatment
Return to ≥ 0,5 x 10^9/L	Resume **CANCALID** at 5 mg once a day continuously in repeating 28 day cycles

⁺ Absolute Neutrophil Count

Patients who experience neutropenia at 5 mg daily should have their dosage adjusted as follows:

If neutropenia develops during treatment at 5 mg daily:

When neutrophils	Recommended course
< 0,5 x 10^9/L for ≥ 7 days or < 0,5 x 10^9/L associated with fever (≥ 38,5 °C)	Interrupt **CANCALID** treatment
Return to ≥ 0,5 x 10^9/L	Resume **CANCALID** at 5 mg once every other day

Other Grade 3/4 Toxicities

For other Grade 3/4 toxicities judged to be related to **CANCALID**, stop treatment and restart at next lower dose level when toxicity has resolved to ≤ Grade 2.

Discontinuation of CANCALID

CANCALID interruption or discontinuation should be considered for Grade 2 - 3 skin rash.

CANCALID must be discontinued for angioedema, Grade 4 rash, exfoliative or bullous rash, or Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) suspected, and should not be resumed following discontinuation from these reactions.

Multiple Myeloma:

Previously Treated Multiple Myeloma

Recommended dosage:

The recommended starting dose of **CANCALID** 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. Treatment should be continued until disease progression or unacceptable toxicity.

Recommended dose adjustments during treatment and restart of treatment:

Dose modification guidelines, as summarised below are recommended to manage Grade 3 or 4 neutropenia or thrombocytopenia or other Grade 3 or 4 toxicity judged to be related to **CANCALID**.

Platelet counts

Thrombocytopenia

See table below entitled, 'Dose Reduction Steps for **CANCALID** in Previously Treated Multiple Myeloma'.

Neutrophil counts (ANC)

Neutropenia

See table below entitled, 'Dose Reduction Steps for **CANCALID** in Previously Treated Multiple Myeloma'.

Other Grade 3/4 Toxicities

For other Grade 3/4 toxicities judged to be related to **CANCALID**, stop treatment and restart at next lower dose level when toxicity has resolved to ≤ Grade 2.

Discontinuation of CANCALID

CANCALID interruption or discontinuation should be considered for Grade 2 - 3 skin rash.

CANCALID must be discontinued for angioedema, Grade 4 rash, exfoliative or bullous rash, or if SJS or TEN is suspected, and should not be resumed following discontinuation from these reactions.

Recommended dose adjustment for previously treated multiple myeloma:

Dosing is continued or modified based upon clinical and laboratory findings.

Dose Reduction Steps for CANCALID in Previously Treated Multiple Myeloma:

Platelet counts

Thrombocytopenia

When platelets	Recommended course	Dose levels	Previously treated Multiple Myeloma (combination with dexamethasone) Days 1 - 21/28 day cycle
Fall to < 30 x 10^9/L	Interrupt **CANCALID** treatment and follow CBC weekly	Starting dose	25 mg
Return to ≥ 30 x 10^9/L	Resume **CANCALID** at dose level – 1	Dose level – 1	15 mg
For each subsequent drop below < 30 x 10^9/L	Interrupt **CANCALID** treatment	Dose level – 2	10 mg
		Dose level – 3	5 mg
Return to ≥ 30 x 10^9/L	Resume **CANCALID** at the next lower dose level -2 or -3 for the indicated dose regimen. Do not dose below the lowest **CANCALID** dose level in the indicated dose regimen		

Absolute neutrophil counts (ANC) Neutropenia

When neutrophils	Recommended course[a]	Dose levels	Previously treated Multiple Myeloma (combination with dexamethasone) Days 1 - 21/28 day cycle
Fall to < 0,5 x 10^9/L	Interrupt **CANCALID** treatment and follow CBC weekly	Starting dose	25 mg
Return to ≥ 0,5 x 10^9/L	Resume **CANCALID** at dose level – 1	Dose level – 1	15 mg
For each subsequent drop below < 0,5 x 10^9/L	Interrupt **CANCALID** treatment	Dose level – 2	10 mg
		Dose level – 3	5 mg
Return to ≥ 0,5 x 10^9/L	Resume **CANCALID** at the next lower dose level -2 or -3 for the indicated dose regimen. Do not dose below the lowest **CANCALID** dose level in the indicated dose regimen		

[a] at the medical practitioner's discretion, if neutropenia is the only toxicity at any dose level, add granulocyte colony stimulating factor (G-CSF) and maintain the dose level of **CANCALID**.

Other Grade 3/4 Toxicities

For other Grade 3/4 toxicities judged to be related to **CANCALID**, stop treatment and restart at next lower dose level when toxicity has resolved to ≤ Grade 2.

Discontinuation of CANCALID

CANCALID interruption or discontinuation should be considered for Grade 2-3 skin rash. **CANCALID** must bediscontinued for angioedema, Grade 4 rash, exfoliative or bullous rash, or if SJS or TEN is suspected, and should not be resumed following discontinuation for these reactions.

Special populations

Elderly patients:

No dose adjustments needed. Because elderly patients are more likely to have decreased renal function, and **CANCALID** is cleared by the kidney, care should be taken in dose selection (see 'Patients with renal impairment').

Patients with renal impairment

CANCALID is primarily excreted unchanged by the kidney, therefore care should be taken in dose selection, and monitoring of renal function is advised. No dose adjustments are required for patients with creatinine clearance (CLcr) ≥ 60 mL/min. The following **CANCALID** dose adjustments are recommended at the start of therapy for patients with CLcr < 60 mL/min.

Renal function (CLcr)	Starting dose 25 mg	Starting dose 10 mg
Moderate Renal Impairment (30 > CLcr < 60 mL/min)	10 mg[a] Every 24 hours	5 mg Every 24 hours
Severe Renal Impairment (CLcr < 30 mL/min, not requiring dialysis)	15 mg Every 48 hours	5 mg Every 48 hours
End Stage Renal Disease (CLcr < 30 mL/min, requiring dialysis)	5 mg Once daily. On dialysis days the dose should be administered following dialysis	5 mg 3 times a week following each dialysis

CLcr = creatinine clearance; [a] The dose may be escalated to 15 mg every 24 hours after 2 cycles if patient is not responding to treatment and is tolerating the medicine.

After initiation of **CANCALID** therapy, subsequent **CANCALID** dose modification should be based on individual patient treatment tolerance, as described elsewhere in this section.

Patients with hepatic impairment

No study has been conducted in patients with hepatic impairment. **CANCALID** is not known to be metabolised by the liver; the elimination of unchanged **CANCALID** is predominantly by the renal route (see section 5.2).

Paediatric population:

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

Method of administration

CANCALID should be taken orally at about the same time each day. The capsules should not be opened, broken, or chewed. **CANCALID** capsules should be swallowed whole, preferably with water, either with or without food.

If less than 12 hours has elapsed since missing a dose, the patient can take the dose. If more than 12 hours has elapsed since missing a dose at the normal time, the patient should not take the dose, but take the next dose at the normal time on the following day. Do not take 2 doses at the same time.

4.3. Contraindications

CANCALID is contraindicated:
- Hypersensitivity to lenalidomide or any of the excipients (see section 6.1)
- In pregnancy and lactation.
- Women of childbearing potential, except when all of the conditions for pregnancy prevention have been met (see sections 4.4 and 4.6).

4.4. Special warnings and precautions for use

General:

Pregnancy warning

CANCALID is contraindicated during pregnancy.

CANCALID is structurally related to thalidomide. Thalidomide is a known human teratogenic active substance that causes severe life-threatening birth defects. Lenalidomide induced in monkeys malformations similar to those described with thalidomide (see section 4.6). If **CANCALID** is taken during pregnancy, a teratogenic effect of lenalidomide in humans is expected. The conditions of the Key Assist Risk Management Program must be fulfilled for all patients unless there is reliable evidence that the patient does not have childbearing potential.

Counselling

For women of childbearing potential, **CANCALID** is contraindicated unless all of the following are met:
- She understands the expected teratogenic risk to the unborn child.
- She understands the need for effective contraception, without interruption, 4 weeks before starting treatment, throughout the entire duration of treatment including dose interruptions, and for 4 weeks after the end of treatment.
- Even if a woman of childbearing potential has amenorrhea she must follow all the advice on effective contraception.
- She should be capable of complying with effective contraceptive measures. She is informed and understands the potential consequences of pregnancy and the need to rapidly consult if there is a risk of pregnancy.
- She understands the need to commence the treatment as soon as **CANCALID** is dispensed following a negative pregnancy test.
- She understands the need and accepts to undergo pregnancy testing every 4 weeks except in case of confirmed tubal sterilisation.
- She acknowledges that she understands the hazards and necessary precautions associated with the use of **CANCALID**.

For male patients taking **CANCALID**, pharmacokinetic data has demonstrated that lenalidomide is present in human semen at extremely low levels during treatment and is undetectable in human semen 3 days after discontinuation of lenalidomide in the healthy subject (see section 5.2). As a precaution, all male patients taking **CANCALID** must meet the following conditions:
- Understand the expected teratogenic risk if engaged in sexual activity with a woman of childbearing potential.
- Understand the need for the use of a condom if engaged in sexual activity with a woman of childbearing potential.

The prescriber must ensure that for women of childbearing potential:
- The patient complies with the conditions of the Key Assist Risk Management Program, including confirmation that she has an adequate level of understanding.
- The patient has acknowledged the aforementioned conditions.

Contraception

Women of childbearing potential must use two reliable methods of contraception for 4 weeks before therapy, during therapy including dose interruptions, and until 4 weeks after **CANCALID** therapy, unless the patient commits to absolute and continuous abstinence confirmed on a monthly basis. If not established on effective contraception, the patient must be referred to an appropriately trained health care professional for contraceptive advice in order that contraception can be initiated.

The following can be considered to be examples of suitable methods of contraception:

Highly effective methods
- Intra Uterine Device (IUD);
- Hormonal (hormonal implants, levonorgestrel-releasing intrauterine system (IUS)), medroxyprogesterone acetate depot injections, ovulation inhibitory progesterone-only pills (e.g. desogestrel);
- Tubal ligation;
- Partner's vasectomy.

Effective methods
- Male condom;
- Diaphragm;
- Cervical cap.

Because of the increased risk of venous thromboembolism in patients with multiple myeloma taking **CANCALID** and dexamethasone, and in patients with myelodysplastic syndromes taking **CANCALID** monotherapy, combined oral contraceptive pills are not recommended (see section 4.5). If a patient is currently using combined oral contraception the patient should switch to two of the effective methods listed above.

The risk of venous thromboembolism continues for 4 - 6 weeks after discontinuing combined oral contraception.

Pregnancy testing

Pregnancy must be excluded by testing blood and/or urine. According to local practice, medically supervised pregnancy tests with a minimum sensitivity of 50 IU/mL must be performed for women of childbearing potential as outlined below. This requirement includes women of childbearing potential who practice absolute and continuous abstinence. Ideally, pregnancy testing, issuing a prescription and dispensing should occur on the same day. Dispensing of **CANCALID** to women of childbearing potential should occur within 7 days of the prescription.

Prior to starting treatment

A medically supervised pregnancy test should be performed 7 days prior to the patient starting **CANCALID**, once the patient had been using effective contraception for at least 4 weeks. The test should ensure the patient is not pregnant when she starts treatment with **CANCALID**.

Follow-up and end of treatment

A medically supervised pregnancy test should be repeated every 4 weeks, including 4 weeks after the end of treatment, except in the case of confirmed tubal sterilisation. These pregnancy tests should be performed on the day of the prescribing visit or in the 7 days prior to the visit to the prescriber.

Male fertility

CANCALID is present in human semen at extremely low levels during treatment and is undetectable in human semen 3 days after discontinuation of **CANCALID** in the healthy subject (see section 5.2). As a precaution, and taking into account special populations with prolonged elimination time such as renal impairment, all male patients should use condoms throughout treatment duration, during dose interruption and for 4 weeks after cessation of treatment if their partner is of childbearing potential and is not established on suitable contraception (even if the male patient has undergone a 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.

Patients should not donate blood during therapy including dose interruptions and for 4 weeks following discontinuation of **CANCALID**.

Educational materials

In order to assist patients in avoiding foetal exposure to **CANCALID**, educational material will be provided to health care professionals to reinforce the warnings about the expected teratogenicity of **CANCALID**, to provide advice on contraception before therapy is started, and to provide guidance on the need for pregnancy testing. Full patient information about the expected teratogenic risk and the strict pregnancy prevention measures as specified in the Key Assist Risk Management Program should be given by the medical practitioner to women of childbearing potential and, as appropriate, to male patients.

Other special warnings and precautions for use:
- *Venous thromboembolic events* (predominantly deep venous thrombosis and pulmonary embolism), in multiple myeloma patients treated with **CANCALID** combination therapy and in MDS patients treated with **CANCALID** monotherapy.
- *Allergic Conditions*: Angioedema and serious dermatologic reactions including SJS and TEN have been reported. These events can be fatal. Patients with a prior history of Grade 4 rash associated with thalidomide treatment should not receive **CANCALID**. **CANCALID** interruption or discontinuation should be considered for Grade 2 - 3 skin rash. **CANCALID** must be discontinued for angioedema, Grade 4 rash, exfoliative or bullous rash, or if SJS or TEN is suspected, and should not be resumed following discontinuation for these reactions.
- *Tumour Lysis Syndrome and Tumour Flare Reaction:* Tumour lysis syndrome (TLS) and tumour flare reaction (TFR) have been observed in patients with Chronic Lymphocytic Leukemia (CLL), and in patients with other lymphomas, who were treated with lenalidomide. Fatal instances of TLS have been reported during treatment with lenalidomide. Patients at risk for TLS and TFR are those with high tumour burden prior to treatment. Caution should be practiced when introducing these patients to **CANCALID**. These patients should be monitored closely, especially during the first cycle or dose-escalation, and appropriate precautions taken. There have been reports of TLS in patients with MM treated with lenalidomide.
- *Myocardial infarction:* Myocardial infarction has been reported in patients receiving lenalidomide, particularly in those with known risk factors and within the first 12 months when used in combination with dexamethasone. Patients with known risk factors – including prior thrombosis – should be closely monitored, and action should be taken to try to minimize all modifiable risk factors (eg. smoking, hypertension, and hyperlipidaemia).
- *Neutropenia and thrombocytopenia:* The major dose limiting toxicities of **CANCALID** include neutropenia and thrombocytopenia. A complete blood cell count, including white blood cell count with differential count, platelet count, haemoglobin, and haematocrit should be performed at baseline, every week for the first 8 weeks of **CANCALID** treatment and monthly thereafter to monitor for cytopenias. A dose reduction may be required (see section 4.2). In case of neutropenia, the medical practitioner should consider the use of growth factors in patient management.
  Patients should be advised to promptly report febrile episodes. Patients and physicians are advised to be observant for signs and symptoms of bleeding, including petechiae and epistaxis, especially in patients receiving concomitant medicines susceptible to induce bleeding. Co-administration of **CANCALID** with other myelosuppressive agents should be undertaken with caution.

Myelodysplastic syndromes (MDS):

Haematologic toxicity (neutropenia and thrombocytopenia) in deletion 5q MDS – A complete blood cell count, including white blood cell count with differential, platelet count, haemoglobin, and haematocrit should be performed weekly for first 8 weeks of **CANCALID** treatment and monthly thereafter to monitor for cytopenias. A dose reduction may be required (see section 4.2).

Multiple myeloma (MM):

Haematological toxicities:
- Previously treated MM:
  Haematologic toxicity (neutropenia and thrombocytopenia) in previously treated multiple myeloma patients treated with **CANCALID** combination therapy – Complete blood cell counts should be monitored every 2 weeks for the first 12 weeks and then monthly thereafter. A dose interruption and/or dose reductions may be required (see section 4.2).

⬆DETACH BEFORE DISPENSING

SCHEDULING STATUS

S4

Patient Information Leaflet

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
2. What you need to know before you take **CANCALID**
3. How to take **CANCALID**
4. Possible side effects
5. How to store **CANCALID**
6. Contents of the pack and other information

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 the lungs and heart.
- 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 medicine.

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 taking **CANCALID**.

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 **CANCALID.**

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 symptom 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

Less frequent side effects:
- 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 and 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.

Capsules are packed in clear PVC film - aluminium foil blister pack. The blisters are further packed in pre-printed cartons with package leaflet.

Pack sizes: 21s (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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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 20 mg: 56/32/0523.516
CANCALID 25 mg: 56/32/0524.517

Black A/s: 350 x 900 mm

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Initiator: Sagar				
Artist: Vision Graphic Designers	Pharmacode: 35377			
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Second Primary Malignancies

- Previously treated MM:

  A numerical imbalance was observed in clinical trials in previously treated multiple myeloma patients with lenalidomide/dexamethasone compared with controls comprising invasive primary malignancies and of basal cell and squamous cell skin cancers. Carefully evaluate patients before and during treatment using standard cancer screening for occurrence of second primary malignancies and institute treatment as appropriate.

Thyroid disorders

Cases of hypothyroidism and cases of hyperthyroidism have been reported.

Optimal control of co-morbid conditions influencing thyroid function is recommended before start of treatment. Baseline and ongoing monitoring of thyroid function is recommended.

Peripheral neuropathy

Lenalidomide is structurally related to thalidomide, which is known to induce severe peripheral neuropathy. There was no increase in peripheral neuropathy observed with lenalidomide in combination with dexamethasone or melphalan and prednisone or lenalidomide monotherapy or with long term use of lenalidomide for the treatment of newly diagnosed multiple myeloma. The combination of lenalidomide with intravenous bortezomib and dexamethasone in multiple myeloma patients is associated with a higher frequency of peripheral neuropathy. The frequency was lower when bortezomib was administered subcutaneously.

Cataract

Cataract has been reported with a higher frequency in patients receiving lenalidomide in combination with dexamethasone particularly when used for a prolonged time. Regular monitoring of visual ability is recommended.

Lactose intolerance

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucosegalactose mal-absorption should not take **CANCALID**.

4.5. Interaction with other medicines and other forms of interaction

Lenalidomide is not a substrate, inhibitor or inducer of cytochrome P450 enzymes *in vitro*. Hence, co-administration of cytochrome P450 substrates or inhibitors with **CANCALID** is not likely to result in clinically relevant medicine interactions. Co-administration of multiple doses of 10 mg of **CANCALID** had no effect on the single dose pharmacokinetics and pharmacodynamic of R- and S-warfarin.

Coadministration of a single 25 mg dose of warfarin had no effect on the pharmacokinetics of **CANCALID**. It is not known whether there is an interaction during concomitant treatment with dexamethasone. Dexamethasone is a weak to moderate enzyme inducer and its effect on warfarin is unknown. Close monitoring of warfarin concentration is advised during treatment.

When digoxin was co-administered with lenalidomide (10 mg/day) the digoxin C_{max} and $AUC_{0-\infty}$ were 14 % higher than when digoxin was administered concomitantly with placebo. Periodic monitoring of digoxin plasma levels is recommended during administration of **CANCALID**.

In patients with multiple myeloma, co-administration of single or multiple doses of dexamethasone (40 mg/day) had no significant effect on the multiple dose pharmacokinetics of **CANCALID** (25 mg/day).

In vitro, **CANCALID** is a weak substrate, but is not an inhibitor of P-glycoprotein (P-gp).

In vitro studies demonstrate that lenalidomide is not a substrate of human multidrug resistance protein MRP1, MRP2 or MRP3 efflux transporters as well as human organic anion and cation uptake transporters OAT1, OAT3, OATP1B1 (OATP2) or OCT1.

Erythropoietic medicines, or other medicines that may increase the risk of thrombosis, such as hormone replacement therapy, should be used with caution in multiple myeloma patients receiving CANCALID with dexamethasone (see section 4.4 and 4.8).

Patients with multiple myeloma taking **CANCALID** and dexamethasone, patients with MDS taking **CANCALID** monotherapy, as well as patients taking combined oral contraceptive pills or hormone replacement therapy, have an increased risk of venous thromboembolic events (VTE).

Statins

There is an increased risk of rhabdomyolysis when statins are administered with lenalidomide, which may be simply additive, Enhanced clinical and laboratory monitoring is warranted notably during the first weeks of treatment.

4.6. Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and female

CANCALID is teratogenic to animals. The teratogenic effect of lenalidomide in humans cannot be ruled out.

Therefore:

- Females of childbearing potential must use effective means of contraception for 28 days before therapy, during **CANCALID** therapy including dose interruptions, and for 28 days following discontinuation of **CANCALID** therapy, or continually abstain from sexual intercourse. There is an increased risk of VTE in patients with multiple myeloma taking **CANCALID** and dexamethasone, and in patients with MDS taking **CANCALID** monotherapy, and an increased risk of VTE in patients taking combined oral contraceptive pills.
- Females of childbearing potential should undergo regular pregnancy-testing during treatment with **CANCALID**.

<u>Males</u>

Clinical data has demonstrated the presence of lenalidomide in human semen. Therefore, male patients taking **CANCALID** should use a condom during **CANCALID** therapy including dose interruptions and for 4 weeks after cessation of treatment. Male patients taking **CANCALID** should not donate sperm or semen during treatment including dose interruptions and for 4 weeks following the discontinuation of treatment.

Criteria for women of non-childbearing potential

A female patient or a female partner of a male patient is considered to have childbearing potential unless she meets at least one of the following criteria:

- Age ≥ 50 years and naturally amenorrhoeic for ≥ 1 year*
- Premature ovarian failure confirmed by a specialist gynaecologist
- Previous bilateral salpingo-oophorectomy, or hysterectomy
- XY genotype, Turner syndrome, uterine agenesis.

*Amenorrhoea following cancer therapy does not rule out childbearing potential.

Pregnancy

CANCALID is contraindicated in pregnancy. If pregnancy occurs, **CANCALID** should be immediately discontinued.

Breastfeeding

Breastfeeding is contraindicated during therapy with **CANCALID**.

Fertility

No clinical data available.

4.7. Effects on ability to drive and use machines

No studies on the effects on the ability to drive or use machines have been performed. **CANCALID** may affect the ability to drive and use machines. Fatigue, dizziness, somnolence and blurred vision have been reported with the use of **CANCALID**. Therefore, caution is recommended when driving or operating machines.

4.8. Undesirable effects

Frequency categories are expressed as: Frequent = very common and common; Less frequent = uncommon, rare and very rare; Frequency unknown = cannot be estimated and post-marketing.

a. *Tabulated list of adverse reactions*

System Organ Class/ Preferred Term	Frequency	All ADRs	Grade 3/4 ADRs	Serious Adverse Drug Reactions (SADRs)
General disorders and administration site conditions	Frequent	Pyrexia, oedema (including peripheral), influenza like illness syndrome (including pyrexia, cough, rhinitis, myalgia, musculoskeletal pain, pharyngitis, headache and rigors), fatigue, asthenia, chest pain	Fatigue, pyrexia, asthenia, fall	
Gastrointestinal disorders	Frequent	Diarrhoea@, vomiting@, nausea@, constipation, abdominal pain (including upper)@, Dry mouth, dyspepsia	Diarrhoea@, nausea@, constipation, toothache	Diarrhoea@
Musculoskeletal and connective tissue disorders	Frequent	Musculoskeletal and connective tissue pain and discomfort (including back pain and pain in extremity), bone pain, muscle spasms, arthralgia, myalgia	Muscular weakness, musculoskeletal and connective tissue pain and discomfort, back pain	Back pain
Nervous system disorders	Frequent	Peripheral neuropathies (excluding motor neuropathy), dizziness, tremor, dysgueusia, headache, lethargy, paraesthesia	Syncope, dizziness	Cerebrovascular accident@
Respiratory, thoracic and mediastinal disorders	Frequent	Dyspnoea, epistaxis	Respiratory distress@, bronchitis	
Infections and infestations#	Frequent	Pneumonia@, bronchitis, bacterial, viral and fungal infections (including opportunistic infections), upper respiratory tract infection, sinusitis	Pneumonia@, bacterial, vi ral and fungal infections (including opportunisti c infections)	Pneumonia@, bacterial,viral and fungal infections (including opportunistic infections)
Skin and subcutaneous tissue disorders	Frequent	Rash+, pruritus, dry skin, hyperhidrosis	Rash, pruritus	
Blood and lymphatic system disorders	Frequent	Neutropenia%, thrombocytopenia@, anaemia@, leukopenia	Neutropenia%, thrombocytopenia@, anaemia@, leukopenia, febrile neutropenia%	Anaemia@, febrile neutropenia%, neutropenia%, thrombocytopenia@
Metabolism and nutrition disorders	Frequent	Decreased appetite, hypokalaemia, hypocalcaemia, dehydration, dypomagnesaemia, iron overload	Hypokalaemia, hypocalcaemia, hypophosphataemia, hyperglycaemia%, decreased appetite	Hyperglycaemia%
Eye disorders	Frequent	Blurred vision	Cataracts	
Renal disorders	Frequent		Renal failure@	Renal failure@
Vascular disorders	Frequent	Venous thromboembolic events, predominantly deep vein thrombosis and pulmonary embolism@, hypertension, hypotension, haematoma	Venous thromboembolic events, predominantly deep vein thrombosis and pulmonary embolism@	Venous thromboembolic events, predominantly deep vein thrombosis and pulmonary embolism@
Psychiatric disorders	Frequent		Depression	Altered mood
Cardiac disorders	Frequent		Acute myocardial infarction@, atrial fibrillation@, tachycardia, cardiac failure congestive@, cardiac failure@	Acute myocardial infarction@, atrial fibrillation@, cardiac failure congestive@, cardiac failure@
Neoplasms benign, malignant and unspecified (including cysts and polyps)	Frequent			B-cell lymphomas
Immune system disorders	Less frequent	Hypersensitivity		
Hepatobiliary disorders	Frequent	Abnormal liver function tests	Abnormal liver function tests	Abnormal liver function tests
Investigations	Frequent	Decreased weight		

@-ADRs with Death as an outcome

%-ADRs which were considered to be Life Threatening (if the outcome of the event was death, it is included with death cases)

- All PTs under SOC of Infections except for rare infections of Public Health interest will be considered listed

+ - All PTs under HLT of Rash will be considered listed

Post-marketing data:

In addition to the above adverse reactions, the following table is derived from data gathered from post-marketing data.

System Organ Class/ Preferred Term	Frequency	All ADRs	Grade 3/4 ADRs
Infections and infestations	Unknown	Viral infections, including herpes zoster and hepatitis B virus reactivation	Viral infections, including herpes zoster and hepatitis B virus reactivation
Neoplasms Benign, Malignant and Unspecified (including cysts and polyps)	Less frequent		Tumour lysis syndrome
Blood and Lymphatic System disorders	Unknown	Acquired haemophilia	
Immune system disorders	Unknown	Solid organ transplant rejection	
Endocrine disorders	Frequent	Hyperthyroidism	
Respiratory, Thoracic and Mediastinal disorders	Unknown		Interstitial pneumonitis
Gastrointestinal disorders	Unknown		Pancreatitis, Gastrointestinal perforation (including diverticular, intestinal and large intestine perforations)
Hepatobiliary disorders	Unknown	Acute hepatic failure, Hepatitis toxic, Cytolytic hepatitis, Cholestatic hepatitis, Mixed cytolytic/ cholestatic hepatitis	Acute hepatic failure, Hepatitis toxic
Skin and subcutaneous tissue disorders	Less frequent		Angioedema, Stevens-Johnson syndrome, toxic epidermal necrolysis
	Unknown		Leukocytoclastic vasculitis, Drug Reaction with Eosinophilia and Systemic Symptoms

b. Description of selected adverse reactions

Hepatic Disorders

Transient liver laboratory abnormalities (predominantly transaminases) were reported in patients treated with lenalidomide. Treatment with **CANCALID** should be interrupted and restarted once the levels return to baseline. Successful re-challenge without recurrence of liver laboratory elevation was reported in some patients.

Teratogenicity

Lenalidomide is structurally related to thalidomide. Thalidomide is a known human teratogenic active substance that causes severe life-threatening birth defects. Lenalidomide induced in monkeys malformations similar to those described with thalidomide (see sections 4.6 and 5.3). If lenalidomide is taken during pregnancy, a teratogenic effect of lenalidomide in humans is expected.

Venous thromboembolism

An increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE) is associated with the use of the combination of lenalidomide with dexamethasone in patients with multiple myeloma, and to a lesser extent in patients treated with lenalidomide in combination with melphalan and prednisone or in patients with multiple myeloma, myelodysplastic syndromes and mantle cell lymphoma treated with lenalidomide monotherapy (see section 4.5). Concomitant administration of erythropoietic agents or previous history of DVT may also increase thrombotic risk in these patients.

Myocardial infarction

Myocardial infarction has been reported in patients receiving lenalidomide, particularly in those with known risk factors.

Haemorrhagic disorders

Haemorrhagic disorders are listed under several system organ classes: Blood and lymphatic system disorders; nervous system disorders (intracranial haemorrhage); respiratory, thoracic and mediastinal disorders (epistaxis); gastrointestinal disorders (gingival bleeding, haemorrhoidal haemorrhage, rectal haemorrhage); renal and urinary disorders (haematuria); injury, poisoning and procedural complications (contusion) and vascular disorders (ecchymosis).

Allergic reactions

Cases of allergic reaction/hypersensitivity reactions have been reported. A possible cross-reaction between lenalidomide and thalidomide has been reported in the literature.

Severe skin reactions

Severe cutaneous reactions including SJS, TEN and DRESS have been reported with the use of lenalidomide. Patients with a history of severe rash associated with thalidomide treatment should not receive lenalidomide (see section 4.4).

Second primary malignancies

In clinical trials in previously treated myeloma patients with lenalidomide/dexamethasone compared to controls, mainly comprising of basal cell or squamous cell skin cancers.

Acute myeloid leukaemia (AML)

- Multiple myeloma

  Cases of AML have been observed in clinical trials of newly diagnosed multiple myeloma in patients taking lenalidomide treatment in combination with melphalan or immediately following HDM/ASCT (see section 4.4). This increase was not observed in clinical trials of newly diagnosed multiple myeloma in patients taking lenalidomide in combination with dexamethasone compared to thalidomide in combination with melphalan and prednisone.
- Myelodysplastic syndromes

  Baseline variables including complex cytogenetics and TP53 mutation are associated with progression to AML in subjects who are transfusion dependent and have a Del (5q) abnormality (see section 4.4). The estimated 2-year cumulative risk of progression to AML were 13,8 % in patients with an isolated Del (5q) abnormality compared to 17,3 % for patients with Del (5q) and one additional cytogenetic abnormality and 38,6 % in patients with a complex karyotype. In a post-hoc analysis of a clinical trial of lenalidomide in myelodysplastic syndromes, the estimated 2-year rate of progression to AML was 27,5 % in patients with IHC-p53 positivity and 3,6 % in patients with IHC-p53 negativity (p = 0,0038). In the patients with IHC-p53 positivity, a lower rate of progression to AML was observed amongst patients who achieved a transfusion independence (TI) response (11,1 %) compared to a non-responder (34,8 %).

Rhabdomyolysis

Rare cases of rhabdomyolysis have been observed, some of them when lenalidomide is administered with a statin.

Tumour flare reaction and tumour lysis syndrome

In study MCL-002, approximately 10 % of lenalidomide-treated patients experienced TFR compared to 0 % in the control arm. The majority of the events occurred in cycle 1, all were assessed as treatment-related, and the majority of the reports were Grade 1 or 2. Patients with high MIPI at diagnosis or bulky disease (at least one lesion that is ≥ 7 cm in the longest diameter) at baseline may be at risk of TFR. In study MCL-002, TLS was reported for one patient in each of the two treatment arms. In the supportive study MCL-001, approximately 10 % of subjects experienced TFR; all report were Grade 1 or 2 in severity and all were assessed as treatment-related. The majority of the events occurred in cycle 1. There were no reports of TLS in study MCL-001 (see section 4.4).

Gastrointestinal disorders

Gastrointestinal perforations have been reported during treatment with lenalidomide. Gastrointestinal perforations may lead to septic complications and may be associated with fatal outcome.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the '6.04 Adverse Drug Reactions Reporting Form', found under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9. Overdose

There is no specific experience in the management of **CANCALID** overdose in patients. In studies, the dose-limiting toxicity was essentially haematological. In the event of overdose, supportive care is advised.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and class: A32 Other - Immunomodulators

Pharmacological Classification: Other immunomodulators

Other immunosuppressants, ATC code: L04AX04

Mechanism of action

Lenalidomide is an oral immunomodulating agent with a pleiotropic mechanism of action involving direct tumouricidal activity, immunomodulation, pro-rythropoiesis, and anti-angiogenesis. Lenalidomide inhibits proliferation of certain aematopoietic tumour cells (including multiple myeloma plasma tumour cells and those with deletions of chromosome 5) and induces expression of tumour suppressor genes, leading to cell cycle arrest. Immunomodulatory properties of lenalidomide include activation of T cells and natural killer (NK) cells, increased numbers of NK T cells, and inhibition of proinflammatory cytokines (e.g. TNF-α and IL-6) by monocytes. Pro-erythropoietic properties of lenalidomide include expansion of CD34+ haematopoietic stem cells and increased foetal haemoglobin production. In multiple myeloma cells, the combination of lenalidomide and dexamethasone induces expression of tumour suppressor genes, activates caspases involved in apoptosis, and synergistically inhibits MM cell proliferation.

In myeloplastic syndromes (MDS) (del 5q), lenalidomide was shown to selectively inhibit the abnormal clone by increasing apoptosis of del 5q cells. Sensitivity to lenalidomide in MDS del (5q) can, at least in part, be explained by upregulation of genes (e.g. SPARC, p21, RPS14) which have reduced expression due to haploinsufficiency caused by del (5q).

Cardiac Electrophysiology

A QTc study was conducted to evaluate the effects of lenalidomide on QT interval at single doses of 10 mg and 50 mg. A single dose of lenalidomide up to 50 mg is not associated with prolongation of the QT interval in healthy male subjects.

5.2. Pharmacokinetic properties

Absorption

Lenalidomide, in healthy volunteers, is rapidly absorbed following oral administration with the maximum plasma concentration (C_{max}) occurring between 0,5 and 1,5 hours post dose. The pharmacokinetic disposition of lenalidomide is linear. C_{max} and AUC increase proportionally with increases in dose. Multiple dosing at the recommended dose-regimen does not result in lenalidomide accumulation.

Co-administration with a high-fat and high-calorie meal in healthy volunteers reduces the extent of absorption, resulting in an approximately 20 % decrease in area under the concentration versus time curve (AUC) and 50 % decrease in C_{max} in plasma. In the pivotal multiple myeloma and MDS registration trials where the efficacy and safety were investigated for lenalidomide, it was administered without regard to food intake. Thus, lenalidomide can be administered with or without food.

In multiple myeloma patients (baseline serum creatinine level ≤ 1,5 mg/dL), C_{max} occurs between 0,5 to 6 hours post dose. Plasma exposure (AUC and Cmax) increases proportionally with dose following single and multiple doses. Multiple doses at 25 mg/day do not cause lenalidomide to accumulate in plasma. Exposure (AUC) in multiple myeloma patients is higher compared to healthy volunteers since lenalidomide clearance is lower in these patients than in healthy volunteers. This is consistent with the compromised renal function in the multiple myeloma patients (dose adjustments are recommended for patients with CLcr < 60 mL/min; see section 4.2).

In patients with low - or intermediate-1-risk MDS, a single 10 mg oral dose of lenalidomide is rapidly absorbed with the Cmax observed at around 1 hour post dose. There is no accumulation of lenalidomide in plasma with multiple doses at 10 mg per day. Because many MDS patients have some degree of renal impairment, the exposure (AUC) is higher in MDS patients as compared with healthy subjects (dose adjustments are recommended for patients with CLcr < 60 mL/min; see section 4.2).

Distribution

In vitro [^{14}C]-lenalidomide binding to plasma proteins is approximately 29 % in healthy volunteers and 23 % in multiple myeloma patients.

Lenalidomide is present in semen (< 0,01 % of the dose) after administration of 25 mg/day and the substance is undetectable in semen 3 days after discontinuation of lenalidomide.

Biotransformation

Lenalidomide is not a substrate of hepatic metabolic enzymes *in vitro*. Unchanged lenalidomide is the predominant circulating component *in vivo* in humans. Two identified metabolites are hydroxy-lenalidomide and N-acetyl-lenalidomide; each constitute less than 5 % of parent levels in circulation.

Elimination

Following a single oral administration of [^{14}C]-lenalidomide (25 mg) to healthy volunteers, approximately 90 % and 4 % of the radioactive dose is eliminated in urine and faeces, respectively. Approximately 82 % of the radioactive dose isexcreted as lenalidomide, almost exclusively via the urinary route. Hydroxylenalidomide and Nacetyl-lenalidomide represent 4,59 % and 1,83 % of the excreted dose, respectively. The renal clearance of lenalidomide exceeds the glomerular filtration rate and therefore is at least actively secreted to some extent.

In MDS patients, urinary excretion of unchanged lenalidomide in 24 hours post-dose averages approximately 65 % of the administered dose.

At recommended doses (5 to 25 mg/day), half-life in plasma is approximately 3 hours in healthy volunteers and ranged from 3 to 5 hours in patients with multiple myeloma or MDS.

Special Populations

Renal impairment

The pharmacokinetics of lenalidomide were studied in patients with renal impairment due to nonmalignant conditions. In this study, 5 patients with mild renal function impairment (creatinine clearance (CLcr) 56 - 74 mL/min), 6 patients with moderate renal function impairment (CLcr 33 - 46 mL/min), 6 patients with severe renal function impairment (CLcr 17-29 mL/min), and 6 patients with end stage renal disease requiring dialysis were administered a single oral 25 mg dose of lenalidomide. Seven (7) healthy subjects of similar age with normal renal function (CLcr 83 - 145 mL/min) were administered a single oral 25 mg dose of lenalidomide. The pharmacokinetics of lenalidomide were similar in patients with mild impairment CLcr 56 - 74 mL/min and healthy subjects. Moderately and severely impaired patients had a 3-fold increase in half-life and a 66 % to 75 % decrease in clearance compared to healthy subjects. Patients on haemodialysis had an approximately 4,5-fold increase in half-life and an 80 % decrease in clearance compared to healthy subjects. Approximately 30 % of the substance in the body was removed by a 4 hour dialysis session.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

CANCALID capsules contain the following inactive ingredients:

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.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months.

6.4. Special precautions for storage

Store at or below 25 °C.

Keep in original packaging until required for use.

KEEP OUT OF REACH OF CHILDREN.

6.5. Nature and contents of container

Capsules are packed in the clear PVC film - aluminium foil blister pack. The blisters are further packed in pre-printed cartons with package leaflet.

Pack sizes: 21s (3 x blister of 7 capsules).

6.6. Special precautions for disposal and other handling

Capsules should not be opened or crushed. If powder from **CANCALID** makes contact with the skin, the skin should be washed immediately and thoroughly with soap and water. If **CANCALID** makes contact with the mucous membranes, they should be thoroughly flushed with water. Any unused product or waste material should be returned to the pharmacist for safe disposal in accordance with local requirements.

7. 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

8. REGISTRATION NUMBER

CANCALID 2,5 mg: 56/32/0518.511
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 20 mg: 56/32/0523.516
CANCALID 25 mg: 56/32/0524.517

9. DATE OF FIRST AUTHORISATION

08 August 2023

P1535377

⬆DETACH BEFORE DISPENSING

SKEDULERINGSTATUS

S4

CANCALID 2,5 mg kapsules
CANCALID 5 mg kapsules
CANCALID 7,5 mg kapsules
CANCALID 10 mg kapsules
CANCALID 15 mg kapsules
CANCALID 20 mg kapsules
CANCALID 25 mg kapsules
(Lenalidomied)
(Bevat Suiker: watervrye laktose)

Lees hierdie inligtingsblad noukeurig deur voordat jy CANCALID neem.

- Hou hierdie inligtingsblad. Dit mag nodig wees om dit weer te lees.
- Indien jy enige verdere vrae het, vra asseblief jou dokter, apteker, verpleegkundige of ander gesondheidsorgverskaffer.
- **CANCALID** is vir jou persoonlik voorgeskryf en jy moenie jou medisyne met ander persone deel nie. Dit kan skadelik wees vir hulle, al is hulle simptome dieselfde as joune.

WAARSKUWING: ERGE LEWENSBEDREIGENDE GEBOORTEAFWYKINGS BY MENSE.

Lenalidomied, die aktiewe bestanddeel wat in **CANCALID** voorkom, is struktureel verwant aan talidomied, 'n verbinding wat erge, lewensbedreigende geboorteafwykings veroorsaak. Lenalidomied het misvormings by ape veroorsaak, soortgelyk aan dié wat met talidomied beskryf is. Indien **CANCALID** tydens swangerskap geneem word, kan dieselfde uitwerking by mense verwag word. **WEENS HIERDIE TOKSIESE EFFEK EN IN 'N POGING OM DIE KANS VIR BLOOTSTELLING AAN CANCALID TYDENS SWANGERSKAP SO KLEIN AS MOONTLIK TE MAAK, IS CANCALID GOEDGEKEUR VIR GEBRUIK BINNE 'N SPESIALE BEPERKTE VERSPREIDINGSPROGRAM. HIERDIE PROGRAM WORD DIE SLEUTEL-BYSTANDRISIKOBESTUURPROGRAM GENOEM.**

Wat is in hierdie inligtingsblad:

1. Wat is **CANCALID** en waarvoor word dit gebruik
2. Wat jy moet weet voordat jy **CANCALID** neem
3. Hoe om **CANCALID** te neem
4. Moontlike newe-effekte
5. Hoe om **CANCALID** te berg
6. Inhoud van die verpakking en ander inligting

1. Wat is CANCALID en waarvoor word dit gebruik

CANCALID behoort aan 'n groep medisynes wat immuunmodulerende medisynes genoem word, wat die werking van die immuunstelsel kan modifiseer of reguleer.

- **CANCALID** in kombinasie met deksametasoon word gebruik om volwasse pasiënte te behandel wat met veelvuldige miëloom gediagnoseer is. Veelvuldige miëloom is 'n tipe bloedkanker wat die witbloedselle affekteer wat teenliggame produseer.
- **CANCALID** word ook gebruik om volwasse pasiënte te behandel wat met miëlodisplastiese sindrome gediagnoseer is. Pasiënte met miëlodisplastiese sindrome het 'n abnormaliteit van hul beenmurg, wat beteken dat hulle nie voldoende gesonde bloedselle vervaardig nie.

2. Wat jy moet weet voordat jy CANCALID neem

Jou dokter sou jou in die SLEUTEL-BYSTANDRISIKOBESTUURPROGRAM **ingeskryf het om seker te maak dat CANCALID veilig gebruik word.**

Moenie CANCALID neem nie:

- indien jy allergies (hipersensitief) vir lenalidomied of vir enige van die ander bestanddele van **CANCALID** is, gelys by die volgende afdeling: "Wat **CANCALID** bevat". Indien jy vermoed dat jy allergies is, vra jou dokter se advies.
- indien jy swanger is, vermoed dat jy swanger kan wees of beplan om swanger te raak, **aangesien CANCALID skadelik vir die ongebore kind is.**
- indien jy in staat is om swanger te raak, behalwe as jy al die nodige maatreëls nakom om te voorkom dat jy swanger raak. Indien jy in staat is om swanger te raak, gaan jou dokter met elke voorskrif aanteken dat die nodige maatreëls geneem is en vir jou hierdie bevestiging gee. Indien enige hiervan op jou van toepassing is, sê vir jou dokter voordat jy **CANCALID** neem.

Waarskuwings en voorsorgmaatreëls

Neem spesiale sorg/ Spesiale sorg moet met **CANCALID** geneem word:

Vir vrouens wat CANCALID neem

Voordat die behandeling begin word, behoort jy jou dokter te vra of dit moontlik is dat jy kan swanger raak, selfs al dink jy dis onwaarskynlik.

Indien jy nog kan swanger raak

- jy sal swangerskapstoetse onder toesig van jou dokter ondergaan (voor behandeling, elke 4 weke tydens behandeling, en 4 weke nadat die behandeling voltooi is), behalwe in die geval waar buissterilisasie bevestig is.
- en jy moet twee doeltreffende voorbehoedmetodes gebruik vir 4 weke voordat met behandeling begin word, tydens behandeling insluitende wanneer dosisse onderbreek word, en tot 4 weke nadat behandeling gestaak is. Jou dokter gaan jou adviseer rakende toepaslike voorbehoedmetodes.

Vir mans wat CANCALID neem

CANCALID word in menslike semen uitgeskei. Indien jou vroulike geslagsmaat swanger is of kan swanger raak, en sy gebruik nie doeltreffende metodes van geboortebeperking nie, moet jy kondome gebruik tydens jou behandeling insluitende wanneer dosisse onderbreek word en tot 4 weke nadat behandeling gestaak is (selfs al het jy 'n vasektomie ondergaan).

Manlike pasiënte wat **CANCALID** neem moenie tydens behandeling sperm of semen skenk nie, insluitende wanneer dosisse onderbreek word en tot 4 weke nadat behandeling gestaak is.

Alle pasiënte

Indien jy in die verlede bloedklonte gehad het, moet jy dit vir jou dokter sê voordat die behandeling begin word. Jy het 'n verhoogde risiko om gedurende behandeling met **CANCALID** bloedklonte in jou are en slagare te ontwikkel. Indien jy miëlodisplastiese sindrome het, wat 'n groep versteurings is veroorsaak deur bloedselle wat swak gevorm is of nie behoorlik werk nie, kan jy meer geneig wees om 'n meer gevorderde toestand, genaamd akute miëloïede leukemie (AML), te ontwikkel. Daarby is dit nie bekend op watter manier **CANCALID** jou kanse om AML op te doen, affekteer nie. Jou dokter kan gevolglik toetse doen om te monitor vir tekens wat die waarskynlikheid beter gaan voorspel dat jy AML tydens behandeling met **CANCALID** kan ontwikkel.

Voor en tydens die behandeling met **CANCALID** gaan jy gereeld bloedtoetse ondergaan, want **CANCALID** kan 'n daling in die bloedselle veroorsaak wat help om infeksie te beveg en die bloed help om te stol. Jou dokter kan jou vra om 'n bloedtoets te ondergaan:

- voor behandeling
- elke week vir die eerste 8 weke van behandeling
- ten minste maandeliks daarna.

Jou dokter kan jou dosis **CANCALID** aanpas of jou behandeling staak, gebaseer op die resultate van jou bloedtoetse en op jou algemene toestand.

Voordat jy met behandeling begin, moet jy jou dokter inlig indien jy

- niersiekte het. Jou dokter kan jou dosis van **CANCALID** aanpas gegrond op hierdie inligting.
- enige tekens van 'n infeksie het, soos hoes of koors.
- 'n virusinfeksie het of voorheen gehad het, veral hepatitis B-infeksie, varicella zona, MIV. Indien jy twyfel, bespreek dit met jou dokter. Behandeling met **CANCALID** kan die virus heraktiveer by pasiënte wat die virus dra, met 'n gevolglike herhaling van die infeksie. Jou dokter behoort na te gaan of jy al ooit hepatitis B-infeksie gehad het.
- 'n hartaanval gehad het, al ooit 'n bloedklont gehad het, of indien jy 'n roker is, hoë bloeddruk of hoë cholesterolvlakke het.
- hart- of longsiekte het, want behandeling met **CANCALID** kan lewensbedreigende hoë bloeddruk in jou long- en hartslagare veroorsaak. Jou dokter gaan jou voor en tydens behandeling vir enige tekens en simptome van hart- of longsiekte evalueer.
- 'n allergiese reaksie gehad het toe jy talidomied geneem het ('n ander medisyne wat gebruik word om veelvuldige miëloom te behandel), soos uitslag, gejeuk, swelling, duiseligheid of moeisame asemhaling.
- in die verlede 'n kombinasie van enige van die volgende simptome ervaar het: uitslag op die gesig of 'n uitgebreide uitslag, hoë koors, griepagtige simptome, vergrote limfknope (tekens van hewige velreaksie, genaamd geneesmiddelreaksie met eosinofilie en sistemiese simptome (DRESS) (sien "Moontlike newe-effekte").

Jou dokter kan nagaan of jy 'n groot aantal tumore versprei deur jou liggaam het, insluitende jou beenmurg. Dit kan lei tot 'n toestand waar die tumore afgebreek word en ongewone vlakke van chemiese verbindings in die bloed vrystel, wat nierversaking kan veroorsaak (hierdie toestand word "tumorlisesindroom" genoem).

Jou dokter kan jou ondersoek om te sien of daar veranderings op jou vel is, soos rooi kolletjies of uitslag.

Jou dokter kan jou dosis van **CANCALID** aanpas of jou behandeling staak, gegrond op die resultate van jou bloedtoetse en op jou algemene toestand. Indien jy onlangs gediagnoseer is, kan jou dokter ook jou behandeling evalueer op grond van jou ouderdom en ander toestande wat jy reeds het.

Jy moenie bloed skenk tydens behandeling nie, insluitende tydens onderbrekings van die dosering en vir 4 weke na die einde van behandeling.

Jou dokter kan jou skildklier en die funksie daarvan nagaan, want **CANCALID** kan 'n effek daarop hê.

CANCALID affekteer die senuwees, wat kan veroorsaak dat jou hande of voete gevoelloos, tintelend of pynlik voel. Dit kan vir jou moeilik wees om knope vas te maak of ander fyn takies uit te voer.

Sê vir jou dokter indien jy hierdie simptome het. Soms moet die medisyne se dosis verlaag word.

CANCALID kan vertroebeling van visie veroorsaak (katarak), dit is belangrik om vir jou dokter te sê as jy enige visuele versteurings ondervind.

Jy moet nooit jou **CANCALID** vir 'n ander persoon gee nie. Neem enige ongebruikte kapsules teen die einde van behandeling terug na jou apteker.

Indien jy nie seker is of enige van bogenoemde op jou van toepassing is nie, bespreek dit met jou dokter of apteker voordat jy **CANCALID** neem.

Kinders en adolessente

CANCALID is nie by kinders of adolessente bestudeer nie en moet gevolglik nie in hierdie pasiëntpopulasie gebruik word nie.

Ander medisyne en CANCALID:

Sê altyd vir jou gesondheidsorgverskaffer indien jy enige ander medisyne neem (dit sluit komplementêre of tradisionele medisynes in).

Gebruik van **CANCALID** saam met hierdie medisynes kan ongewenste interaksies veroorsaak.

Sê veral vir jou dokter indien jy medisynes gebruik wat die volgende aktiewe bestanddele bevat:

- Warfarien (medisyne om bloedstolling te voorkom);
- Digoksien (medisyne gebruik om hartprobleme te behandel);
- Medisynes wat die vorming van rooibloedselle stimuleer, of ander middels wat die risiko van bloedklonte (trombose) kan verhoog, soos hormoonvervangingsterapie;
- Statiene (medisynes gebruik om hoë cholesterol te behandel).

Swangerskap, borsvoeding en vrugbaarheid

Indien jy swanger is of jou baba borsvoed, vermoed dat jy swanger mag wees of beplan om swanger te raak, raadpleeg asseblief jou dokter, apteker of ander gesondheidsorgverskaffer voordat jy **CANCALID** neem.

Swangerskap:

Jy moenie **CANCALID** neem wanneer jy swanger is nie, want daar word verwag dat dit skadelik vir die ongebore baba gaan wees. Daarby moet jy ook nie swanger raak terwyl jy **CANCALID** neem nie. Gevolglik moet jy twee doeltreffende metodes van voorbehoeding gebruik indien jy 'n vrugbare vrou is. Indien jy wel swanger raak tydens **CANCALID** behandeling, moet jy onmiddellik die behandeling staak en jou dokterinlig.

Mans wat **CANCALID** neem, verwys asseblief na die afdeling: "Waarskuwings en voorsorgmaatreëls". Indien jou geslagsmaat swanger raak terwyl jy **CANCALID** neem, moet jy onmiddellik jou dokter inlig. Dit word aanbeveel dat jou maat mediese advies inwin.

Borsvoeding:

Jy moenie borsvoed wanneer jy **CANCALID** neem nie.

Bestuur en gebruik van masjiene

Moenie 'n voertuig bestuur of masjiene hanteer indien jy newe-effekte ervaar nie, soos duiseligheid, moegheid, slaperigheid of dowwe visie.

Dit is nie altyd moontlik om te voorspel tot watter mate **CANCALID** met jou daaglikse aktiwiteite mag inmeng nie. Verseker asseblief dat jy nie bogenoemde aktiwiteite uitvoer nie, totdat jy weet tot watter mate **CANCALID** jou affekteer.

CANCALID bevat suiker

Indien jou dokter jou ingelig het dat jy onverdraagsaam vir sekere suikers is, kontak jou dokter voordat jy **CANCALID** neem.

3. Hoe om CANCALID te neem

Moenie medisynes wat vir jou voorgeskryf is, met enigiemand anders deel nie. Neem **CANCALID** altyd presies soos wat jou dokter vir jou gesê het. Vra gerus jou dokter of apteker indien jy onseker is.

CANCALID word alleen of in kombinasie met deksametasoon geneem. Neem altyd **CANCALID** alleen of **CANCALID** en deksametasoon in kombinasie, presies soos wat jou dokter vir jou gesê het. Kontroleer met jou dokter of apteker indien jy onseker is. Verwys na deksametasoon se inligtingsblad vir verdere inligting oor die gebruik en effekte daarvan.

Die gebruiklike dosis vir miëlodisplastiese sindrome is: 10 mg een keer per dag mondeliks geneem, op dae 1 – 21 van herhaalde 28 dag behandelingsiklusse.

Die gebruiklike dosis vir veelvuldige miëloom is: 25 mg/dag mondeliks op Dae 1 – 21 van herhaalde 28 dag siklusse. Die aanbevole dosis deksametasoon is 40 mg/dag op Dae 1 – 4, 9 – 12 en 17 – 20 van elke 28 dag siklus vir die eerste 4 siklusse van terapie en dan 40 mg/dag mondeliks op Dae 1 – 4, elke 28 dae.

Jou dokter sal die korrekte dosis vir jou toestand voorskryf. Jou dokter kan jou dosis **CANCALID** aanpas of jou behandeling staak, gegrond op die resultate van jou bloedtoetse en jou algemene toestand. Jy behoort die **CANCALID** kapsules heel in te sluk, verkieslik met water, een keer 'n dag. Moenie die kapsules breek, oopmaak of kou nie. Die **CANCALID** kapsules kan met of sonder kos geneem word.

Jy behoort **CANCALID** op omtrent dieselfde tyd elke dag te neem.

Jou dokter gaan vir jou sê hoe lank jou behandeling met **CANCALID** gaan duur. Moenie enige behandeling staak nie, behalwe as jou dokter sê jy moet.

CANCALID word in behandelingsiklusse geneem, waar elke siklus 28 dae duur. Jy moet volhou met die behandelingsiklusse totdat jou dokter jou aansê om op te hou.

Indien jy die indruk kry dat die uitwerking van **CANCALID** te sterk of te swak is, bespreek dit met jou dokter of apteker.

Indien jy meer CANCALID neem as wat jy behoort te neem

In geval van oordosering, raadpleeg jou dokter of apteker. Indien nie een van hulle beskikbaar is nie, kontak die naaste hospitaal of gifsentrum.

Indien jy vergeet om CANCALID te neem

Indien minder as 12 uur verloop het sedert 'n dosis oorgeslaan is, kan jy die dosis neem. Indien meer as 12 uur verloop het sedert 'n dosis op die gewone tyd oorgeslaan is, moet jy nie die dosis neem nie, maar die volgende dosis op die gebruiklike tyd die volgende dag neem.

Moenie 'n dubbele dosis neem om te vergoed vir die individuele dosisse wat oorgeslaan is nie.

4. Moontlike newe-effekte

CANCALID kan newe-effekte hê.

Nie alle newe-effekte wat vir **CANCALID** gerapporteer is, word in hierdie inligtingsblad ingesluit nie. Indien jou algemene gesondheid sou verswak of indien jy enige ongunstige effekte ondervind terwyl jy **CANCALID** neem, moet jy asseblief jou dokter, apteker of ander gesondheidsorgverskaffer raadpleeg.

CANCALID kan die getal witbloedselle verlaag wat infeksie beveg, asook die bloedselle wat die bloed help om te stol (plaatjies). **CANCALID** kan ook bloedklonte in die are veroorsaak (trombose).

Indien enige van die volgende voorkom, hou op om **CANCALID** te neem en sê onmiddellik vir jou dokter of gaan na die ongevalle-afdeling by jou naaste hospitaal:

- Swelling om die oë, in die gesig of die tong (wat in seldsame gevalle 'n ernstige allergiese reaksie kan wees);
- Uitslag wat versprei, met vel wat afgaan;
- Swelling in die enkels, gewrigte, arms en bene;
- Enige koors, kouekoors, seer keel, hoes, mondsere of enige ander simptome van infeksie
- Enige bloeding of kneusing in afwesigheid van 'n besering
- Enige pyn in die borskas of been;

Gehyg, enige kortasemheid, droë hoes.

Hierdie is baie ernstige newe-effekte. Indien jy enige daarvan ondervind, mag jy 'n ernstige reaksie op **CANCALID** gehad het. Jy mag dringend mediese bystand of hospitalisasie benodig.

Dit is belangrik om kennis te neem dat pasiënte met veelvuldige miëloom bykomende soorte kanker kan ontwikkel, en dit is moontlik dat hierdie risiko verhoog kan word met **CANCALID** behandeling, daarom moet jou dokter die voordeel en risiko noukeurig evalueer wanneer **CANCALID** vir jou voorgeskryf word.

Sê vir jou dokter indien jy enige van die volgende opmerk:

<u>Newe-effekte wat dikwels voorkom:</u>

- 'n Vermindering in die getal witbloedselle (die selle wat infeksie beveg), plaatjies (die selle wat die bloed help om te stol, wat bloedingsversteurings kan veroorsaak) en rooibloedselle (anemie, wat lei tot moegheid en swakheid)
- Hardlywigheid, diarree, naarheid, rooiheid van die vel, uitslag, braking, spierkrampe, knaende pyn in die spiere, beenpyn, gewrigspyn, moegheid, veralgemeende swelling insluitende swelling van die ledemate
- Koors en griepagtige simptome, insluitende koors, knaende spierpyn, hoofpyn en kouekoors
- Gevoelloosheid, tintelende of brandsensasie op die vel, pyn in die hande of voete, duiseligheid, tremor
- Smaakversteuring
- Verminderde eetlus, lae kaliumvlakke in die bloed
- Beenpyn (wat 'n simptoom van bloedklonte (trombose) kan wees), pyn in die bors, kortasemheid (wat 'n simptoom van bloedklonte in die longe kan wees)
- Infeksie van die long en boonste lugweg, kortasemheid, neusbloeding
- Dowwe visie
- Hoofpyn
- Borskaspyn
- Moeisame asemhaling
- Alle soorte infeksies
- Infeksie van die sinusse by die neus
- Bloeding in die tandvleis, maag of derms, kneusing
- Styging of val in bloeddruk, stadige, vinnige of onegalige hartklop
- Uitbarstings op die vel, vel bars, skilfer af
- Galbulte, gejeuk, droë vel, verhoogde sweetafskeiding, ontwatering
- Seer, ontsteekte mond, droë mond
- Buikpyn
- Produseer baie meer of baie minder urine as gewoonlik (wat 'n simptoom van nierversaking kan wees)
- Kortasemheid, veral wanneer jy plat lê (wat 'n simptoom van hartversaking kan wees)
- Sukkel om 'n ereksie te kry
- Pyn in die bors wat versprei na die arms, nek, kaak, rug of maag, voel sweterig en uitasem, voel naar of gooi op (wat simptome van 'n hartaanval/miokardiale infarksie kan wees)
- Beroerte, floute
- Spierswakheid
- Gewrigswelling
- Lae vlakke van kalsium, fosfaat of magnesium in die bloed
- Depressie
- Katarak
- Belemmerde visie
- Abnormale lewertoetsresultate
- Ysteroorlading
- Veranderende bui
- Tandpyn

<u>Newe-effekte wat minder dikwels voorkom:</u>

- Bloeding in die brein
- Bloedsomloopprobleme
- Sekere soorte velkanker
- Hipersensitiwiteit of 'n allergiese reaksie (angio-edeem), 'n soort allergiese reaksie wat simptome soos galbulte, veluitslag, swelling van die oë, mond of gesig, sukkel om asem te haal, of 'n gejeuk het
- Tumorlisesindroom – metaboliese komplikasies wat tydens behandeling van kanker en soms selfs sonder behandeling kan voorkom.

Ander newe-effekte waar die frekwensie onbekend is, is skielike of geringe maar verergerende pyn in die bo-buik en/of rug, wat vir 'n paar dae volhou, moontlik met gepaardgaande naarheid, braking, koors en 'n vinnige polsspoed – hierdie simptome kan as gevolg van inflammasie van die pankreas voorkom.

Indien jy enige newe-effekte opmerk wat nie in hierdie inligtingsblad genoem word nie, lig asseblief jou dokter of apteker daaroor in.

Rapportering van newe-effekte

Indien jy enige newe-effekte ondervind, bespreek dit met jou dokter, apteker of verpleegkundige. Dit sluit enige moontlike newe-effekte wat nie in hierdie inligtingsblad gelys word nie, in. Jy kan ook newe-effekte aan SAHPRA rapporteer via https://www.sahpra.org.za/Publications/Index/8. Deur newe-effekte te rapporteer, kan jy help om meer inligting rakende die veiligheid van **CANCALID** te verskaf.

5. Hoe om CANCALID te berg

BERG ALLE MEDISYNES BUITE BEREIK VAN KINDERS.

CANCALID gaan in die apteek gestoor word.

Bêre by of onder 25 °C.

Hou die houer in die buitenste karton om teen lig te beskerm.

Moenie gebruik ná die vervaldatum wat op die flessie en die karton voorkom nie.

Neem alle ongebruikte medisyne terug na jou apteker.

Moenie ongebruikte medisyne in dreine en rioolstelsels (bv. toilette) wegdoen nie.

6. Inhoud van die verpakking en ander inligting

Die aktiewe bestanddeel is lenalidomied.

CANCALID 2,5 mg:
Elke kapsule bevat 2,5 mg lenalidomied.
Bevat suiker: watervrye laktose 20,0 mg.

CANCALID 5 mg:
Elke kapsule bevat 5 mg lenalidomied.
Bevat suiker: watervrye laktose 40,0 mg.

CANCALID 7,5 mg:
Elke kapsule bevat 7,5 mg lenalidomied.
Bevat suiker: watervrye laktose 60,0 mg.

CANCALID 10 mg:
Elke kapsule bevat 10 mg lenalidomied.
Bevat suiker: watervrye laktose 80,0 mg.

CANCALID 15 mg:
Elke kapsule bevat 15 mg lenalidomied.
Bevat suiker: watervrye laktose 120,0 mg.

CANCALID 20 mg:
Elke kapsule bevat 20 mg lenalidomied.
Bevat suiker: watervrye laktose 160,0 mg.

CANCALID 25 mg:
Elke kapsule bevat 25 mg lenalidomied.
Bevat suiker: watervrye laktose 200,0 mg.

Die ander bestanddele van **CANCALID** is watervrye laktose, mikrokristallyne sellulose, natriumkruiskarmellose en magnesiumsteraat.

Samestelling van kapsuledoppie:

CANCALID 2,5 mg: Gelatien, titaandioksied, geel ysteroksied, FD &C Blue 2
CANCALID 5 mg: Gelatien, titaandioksied
CANCALID 2,5 mg: Gelatien, titaandioksied, geel ysteroksied, FD &C Blue 2
CANCALID 7,5 mg: Gelatien, titaandioksied
CANCALID 10 mg: Gelatien, titaandioksied, geel ysteroksied, rooi ysteroksied, FD &C Blue 2
CANCALID 15 mg: Gelatien, titaandioksied, rooi ysteroksied
CANCALID 20 mg: Gelatien, titaandioksied, geel ysteroksied, rooi ysteroksied
CANCALID 25 mg: Gelatien, titaandioksied

Samestelling van ink vir drukwerk: Skilferlak, gedehidreerde alkohol, isopropielalkohol, butielalkohol, sterk ammoniakoplossing, swart ysteroksied, kaliumhidroksied.

Hoe CANCALID lyk en inhoud van die verpakking:

CANCALID 2,5 mg: Naaswit tot dowwe geel poeier binne in groen, ondeursigtige kapsules, met "L 2.5" in swart ink op die doppie gedruk en 'n skoon romp, grootte 4, harde gelatienkapsule.

CANCALID 5 mg: Naaswit tot dowwe geel poeier binne in wit, ondeursigtige kapsules, met "L 5" in swart ink op die doppie gedruk en 'n skoon romp, grootte 2, harde gelatienkapsule.

CANCALID 7,5 mg: Naaswit tot dowwe geel poeier binne in wit, ondeursigtige kapsules, met "L 7.5" in swart ink op die doppie gedruk en 'n skoon romp, grootte 2, harde gelatienkapsule.

CANCALID 10 mg: Naaswit tot dowwe geel poeier binne in olyfgroen en oranje ondeursigtige kapsules, met "L10" in swart ink op die doppie gedruk en 'n skoon romp, grootte 0, harde gelatienkapsule.

CANCALID 15 mg: Naaswit tot dowwe geel poeier binne in donkeroranje, ondeursigtige kapsules, met "L 15" in swart ink op die doppie gedruk en 'n skoon romp, grootte 0, harde gelatienkapsule.

CANCALID 20 mg: Naaswit tot dowwe geel poeier binne in oranje ondeursigtige kapsules, met "L 20" in swart ink op die doppie gedruk en 'n skoon romp, grootte 0, harde gelatienkapsule.

CANCALID 25 mg: Naaswit tot dowwe geel poeier binne in wit, ondeursigtige kapsules, met "L 25" in swart ink op die doppie gedruk en 'n skoon romp, grootte 0, harde gelatienkapsule.

Kapsules word verpak in deurskynende PVC-film en aluminiumfoelie-stulpstrook. Die stulpstroke word verder in voorafbedrukte kartonne verpak, saam met 'n inligtingsblad.

Verpakkingsgroottes: 21s (3 x stulpstroke van 7 kapsules).

Houer van Registrasiesertifikaat

AUROGEN SA (EDMS.) BPK.
Woodhill Office Park, Gebou 1, Eerste Vloer
Phillip Engelbrechtlaan 53
Meyersdal, Uitbr. 12
1448 Johannesburg
Suid-Afrika

Hierdie inligtingsblad is laas hersien

08 Augustus 2023

Registrasienommers

CANCALID 2,5 mg: 56/32/0518.511
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 20 mg: 56/32/0523.516
CANCALID 25 mg: 56/32/0524.517

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