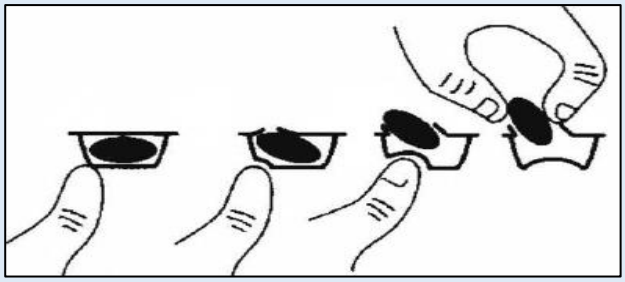
It is recommended to press only on one site at the end of the capsule (see figure), as therefore the pressure is located to one site only, which reduces the risk of capsule deformation or breakage.



Healthcare professionals and caregivers should wear disposable gloves when handling the blister or capsule. Gloves should then be removed carefully to prevent skin exposure, placed in a sealable plastic polyethylene bag and disposed of in accordance with local requirements. Hands should then be washed thoroughly with soap and water. Women who are pregnant or suspect they may be pregnant should not handle the blister or capsule.

Refer below for further guidance.

When handling the medicinal product, use the following precautions to prevent potential exposure if you are a healthcare professional or caregiver

- If you are a woman who is pregnant or suspect that you may be pregnant, you should not handle the blister or capsule
- Wear disposable gloves when handling the product and / or its packaging (e.g. blister or capsule).
- Use proper technique when removing gloves to prevent potential skin exposure (see below)
- Put gloves in a sealable plastic polyethylene bag and dispose of them according to local requirements.
- Wash hands thoroughly with soap and water after removing gloves.

If a drug product package appears visibly damaged, use the following extra precautions to prevent exposure.

- If the outer carton is visibly damaged - **Do Not Open.**
- If the blister strips are damaged or leaking or capsules are noted to be damaged or leaking,
- **Close the outer carton immediately.**
- Place the product in a sealed plastic polyethylene bag.
- Return unused packs to the pharmacist for safe disposal as soon as possible.

If the product is released or spills, take appropriate precautions to minimise exposure by using appropriate personal protection:

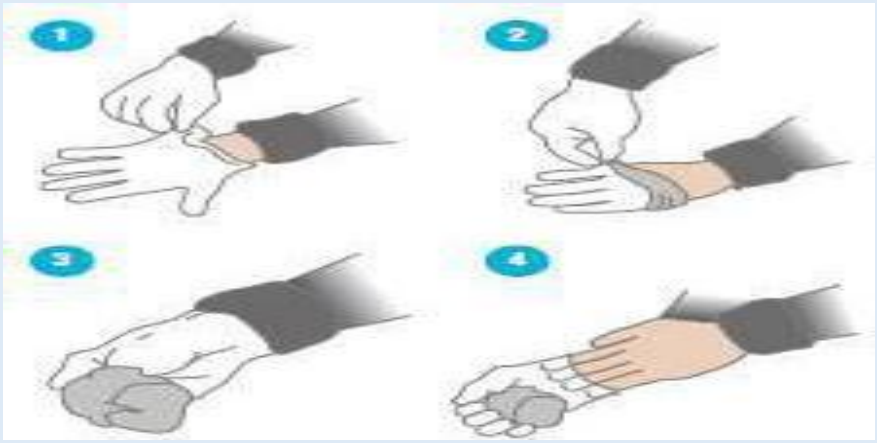
- If the capsules are crushed or broken, dust-containing drug substance may be released. Avoid dispersing the powder and avoid breathing the powder.
- Wear disposable gloves to clean up the powder.
- Place a damp cloth or towel over the powder area to minimise the entry of powder into the air. Add excess liquid to allow the material to enter the solution. After handling, clean the area thoroughly with soap and water and dry it.
- Place all contaminated materials, including damp cloths or towels and gloves, into a sealable polyethylene plastic bag and dispose of them in accordance with local requirements for the disposal of medicinal products.
- Wash your hands thoroughly with soap and water after removing the gloves.

Please report to Cipla immediately to Lenalidomide.cipla@cipla.com

If the contents of the capsules are attached to the skin or mucous membranes

- If you touch the powder, wash the exposed area thoroughly under running water and soap.
- If the powder gets in contact with your eye, if worn and easy to do, remove contact lenses and discard them. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs, please contact an ophthalmologist.

Proper technique for removing gloves:



- Grasp the outer edge near the wrist (1).
- Peel away from the hand, turning the glove inside out (2).
- Hold in opposite gloved hand (3).
- Slide ungloved fingers under the wrist of the remaining glove. Be careful not to touch the outside of this glove (4).
- Peel off from inside, creating a bag for both gloves.
- Discard in the appropriate container.
- Wash your hands with soap and water thoroughly.

6.2 Blood/Semen Donation

Patients should not donate blood/semen during treatment and for at least seven days after cessation of treatment with lenalidomide.

7. Prescribing lenalidomide

7.1 Maximum Prescription Lengths

Prescriptions for women of childbearing potential can be for a maximum duration of 4 weeks according to the approved indications dosing regimens (posology). For all other patients, prescriptions of lenalidomide should be limited to a maximum duration of 12 weeks and continuation of treatment requires a new prescription. Lenalidomide treatment must be initiated and monitored under the supervision of physicians with expertise in managing immunomodulatory or chemotherapeutic agents and a full understanding of the risks of lenalidomide therapy and monitoring requirements

7.2 Initial prescription

Before issuing the initial prescription, you must:

- Counsel the patient on the safe use of lenalidomide in accordance with the measures described in this brochure and the PI, which can be found on the TGA website: https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2019-PI-02101-1&d=20220418172310101
- Obtain their written confirmation (using the correct Treatment Initiation Form) that they have received and understood this information, and provide the patient with a copy
- Provide the patient with a Patient Brochure and a Patient Card. Provide an 'electronic Prescription Authorisation Form' to the patient with each lenalidomide prescription, and this will contain:
  - Patient initials, date of birth and diagnosis
  - Prescriber name, signature and date
  - Patient category (women of childbearing potential, women of non-childbearing potential or male)
  - Confirmation that they have received counselling about the teratogenic risk of lenalidomide and the required contraceptive measures for women of childbearing potential and male patients
  - For women of childbearing potential, the pregnancy test date and result.
  - That your patient is using effective contraception (if appropriate)

The patient must present their 'electronic Prescription Authorisation Form' to the pharmacy along with their prescription, and the pharmacy will check this form prior to dispensing lenalidomide.

7.3 Repeat of Subsequent Prescriptions

The patient must return to a prescriber for every repeat prescription of lenalidomide and a new ePAF must be completed and submitted.

8. Dispensing lenalidomide

It is a requirement of the Pregnancy Prevention Program that pharmacies wishing to purchase and dispense lenalidomide are registered with Cipla. Registration involves receiving a Healthcare Professional's Information Pack.

Dispensing of lenalidomide will only be allowed from pharmacies registered with Cipla. Cipla will not authorise the purchase and supply of lenalidomide to pharmacies not registered with Cipla.

Lenalidomide is supplied to pharmacies registered with Cipla's Risk Minimisation Program, known as the web-based platform named 'Cipla lenalidomide aRMM Program', only for the purpose of dispensing the product by the PPP registered pharmacy to the patient.

In order to be registered, the Chief Pharmacist or appointed deputy of the institution wishing to dispense must agree to implement the use of an electronic Prescription Authorisation Form.

When completing ePAF, it asks the prescriber to confirm:

- The patient's diagnosis
- Whether the patient is male or female
- If female, the patient's childbearing potential
- If of childbearing potential that adequate contraception is in place and the date of the last negative pregnancy test, which must be within the three days prior to the date of the prescription
- If male, counselling regarding the use of condoms has taken place

- That informed consent has been completed by the patient
- That the prescriber has read and understood the contents of this Healthcare Professional's Information Pack.

When completing ePAF, it asks the pharmacist to confirm:

- That the electronic Prescription Authorisation Form has been completed in full by the prescriber

- That dispensing for women of childbearing potential is taking place within **seven days** of the prescription date
- That the pharmacist has read and understood the contents of this Healthcare Professional's Information Pack.

For women of childbearing potential, prescriptions for lenalidomide should be limited to 4 weeks of treatment and continuation of treatment requires a new prescription. Ideally, pregnancy testing, issuing a prescription and dispensing should occur on the same day.
Dispensing of lenalidomide should occur within a maximum of 7 days of the prescription, and the date of the last negative pregnancy test must be within 3 days prior to the date of the prescription.

For males and women of non-childbearing potential, prescriptions of lenalidomide should be limited to 12 weeks and continuation of treatment requires a new prescription.

Pharmacists are required to send a copy of **every** electronic Prescription Authorisation Form to Cipla immediately after dispensing (Lenalidomide.cipla@cipla.com).

8.1 Dispensing Advice

- Please ensure that you dispense lenalidomide blisters intact; capsules must not be removed from blisters and packaged into bottles
- For each prescription, dispense a maximum of a 4-week supply for women of childbearing potential or a 12-week supply for all other patients
- Please educate all pharmacists within your pharmacy about the dispensing procedures for
- lenalidomide
- Instruct patients to return any unused lenalidomide to the pharmacy. Pharmacies must accept any unused lenalidomide returned by patients for destruction and follow Good Pharmacy Practice guidelines for the destruction of dangerous medicines.

8.2 Follow-up Assessment of the Effectiveness of the Program

The terms of the lenalidomide Marketing Authorisation require Cipla to assess the effectiveness of the Pregnancy Prevention Program in order to ensure that all reasonable steps are being taken to reduce the risk of foetal exposure to lenalidomide.

Cipla is therefore obliged to perform audits at regular intervals and to report appropriately anonymous and aggregated results to the TGA.

Cipla will conduct the audit from all of the completed electronic Prescription Authorisation Forms received.

Pharmacies must send a copy of every completed electronic Prescription Authorisation Form immediately after dispensing to Cipla, then Cipla will be able to conduct the pharmacy audit using these forms (a manual self-audit by pharmacies will not be required). It is critical, therefore, that electronic Prescription Authorisation Forms are completed accurately and that pharmacies thereby assist Cipla in auditing the effectiveness of the Pregnancy Prevention Program.

9. Posology

9.1 Multiple Myeloma (MM)

9.1.1 Lenalidomide Maintenance in Patients who have undergone autologous stem cell transplantation (ASCT)

The recommended starting dose is lenalidomide 10 mg orally once daily continuously (on Days 1 to 28 of repeated 28-day cycles) given until disease progression or intolerance. After 3 cycles of lenalidomide maintenance, the dose can be increased to 15 mg orally once daily if tolerated.

Dose reduction steps are provided in Section 4.2 of the PI.

9.1.2 Lenalidomide in Combination with Dexamethasone Until Disease Progression in Patients who are Not Eligible for Transplant.

The recommended starting dose of lenalidomide is 25 mg orally once daily on Days 1 to 21 of repeated 28-day cycles.

The recommended dose of dexamethasone is 40 mg orally once daily on Days 1, 8, 15 and 22 of repeated 28-day cycles. Patients may continue lenalidomide and dexamethasone therapy until disease progression or intolerance.

Dose reduction steps are provided in Section 4.2 of the PI.

9.1.3 Lenalidomide in Combination with Bortezomib and Dexamethasone Followed by Lenalidomide and Dexamethasone until Disease Progression in Patients who are Not Eligible for Transplant

The recommended starting dose of lenalidomide is 25 mg orally once daily on Days 1 to 14 of each 21-day cycle in combination with bortezomib and dexamethasone. The recommended dose of bortezomib is 1.3 mg/m2 body surface area subcutaneously twice weekly on Days 1, 4, 8 and 11 of each 21-day cycle. Up to eight 21-day treatment cycles (24 weeks of initial treatment) are recommended. Continue lenalidomide 25 mg orally once daily on Days 1 to 21 of repeated 28-day cycles in combination with dexamethasone. Treatment should be continued until disease progression or unacceptable toxicity.

Dose reduction steps are provided in Section 4.2 of the PI

9.1.4 Lenalidomide in Combination with Melphalan and Prednisone Followed by Lenalidomide Maintenance in Patients who are Not Eligible for Transplant

The recommended starting dose is lenalidomide 10 mg orally once daily on Days 1 to 21 of repeated 28-day cycles for up to 9 cycles, melphalan 0.18 mg/kg orally on Days 1 to 4 of repeated 28-day cycles, prednisone 2 mg/kg orally on Days 1 to 4 of repeated 28-day cycles. Patients who complete 9 cycles or who are unable to complete the combination therapy due to intolerance are treated with lenalidomide monotherapy as follows: 10 mg orally once daily on Days 1 to 21 of repeated 28-day cycles given until disease progression.

Dose reduction steps are provided in Section 4.2 of the PI.

9.1.5 Multiple Myeloma with at Least One Prior Therapy

The recommended starting dose of lenalidomide is 25 mg orally once daily on Days 1 to 21 of repeated 28-day cycles.

The recommended dose of dexamethasone is 40 mg orally once daily on Days 1 to 4, 9 to 12, and 17 to 20 of each 28-day cycle for the first 4 cycles of therapy and then 40 mg once daily on Days 1 to 4 every 28 days. Prescribers should carefully evaluate which dose of dexamethasone to use, taking into account the condition and disease status of the patient.

Dose reduction steps are provided in Section 4.2 of the PI.

9.2 Myelodysplastic Syndromes (MDS)

For patients on therapy for del 5q MDS, CBC should be monitored weekly for the first eight weeks of therapy and at least monthly thereafter.

The recommended starting dose of lenalidomide is 10 mg given orally once a day on Days 1 to 21 of repeating 28-day treatment cycles. Dosing is continued or modified based upon clinical and laboratory findings

Dose reduction steps are provided in Section 4.2 of the PI.

9.3 Mantle Cell Lymphoma

The recommended starting dose of lenalidomide is 25 mg once daily on Days 1 to 21 of repeated 28-day cycles. Dose reduction steps are provided in Section 4.2 of the PI.

10. Selected Risks of lenalidomide

The following section contains advice to Healthcare Professionals about how to minimise some of the main risks associated with the use of lenalidomide. Please also refer to PI (Section 4.2 Dose and Method of Administration, 4.3 Contraindications, 4.4 Special warnings and precautions for use and 4.8 Adverse Effects (Undesirable Effects).

10.1 Tumour flare reaction and tumour lysis syndrome

Tumour flare reaction (TFR) has commonly been observed in patients with mantle cell lymphoma who were treated with lenalidomide. The patients at risk of TFR are those with high tumour burden prior to treatment. Caution should be practiced when introducing these patients to lenalidomide. These patients should be monitored closely, especially during the first cycle or dose-escalation and appropriate precautions taken.

At the prescriber's discretion, lenalidomide may be continued in patients with Grade 1 or 2 TFR without interruption or modification. At the prescriber's discretion, therapy with non-steroidal anti-inflammatory drugs (NSAIDs), limited duration corticosteroids, and/or narcotic analgesics may be administered. In patients with Grade 3 or 4 TFR, withhold treatment with lenalidomide and initiate therapy with NSAIDs, corticosteroids and/or narcotic analgesics. When TFR resolves to ≤ Grade 1, restart lenalidomide treatment at the same dose level for the rest of the cycle. Patients may be treated for management of symptoms per the guidance for treatment of Grade 1 and 2 TFR.

There have been rare reports of tumour lysis syndrome (TLS) in patients with MM treated with lenalidomide and no reports in patients with MDS treated with lenalidomide (see section 4.4 of PI).

10.2 Second Primary Malignancies (SPM)

In clinical trials in NDMM patients not eligible for ASCT, a 4.9-fold increase in the incidence rate of haematologic second primary malignancies (SPM) (cases of AML and MDS) has been observed in patients receiving lenalidomide in combination with melphalan and prednisone (MPR+R) until progression (1.75 per 100 person-years) compared with melphalan in combination with prednisone (MPp+p) (0.36 per 100 person-years). A 2.12-fold increase in the incidence rate of solid tumour SPM has been observed in patients receiving MPR+R (9 cycles) (1.57 per 100 person-years) compared with MPp+p (0.74 per 100 person-years).

In NDMM patients receiving lenalidomide in combination with dexamethasone (len/dex) until progression or for 18 months, the haematologic SPM incidence rate (0.16 per 100 person-years) was not increased as compared to thalidomide in combination with melphalan and prednisone (MPT) (0.79 per 100 person-years). A 1.3-fold increase in the incidence rate of solid tumour SPM has been observed in patients receiving len/dex until progression or for 18 months (1.58 per 100 person-years) compared to MPT (1.19 per 100 person-years).

In clinical trials of NDMM patients eligible for ASCT, an increased incidence rate of haematologic SPM (most notably AML, MDS and B-cell malignancies [including Hodgkin's lymphoma] has been observed in patients receiving lenalidomide maintenance immediately following high-dose melphalan/ASCT (1.31 per 100 person-years) compared with patients who received placebo (0.58 per 100 person-years). The incidence rate of solid tumour SPMs was 1.36 per 100 person-years for the lenalidomide arms and 1.05 per 100 person-years for the placebo arms.

Based on a low number of cases, a numerical imbalance in SPM (comprising mainly of basal cell and squamous cell skin cancers) has been observed in clinical trials in previously treated MM patients with len/dex (3.98 per 100 patient-years) compared with placebo/dex (1.38 per 100 patient-years).

Subjects who received lenalidomide-containing therapy until disease progression did not show a higher incidence of invasive SPM than subjects treated in the fixed duration lenalidomide-containing arms. These results suggest that the duration of lenalidomide treatment is not associated with an increased risk for the occurrence of invasive SPM.

Both the benefit achieved with lenalidomide and the risk of SPMs should be considered and discussed with patients before initiating treatment with the product. Physicians should also carefully evaluate patients before and during treatment using standard cancer screening for the occurrence of SPMs and institute treatment as appropriate.

11. Disposal and other handling of unwanted medicine

Capsules should not be opened or crushed. If powder from lenalidomide makes contact with the skin, the skin should be washed immediately and thoroughly with soap and water. If lenalidomide makes contact with the mucous membranes, they should be thoroughly flushed with water.

Healthcare professionals and caregivers should wear disposable gloves when handling the blister or capsule.

Gloves should then be removed carefully to prevent skin exposure, placed in a sealable plastic polyethylene bag and disposed of in accordance with local requirements. Hands should then be washed thoroughly with soap and water. Women who are pregnant or suspect they may be pregnant should not handle the blister or capsule.

Patients should be instructed never to give lenalidomide to another person and to return any unused capsules to the pharmacist at the end of treatment for safe disposal in accordance with local requirements.

12. Reporting of adverse reactions, Suspected and Confirmed Pregnancies, and Foetal Exposures

The safe use of lenalidomide is of paramount importance. As part of the safety monitoring, Cipla wants to know about the side effects that have occurred with lenalidomide. Adverse event and pregnancy reporting forms are included in Healthcare Professional's Information Pack. Adverse event form should be forwarded to Cipla via drugsafety@Cipla.com, and the pregnancy reporting form should be forwarded to Cipla via Lenalidomide.cipla@cipla.com.

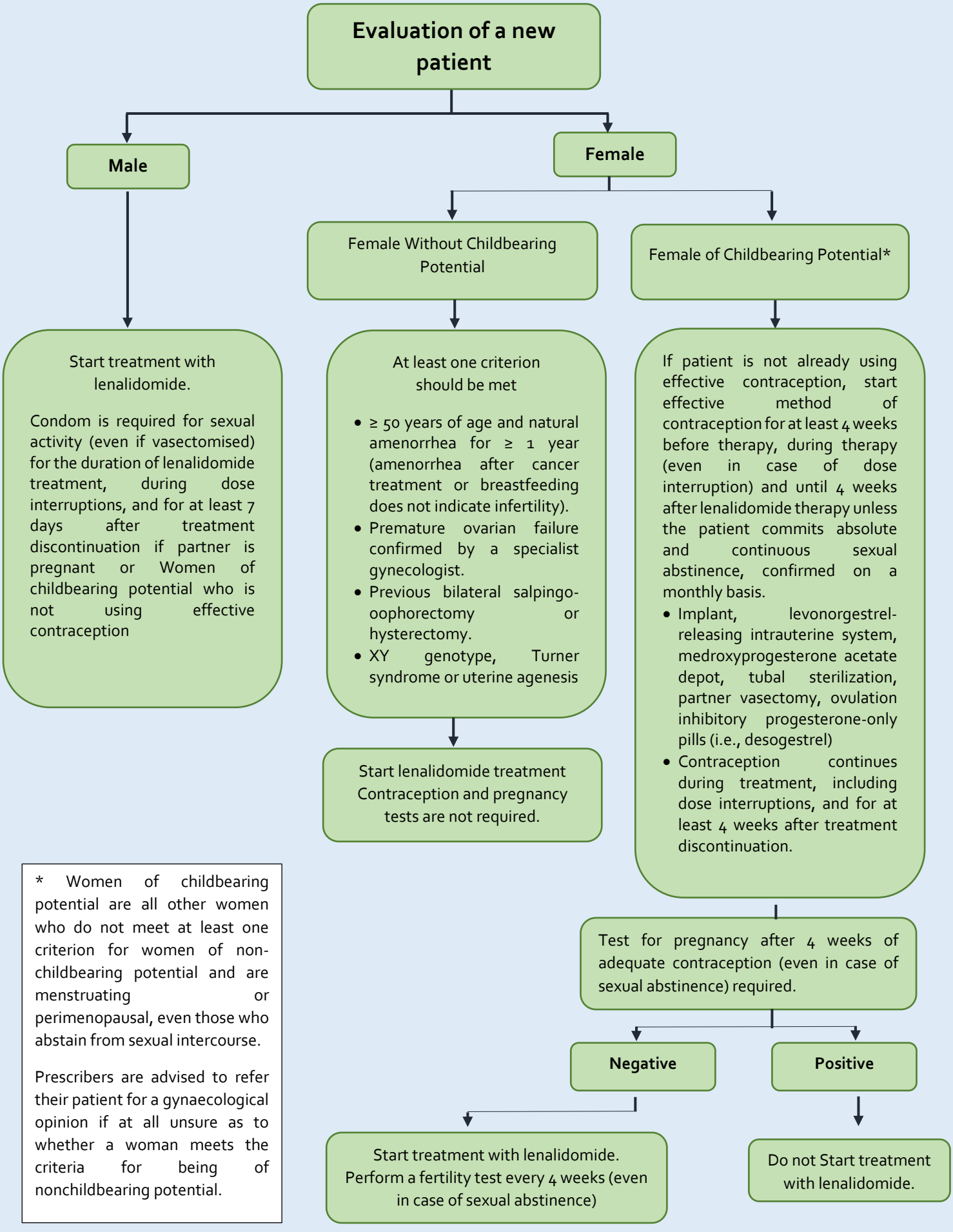
Report the suspected pregnancy to the TGA via the Blue Card Scheme website: www.tga.gov.au/reporting-problems

- You can report the suspected pregnancy online via the Blue Card website: www.tga.gov.au/reporting-problems
- Alternatively, Blue Cards for reporting are available:
    - by mail to Pharmacovigilance and Special Access Branch, Reply Paid 100, Woden ACT 2606;
    - by emailing adr.reports@tga.gov.au ;
    - by FAX to 02 6232 8392;

13. Patient Categorisation Algorithm

The description of the Pregnancy Prevention Program and the categorisation of patients based on sex and childbearing potential is presented in the below-given algorithm.

Patient Categorization Algorithm



* Women of childbearing potential are all other women who do not meet at least one criterion for women of non-childbearing potential and are menstruating or perimenopausal, even those who abstain from sexual intercourse.

Prescribers are advised to refer their patient for a gynaecological opinion if at all unsure as to whether a woman meets the criteria for being of nonchildbearing potential.

14. Contact Details

For information and questions on the Risk Management of Cipla products, the Pregnancy Prevention Program, pregnancy reporting form and pharmacy registrations, please contact Cipla:
Email: Lenalidomide.cipla@cipla.com

For adverse event form: drugsafety@Cipla.com

Phone no: 1800 87 86 85

Approved by TGA:Jul 2023