# Lenalidomide Pregnancy Prevention Programme

## And

## Information for Healthcare Professionals Prescribing or Dispensing Lenalidomide

**Important Safety Information:**

Healthcare Professionals involved in the prescribing or dispensing of lenalidomide must read and understand the information contained within this brochure.
For complete safety information please refer to the Summary of Product Characteristics (SmPC) for lenalidomide, available on the electronic medicines compendium (emc) website: www.medicines.org.uk/emc

Pathfinder
Risk Management Platform

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This guide contains the information needed for the prescribing and dispensing of lenalidomide, including information about the Pregnancy Prevention Programme (PPP) and important safety information. This guide will help you understand these problems and make sure you know what to do before prescribing and dispensing lenalidomide.

# Pregnancy Prevention Programme:

If lenalidomide is taken during pregnancy it is expected to cause severe birth defects or death to an unborn baby. This Programme is designed to make sure that unborn babies are not exposed to lenalidomide. It will provide you with information about how to follow the programme and explain your responsibilities.

It is a requirement of the Pregnancy Prevention Programme that all healthcare professionals (HCPs) ensure that they have read and understood the Healthcare Professionals Information guide before prescribing or dispensing lenalidomide for any patient.

Important information about the safe disposal of unwanted capsules and restrictions on donating blood during treatment is also included in this guide.

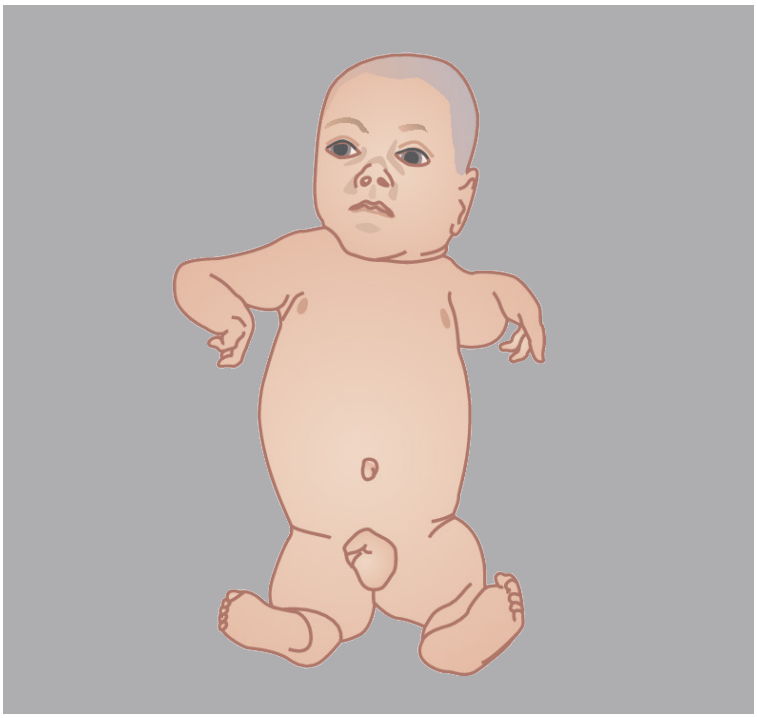
To ensure your patients' health and safety, please read this guide carefully. You must ensure that your patients fully understand what you have told them about lenalidomide and that they have provided written confirmation on the Treatment Initiation Form, before starting treatment.

For full information regarding the requirements of the Pregnancy Prevention Programme, as well as safety information, side effects and recommended precautions please also refer to the relevant Summary of Product Characteristics (SmPC), which is available at the following websites www.mhra.gov.uk ; www.ema.europe.eu

# Lenalidomide - Risk of Teratogenicity

Lenalidomide is structurally related to thalidomide. Thalidomide is a known human teratogenic substance that causes severe life-threatening birth defects. An embryofoetal development study has been conducted in monkeys administered lenalidomide at doses up to 4mg/kg/day. Findings from this study showed that lenalidomide produced external malformations (short limbs, bent digits, wrist and/or tail, supernumerary or absent digits) in the offspring of female monkeys who received the drug during pregnancy. Thalidomide produced similar types of malformations in the same study.

If lenalidomide is taken during pregnancy, a teratogenic effect is expected. Therefore, lenalidomide is contraindicated in pregnancy and in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are met.



## Lenalidomide Pregnancy Prevention Programme

- It is a requirement of the Pregnancy Prevention Programme that all Healthcare Professionals ensure that they have read and understood this guide before prescribing or dispensing lenalidomide for any patient.

- All men and all women of childbearing potential should undergo, at treatment initiation, counselling regarding the need to avoid foetal exposure to lenalidomide during pregnancy. Treatment Initiation Forms and a treatment initiation checklist are available for this purpose. The patient should receive a copy of the Treatment Initiation Form when completed.

- The description of the Pregnancy Prevention Programme and the categorisation of patients based on sex and childbearing potential is set out in the algorithm available on Pathfinder RMP and is also available in this Healthcare Professional`s Information Guide, see section 7.0.

- Patients should be capable of complying with the requirements of safe use of lenalidomide.

- Patients must be provided with the appropriate Patient Brochure, Treatment Initiation Form and Patient Pocket Information Card.

The lenalidomide MAH licence holders Pregnancy Prevention Programme materials are contained within the Pathfinder RMP and additional hard copies can be obtained by using the contact details displayed on the back of this guide. Electronic copies of the materials are also available for download on the website www.medicines.org.uk (enter 'Lenalidomide' under 'Find a Medicine' and click 'EdM' under the 'Documents' column for the relevant Lenalidomide product).

You must ensure that your patient fully understands what you have told them about lenalidomide before starting the treatment.

In order to obtain lenalidomide, it is a requirement of the Pregnancy Prevention Programme that all healthcare professionals ensure that they have read and understood this pack before prescribing or dispensing lenalidomide for **any** patient.

- Prescribers must complete the appropriate treatment initiation form for the patient before the first prescription is issued
- Pharmacies must register with Pharmacare Group to be able to order and dispense lenalidomide. To do this, the pharmacist must either; contact Pharmacare Group using the details at the front of this brochure or use the Pharmacy Registration Form on the Pathfinder RMP platform
- Every prescription for Lenalidomide must be accompanied by a paper Prescription Authorisation Form, which must be completed by the prescriber and the pharmacist. A copy of each PAF must be sent to Pharmacare group.
- The pharmacy registration form and Prescription Authorisation Forms are in subsequent sections of this pack.

All patients should be given a Patient Brochure and a Patient Pocket Information Card to take home – these materials remind patients of the key educational information and risks of treatment and can be found in the Information for Patients section.For women of childbearing potential, prescriptions of lenalidomide should be limited to a maximum duration of 4 weeks according to the approved indications dosing regimens (posology) 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 the 3 days prior to the date of the prescription.

For all other patients, prescriptions of lenalidomide should be limited to 12 weeks and continuation of treatment requires a new prescription. Pharmacists are required to send copies of every Prescription Authorisation Form immediately after dispensing to (email for paper submission to support@pharmacaregroup.co.uk)

In order to ensure that the actions to minimise the risk of foetal exposure are carried out for all patients, dispensing of lenalidomide will only be allowed from pharmacies registered with the NHS Licence holders Pregnancy Prevention Programme. The Marketing Authorisation Holders will not authorise supply of their respective lenalidomide products to pharmacies that are not registered.

The following are core requirements of the lenalidomide Pregnancy Prevention Programme:

- A controlled distribution system
- All healthcare professionals dispensing or prescribing lenalidomide must read and understand the Lenalidomide Healthcare Professional's Information Guide.
- All pharmacies who dispense lenalidomide from MAH licence holders must agree to implement risk minimisation by registering with the Lenalidomide MAH licence holders Pregnancy Prevention Programme
- Every prescription for lenalidomide must be accompanied by a Prescription Authorisation Form which must be completed by the prescriber and the pharmacist.

# Table of Contents

# 1.0 Introduction

Lenalidomide is an immunomodulating medicinal product.

Two Phase III clinical studies assessed lenalidomide maintenance in patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation (ASCT) was assessed in (CALGB 100104 and IFM 2005 02).
In Study CALGB 100104, patients were randomised 1:1 within 90 to 100 days after ASCT to receive either lenalidomide or placebo maintenance. The maintenance dose was 10 mg once daily on Days 1 to 28 of repeated 28-day cycles (increased up to 15 mg once daily after 3 months in the absence of dose limiting toxicity), and treatment was continued until disease progression.

The results of progression free survival (PFS) at unblinding (cut-off of 17 December 2009) showed a 62% reduction in risk of disease progression or death favouring lenalidomide over placebo. The Hazard Ratio was 0.38 (95% CI 0.27, 0.54; p <0.001). The median overall PFS was 33.9 months (95% CI not evaluable [NE], NE) in the lenalidomide arm versus 19.0 months (95% CI 16.2, 25.6) in the placebo arm. The updated PFS, using a cut-off of 01 February 2016, continued to show a PFS advantage for lenalidomide (Hazard Ratio = 0.61; p <0.001).

In Study IFM 2005-02, patients who had undergone ASCT and had achieved at least a stable disease response at the time of haematologic recovery were randomised 1:1 to receive either lenalidomide or placebo maintenance (10 mg once daily on Days 1 to 28 of repeated 28-day cycles increased up to 15 mg once daily after 3 months in the absence of dose-limiting toxicity) following 2 courses of lenalidomide consolidation (25 mg/day, Days 1 to 21 of a 28-day cycle). Treatment was to be continued until disease progression. The study was unblinded upon the recommendations of the data monitoring committee after surpassing the threshold for a preplanned interim analysis of PFS. After unblinding, patients receiving placebo were not crossed over to lenalidomide therapy prior to progressive disease. The lenalidomide arm was discontinued, as a proactive safety measure, after observing an imbalance of second primary malignancies (SPM). The results of PFS at unblinding, following a preplanned interim analysis, using a cut-off of 07 July 2010 (31.4 months follow up) showed a 48% reduction in risk of disease progression or death favouring lenalidomide over placebo. The Hazard Ratio was 0.52 (95% CI 0.41, 0.66; p <0.001). The median overall PFS was 40.1 months (95% CI 35.7, 42.4) in the lenalidomide arm versus 22.8 months (95% CI 20.7, 27.4) in the placebo arm. The updated PFS, using a cut-off of 01 February 2016 (96.7 months follow-up) continued to show a PFS advantage for lenalidomide (Hazard Ratio = 0.57; p <0.001).

A Phase III clinical study in newly diagnosed multiple myeloma (MM-020) compared lenalidomide and dexamethasone (Rd) given for 2 different durations of time (i.e. until progressive disease [Arm Rd] or for up to eighteen 28-day cycles [72 weeks, Arm Rd18]) to that of melphalan, prednisone and thalidomide (MPT) for a maximum of twelve 42-day cycles (72 weeks). The study showed a statistically significant prolongation of PFS benefit in patients receiving Rd compared to MPT. The Hazard Ratio was 0.69 (p <0.001).

Another Phase III study in newly diagnosed multiple myeloma (MM-015) was conducted to evaluate the safety and efficacy of lenalidomide in combination with melphalan and prednisone (MPR) with or without lenalidomide maintenance therapy until disease progression, to that of melphalan and prednisone for a maximum of 9 cycles.
The study showed a statistically significant prolongation of PFS benefit in patients receiving MPR+R compared to MPp+p (melphalan, prednisone, placebo + placebo maintenance). The Hazard Ratio was 0.37 (p <0.001).*

In Phase III clinical studies in multiple myeloma with at least one prior therapy, the median time to progression (TTP) was 60.1 weeks in patients treated with lenalidomide/dexamethasone versus 20.1 weeks in patients treated with placebo/dexamethasone. The median PFS was 48.1 weeks in patients treated with lenalidomide/dexamethasone versus 20.0 weeks in patients treated with placebo/-dexamethasone.*

In a Phase III clinical study in myelodysplastic syndromes (MDS-004), a significant larger proportion of patients achieved the primary endpoint of transfusion independence (>182 days) on lenalidomide 10 mg compared with placebo (55.1% vs. 6.0%). The median time to transfusion independence in the lenalidomide 10 mg arm was 4.6 weeks. The median duration of transfusion independence was not reached in any of the treatment arms, but should exceed 2 years for the lenalidomide-treated subjects. The median increase in haemoglobin (Hgb) from baseline in the 10 mg arm was 6.4 g/dL.*

In a phase II study of lenalidomide (N=170) versus single agent of investigator's choice of monotherapy with either chlorambucil, cytarabine, rituximab, fludarabine, or gemcitabine (N=84) in patients with mantle cell lymphoma (MCL) who were refractory to their last regimen or had relapsed one to three times (Study MCL-002), median PFS was significantly improved for lenalidomide versus investigator's choice (37.6 versus 22.7 weeks; Hazard Ratio = 0.61, p = 0.004).*

*text according to SmPC

## 1.1 Licenced Indication

Lenalidomide is an immunomodulating medicinal product.

Lenalidomide MAH Licence holders:

- Lenalidomide as monotherapy is indicated for the maintenance treatment of adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation.

AND

- Lenalidomide as combination therapy with dexamethasone, or bortezomib and dexamethasone, or melphalan and prednisone is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant.

AND

- Lenalidomide in combination with dexamethasone is indicated for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.

AND

- Lenalidomide as monotherapy is indicated for the treatment of adult patients with transfusion-dependent anaemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate.

AND

- Lenalidomide as monotherapy is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma.

AND

- Lenalidomide in combination with rituximab (anti-CD20 antibody) is indicated for the treatment of adult patients with previously treated follicular lymphoma (Grade 1 – 3a).

When lenalidomide is given in combination with other medicinal products, the corresponding SmPC must be consulted prior to initiation of treatment.

Safety Advice Relevant to all Patients In addition to information about the Pregnancy Prevention Programme, this brochure contains important advice for healthcare professionals about how to minimise the risk of adverse events during treatment with lenalidomide.

For further information about the appropriate use and safety profile of lenalidomide, please refer to the SmPC, which can be found on the eMC website: www.medicines.org.uk

**You must send a copy of every completed Prescription Authorisation Form immediately to PCG, for ALL patients, regardless of indication. This is an absolute requirement so that MA holders can fulfil regulatory obligations to monitor PPP adherence and off-label usage. MA holders is obliged to provide anonymous reports on this data to the regulatory agencies, to assess the effectiveness of risk minimisation activities and will not be able to comply if pharmacies do not provide ALL their Prescription Authorisation Forms to Pharmacare Group. Prescription Authorisation Forms can be sent via email, fax or post (a photocopy of the form), using the following contact details: Support@pharmacaregroup.co.uk**

# 2.0 Safety Advice to Avoid Foetal Exposure

## 2.1 Women of Non-childbearing Potential

Women in the following groups are considered **not** to have childbearing potential and do not need to undergo pregnancy testing or receive contraceptive advice;

- Age ≥ 50 years and naturally amenorrhoeaic for ≥ 1 year. Please note amenorrhoea following cancer therapy or during breastfeeding does not rule out childbearing potential
- Premature ovarian failure confirmed by a specialist gynaecologist
- Previous bilateral salpingo-oophorectomy, or hysterectomy
- XY genotype, Turner syndrome, uterine agenesis.

Women of childbearing potential are all other women who 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 non-childbearing potential.

If a patient does not meet at least one of above criteria, but the prescriber considers the patient to be of nonchildbearing potential, then prior approval of any deviation from these stipulated criteria should be sought from the MAH via their Medical Information Team.

The following information is required to assess whether a patient, who does not meet at least one of the above criteria, can be treated as a women of non-childbearing potential:

- DOB and Initials of the Patient
- Details of why the prescriber considers the patient to be of non-childbearing potential
- Background to why a deviation has been requested.

## 2.2 Women of Childbearing Potential

Women of childbearing potential must never take lenalidomide if they are:

- Pregnant
- Able to become pregnant, even if not planning to become pregnant, unless all of the conditions of the Pregnancy Prevention Programme are met.

In view of the expected teratogenic risk of lenalidomide, foetal exposure must be avoided.

Women of childbearing potential (even if they have amenorrhoea) must:

– use at least one effective method of contraception for at least 4 weeks before therapy, during therapy, and until at least 4 weeks after lenalidomide therapy, and even in case of dose interruption **or**
– commit to absolute and continuous abstinence confirmed on a monthly basis

**AND**
– have a medically supervised negative pregnancy test (with a minimum sensitivity of 25 mIU/mL) once she has been established on contraception for at least 4 weeks, at least in 4-weekly intervals during therapy (this includes dose interruptions) and at least 4 weeks after the end of therapy (unless confirmed tubal sterilisation). This includes those women of childbearing potential who confirm absolute and continued sexual abstinence.

There must be no more than **3 days** between the dates of the last negative pregnancy test and the prescription.
Best practice is for the pregnancy test, prescribing and dispensing to take place on the same day.

If not established on effective contraception, the patient must be referred to an appropriately trained healthcare professional for contraceptive advice in order that contraception can be initiated.

The following can be considered to be examples of suitable methods of contraception:
- Implant
- Levonorgestrel-releasing intrauterine system (IUS)
- Medroxyprogesterone acetate depot
- Tubal sterilisation
- Sexual intercourse with a vasectomised male partner only; vasectomy must be confirmed by two negative semen analyses
- Ovulation inhibitory progesterone-only pills (i.e. desogestrel).

Patients should be advised to inform the healthcare professional prescribing her contraception about the lenalidomide treatment.

Patients should be advised to inform you if a change or stop of method of contraception is needed.

**TREATMENT FOR A WOMAN OF CHILDBEARING POTENTIAL CANNOT START UNTIL THE PATIENT IS ESTABLISHED ON AT LEAST ONE EFFECTIVE METHOD OF CONTRACEPTION FOR AT LEAST 4 WEEKS OR COMMITS TO ABSOLUTE AND CONTINUOUS ABSTINENCE AND PREGNANCY TEST IS NEGATIVE.**

Because of the increased risk of venous thromboembolism in patients with multiple myeloma taking lenalidomide in combination therapy, and to a lesser extent in patients with multiple myeloma, myelodysplastic syndromes and mantle cell lymphoma taking lenalidomide monotherapy, combined oral contraceptive pills are not recommended. If a patient is currently using combined oral contraception, the patient should switch to at least one of the effective methods listed above. The risk of venous thromboembolism continues for 4 to 6 weeks after discontinuing combined oral contraception. The efficacy of contraceptive steroids may be reduced during co-treatment with dexamethasone.

Implants and levonorgestrel-releasing intrauterine systems are associated with an increased risk of infection at the time of insertion and irregular vaginal bleeding. Prophylactic antibiotics should be considered particularly in patients with neutropenia.

Insertion of copper-releasing intrauterine devices are generally not recommended due to the potential risks of infection at the time of insertion and menstrual blood loss which may compromise patients with neutropenia or thrombocytopenia.

**Your patient should be advised that if a pregnancy does occur whilst she is receiving lenalidomide, she must stop treatment immediately and immediately inform her prescriber.**

**Requirements in the event of a suspected pregnancy while on treatment with lenalidomide:**

- **Stop treatment immediately**
- **Refer the patient to a physician specialised or experienced in teratology for evaluation and advice.**
- **Immediately notify the relevant Marketing Authorisation Holder Risk Management (see section 6.0 for contact details) immediately of all such occurrences. Please also complete the Pregnancy Reporting Form for the relevant Marketing Authorisation Holder. The relevant Marketing Authorisation Holder will wish to follow-up with you on the progress of all suspected pregnancies in female patients or partners of male patient cases.**

**Suspected pregnancies can also be reported online via the Yellow Card Website https://yellowcard@mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store. Alternatively, prepaid Yellow Cards for reporting are available:**

- **By writing FREEPOST YELLOW CARD (no other address details necessary);**
- **By emailing yellowcard@mhra.gov.uk**
- **By telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789 Or by downloading and printing a form from the Yellow Card section of the MHRA website**

## 2.3 Men

In view of the expected teratogenic risk of lenalidomide, foetal exposure should be avoided.

Inform your patient about the effective contraceptive methods that his female partner can use.

Lenalidomide is present in semen. Therefore all male patients should use condoms throughout treatment duration, during dose interruption and for at least 7 days after cessation of treatment if their partner is pregnant or of childbearing potential who is not using effective contraception and even if the male patient has undergone vasectomy.

Patients should be instructed that if their partner does become pregnant whilst he is taking lenalidomide or within 7 days after he has stopped taking lenalidomide, he should inform his prescriber immediately. The partner should inform her doctor immediately. It is recommended that she be referred to a physician specialised in teratology for evaluation and advice.

Male patients should not donate semen or sperm during treatment, including during dose interruptions and for at least 7 days following discontinuation of lenalidomide.

**If the partner of a male patient taking lenalidomide becomes pregnant, then he must inform his prescriber immediately. Then:**

**refer the female partner to a physician specialised or experienced in dealing with teratology for advice and evaluation.**

**Immediately notify the relevant Marketing Authorisation Holder Risk Management (see section 6.0 for contact details) immediately of all such occurrences. Please also complete the Pregnancy Reporting Form for the relevant Marketing Authorisation Holder. The relevant Marketing Authorisation Holder will wish to follow-up with you on the progress of all suspected pregnancies in female patients or partners of male patient cases.**

**Suspected pregnancies can also be reported via the MHRA Pharmacovigilance website: www.mhra.gov.uk or via the Pathfinder RMP Platform on the "Report an AE or Pregnancy" page, allowing you to download the adverse event forms and report it directly to the relevant MA holders AE reporting team.**

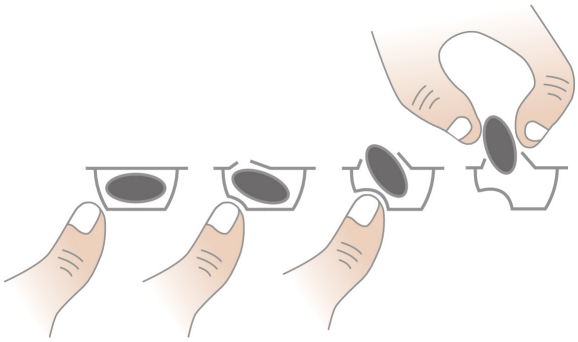
## 2.4.1 Points to Consider for Handling the Medicinal Product: Advice to all Patients, Healthcare Professionals and Caregivers

**Please note the method of removal of the capsule from the blister may differ between different lenalidomide products. Please refer to the SmPC for the lenalidomide product you are handling for specific handling advice**

Keep the blisters with the capsules in the original pack.

Care must be taken when removing capsules from the blister packaging to ensure that capsules are not broken. Please refer the patient to the package leaflet that comes with the medicine for instructions on how to remove the capsule from the blister to reduce the risk of damage to the capsule.

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.



**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 product and/or packaging (i.e. blister or capsule)
- Use proper technique when removing gloves to prevent potential skin exposure (see below)
- Place gloves in sealable plastic polyethylene bag and dispose 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 outer carton is visibly damaged – **Do Not Open**
- If blister strips are damaged or leaking or capsules are noted to be damaged or leaking – **Close Outer Carton Immediately**
- Place the product inside a sealable plastic polyethylene bag
- Return unused pack to the pharmacist for safe disposal as soon as possible.

**If product is released or spilled, take proper precautions to minimise exposure by using appropriate personal protection**

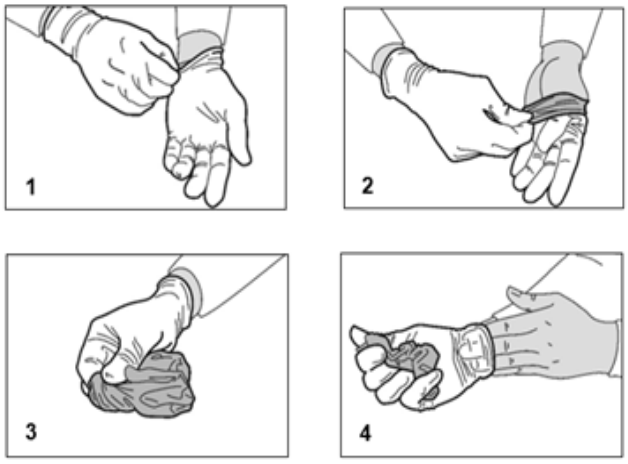
- If capsules are crushed or broken, dust containing drug substance may be released. Avoid dispersing the powder and avoid breathing the powder
- Wear disposable gloves to clean up the powder
- Place a damp cloth or towel over the powder area to minimise entry of powder into the air. Add excess liquid to allow the material to enter solution. After handling, clean the area thoroughly with soap and water and dry it
- Place all contaminated materials including damp cloth or towel and the gloves into a sealable polyethylene plastic bag and dispose in accordance to local requirements for medicinal products
- Wash your hands thoroughly with soap and water after removing the gloves
- Please report to the relevant Marketing Authorisation Holder (see section 8 for contact details)

**If the contents of the capsule are attached to the skin or mucous membranes**

- If you touch the drug powder, please wash exposed area thoroughly with running water and soap
- If the powder gets in contact with your eye, if worn and if 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 outside edge near wrist (1)
- Peel away from hand, turning glove inside-out (2)
- Hold in opposite gloved hand (3)
- Slide ungloved finger under the wrist of the remaining glove, be careful not to touch the outside of the glove (4)
- Peel off from inside, creating a bag for both gloves.
- Discard in appropriate container
- Wash your hands with soap and water thoroughly.



### 2.4.2 Blood Donation

Patients should not donate blood during treatment and for at least 7 days after cessation of treatment with lenalidomide.

## 2.5 The physicians guide to prescribing lenalidomide

### 2.5.1 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.

### 2.5.2 Initial Prescription

Before issuing the initial prescription, you must:

- Have read and understood the Healthcare Professional`s Information Guide
- Counsel the patient on the safe use of lenalidomide in accordance with the measures described in this guide and the SmPC.
- Obtain written confirmation (using the Treatment Initiation Form for the appropriate patient category) that they have received and understood this information, and provide the patient with a copy
- Provide the patients with a Patient Brochure and Patient Pocked information Card
- Ensure that your patient is using an effective method of contraception, if appropriate

**Pharmacy notification**

When a patient is first initiated on lenalidomide, they will nominate a pharmacy to supply their medication. Prescribers must notify the nominated pharmacy that they will shortly be receiving an initial prescription for lenalidomide on the first occasion that the patient is being prescribed lenalidomide.

Initial and subsequent Prescriptions

- If using the Pathfinder RMP platform you must complete the necessary fields on the digital prescription authorisation form and provide the patient with just the prescription.
- A 'Prescription Authorisation Form' must be provided to the pharmacy with each lenalidomide prescription. This will contain:
- Date of birth, patient initials, and indication.
- Name of treating hospital, prescriber name, address and date
- Patient category (woman of childbearing potential, woman 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 date of the last negative pregnancy test, which must be within the 3 days prior to the date of the prescription.
- That your patient is using an effective contraception (if applicable)
- The patients must present their paper prescription authorisation form to the pharmacy with their prescription and the pharmacy will check this form prior to dispensing lenalidomide.

The pharmacy will check the prescription authorisation form prior to dispensing lenalidomide.

The patient must return to their a prescriber for every repeat prescription of lenalidomide and a new Prescription Authorisation Form must be completed and submitted.

## 2.6 The pharmacists guide to dispensing Lenalidomide PPP

**Pharmacy registration**

It is a requirement of the Lenalidomide Pathfinder RMP that pharmacies wishing to purchase and dispense lenalidomide products are registered with these marketing authorisation holders. Registration involves reading and understanding the Healthcare Professional's Information Guide and completing a Pharmacy Registration form indicating agreement and compliance with the requirements of the lenalidomide Pathfinder RMP pregnancy prevention programme.

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

Dispensing of lenalidomide MAH licence holders products will only be allowed from pharmacies registered with the Pathfinder RMP. The relevant distributor will not authorise purchase and supply of these lenalidomide products to pharmacies not registered with the Lenalidomide MAH licence holders

**Lenalidomide is supplied to pharmacies registered with the Pathfinder RMP only for the purpose of dispensing the product by the PPP registered pharmacy to the patient.**

**Prescription Authorisation Form (PAF)**
**Every prescription for lenalidomide must be accompanied by a complete Prescription Authorisation Form**

The prescriber must confirm the following on the Prescription Authorisation Form or through the portal:

- The indication for which lenalidomide is being prescribed.
- Whether the patient is male, a woman of childbearing potential or a woman of non-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 3 days prior to the date of the prescription
- If male, that the required counselling has taken place
- That the treatment initiation form has been completed and signed by the patient.
- That the prescriber has read and understands the contents of the Healthcare Professional's Information Guide.

**The Pharmacist must confirm the following on the Prescription Authorisation Form:**

- That the Prescription Authorisation Form has been completed in full by the prescriber
- That dispensing for a woman of childbearing potential is taking place 7 days or less from the date of prescribing
- That the pharmacist is dispensing the appropriate supply for the patient category
- That the pharmacist has read and understood the contents of the Healthcare Professional's Information Guide

## 2.6.1 Dispensing Advice

**For women of childbearing potential:**

- The date of the last negative pregnancy test, must be within the 3 days prior to the date of the prescription.
- Dispensing of lenalidomide should occur within a maximum of 7 days of the prescription.
- 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

**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.

**For all patients:**

- Please ensure that you dispense Lenalidomide blisters intact; capsules must not be removed from blisters and packaged into bottles.

- Instruct patients to return any unused lenalidomide capsules to the pharmacy. Pharmacies must accept any unused lenalidomide capsules returned by patients for destruction, and follow Good Pharmacy Practice guidelines for destruction of dangerous medicines.

**Please ensure that all pharmacists within your pharmacy are educated about and familiar with the requirements for the Pregnancy Prevention Programme and the dispensing procedures for lenalidomide.**

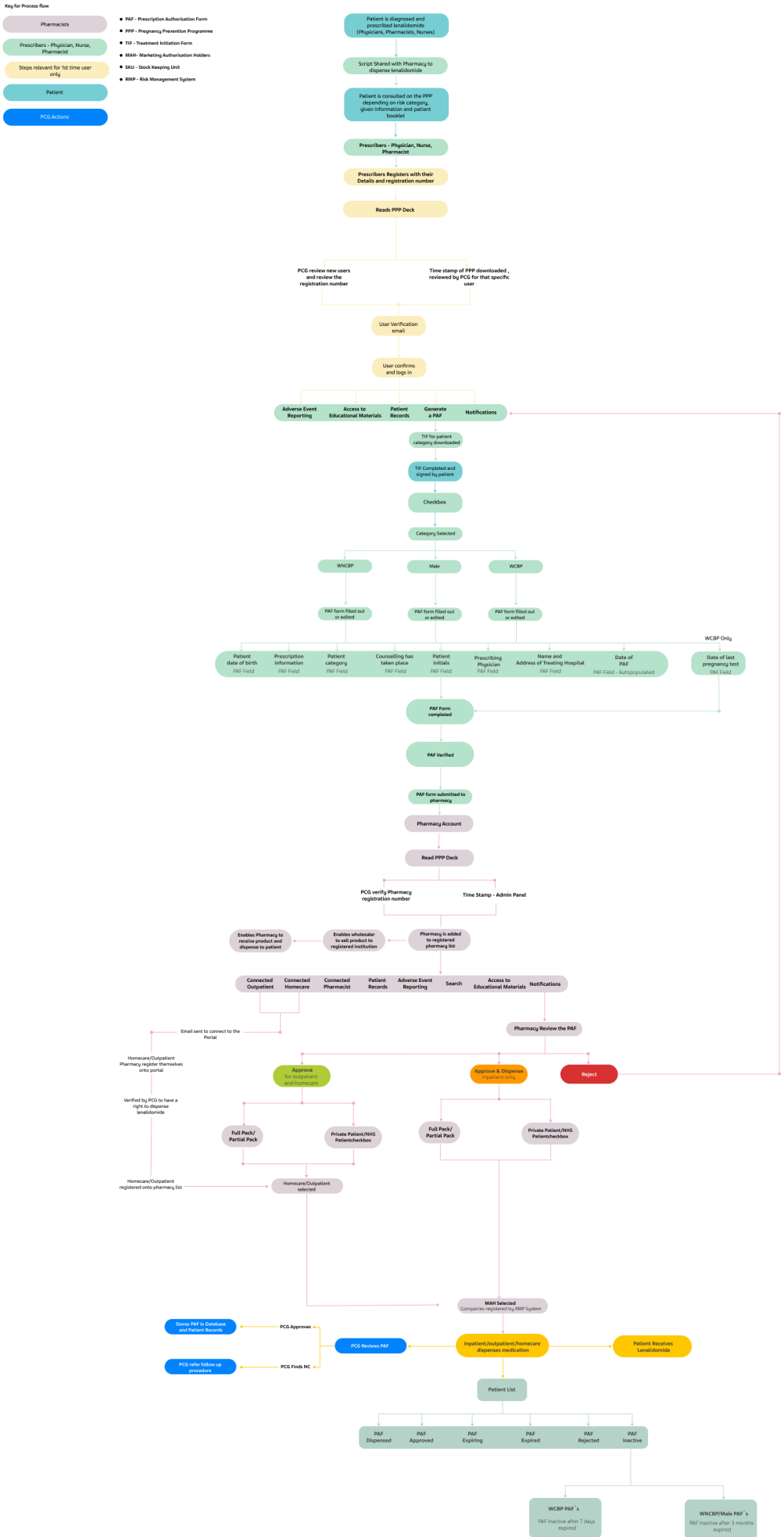
# 3.0 Follow Up Assessment of the Effectiveness of the Programme.

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

The MAH licence holders are therefore obliged to perform audits at regular intervals and to report appropriately anonymous and aggregated results to the MHRA and European medicines Agency (EMA). An audit of **ALL** completed prescription authorisation forms will be carried out.

**Pharmacies must complete via the Pathfinder RMP or send a copy of every completed PAF from immediately** after dispensing lenalidomide to the appointed service provider (acting on behalf of the MAHs) who will then be able to conduct the pharmacy audit using these forms and a manual self audit by pharmacies will not be required. It is CRITICAL, therefore that the Prescription Authorisation Forms are completed accurately and that pharmacies assist the service provider to audit the effectiveness of the Pregnancy Prevention Programme).

## 3.1 The Prescribing and Dispensing of Lenalidomide using the Pathfinder RMP



# 4.0 Posology

## 4.1 Newly Diagnosed

### 4.1.1 Lenalidomide Maintenance in patients who have undergone Autologous Stem Cell Transplantation (ASCT)

The recommended starting dose of lenalidomide is 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 SmPC.

### 4.1.2 Lenalidomide in Combination with Dexamethasone until Disease Progression in Patients who are Not Eligible in 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 SmPC.

### 4.1.3 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 SmPC.

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

The recommended starting dose of lenalidomide is 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 SmPC.

## 4.2 Multiple Myeloma Patients 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. The prescriber 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 SmPC.

## 4.3 Myelodysplastic Syndromes

The recommended starting dose of lenalidomide is 10 mg orally once daily on Days 1 to 21 of repeated 28-day cycles. Dose reduction steps are provided in Section 4.2 of the SmPC.

## 4.4 Mantle Cell Lymphoma

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

## 4.5 Follicular lymphoma

The recommended starting dose of lenalidomide is 20 mg orally once daily on Days 1 to 21 of repeated 28-day cycles for up to 12 cycles of treatment. The recommended starting dose of rituximab is 375 mg/m2 intravenously every week in Cycle 1 (Days 1, 8, 15, and 22) and Day 1 of every 28-day cycle for Cycles 2 through 5. Dose reduction steps are provided in Section 4.2 of the SmPC.

# 5.0 Other 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 refer also to SmPC (Section 4.2 Posology and method of administration, 4.3 Contraindications, 4.4 Special warnings and precautions for use and 4.8 Undesirable effects).

## 5.1 Tumour Flare Reaction in Mantle Cell Lymphoma and Follicular Lymphoma Patients

Tumor Flare Reaction (TFR) has commonly been observed in patients with mantle cell lymphoma, who were treated with lenalidomide or with follicular lymphoma treated with lenalidomide and rituximab. The patients at risk of TFR are those with high tumour burden prior to treatment. Caution should be practised 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.

## 5.2 Second Primary Malignancies

The risk of occurrence of Second Primary Malignancies (SPM) must be taken into account before initiating treatment with lenalidomide either in combination with melphalan or immediately following high dose melphalan and ASCT. Prescribers should carefully evaluate patients before and during treatment using standard cancer screening for occurrence of SPM and institute treatment as indicated.

An increase of SPM has been observed in clinical trials in previously treated myeloma patients with lenalidomide/dexamethasone compared to controls, mainly comprising of basal cell or squamous cell skin cancers.

Cases of haematological SPM such as acute myeloid leukaemia (AML) have been observed in clinical trials of newly diagnosed multiple myeloma in patients taking lenalidomide in combination with melphalan or immediately following high dose melphalan and ASCT (HDM/ASCT; see Section 4.4 of the SmPC). 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.

## 5.3 Progression to Acute Myeloid Leukaemia in Low- and Int-1-risk MDS Patients

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 of the SmPC).

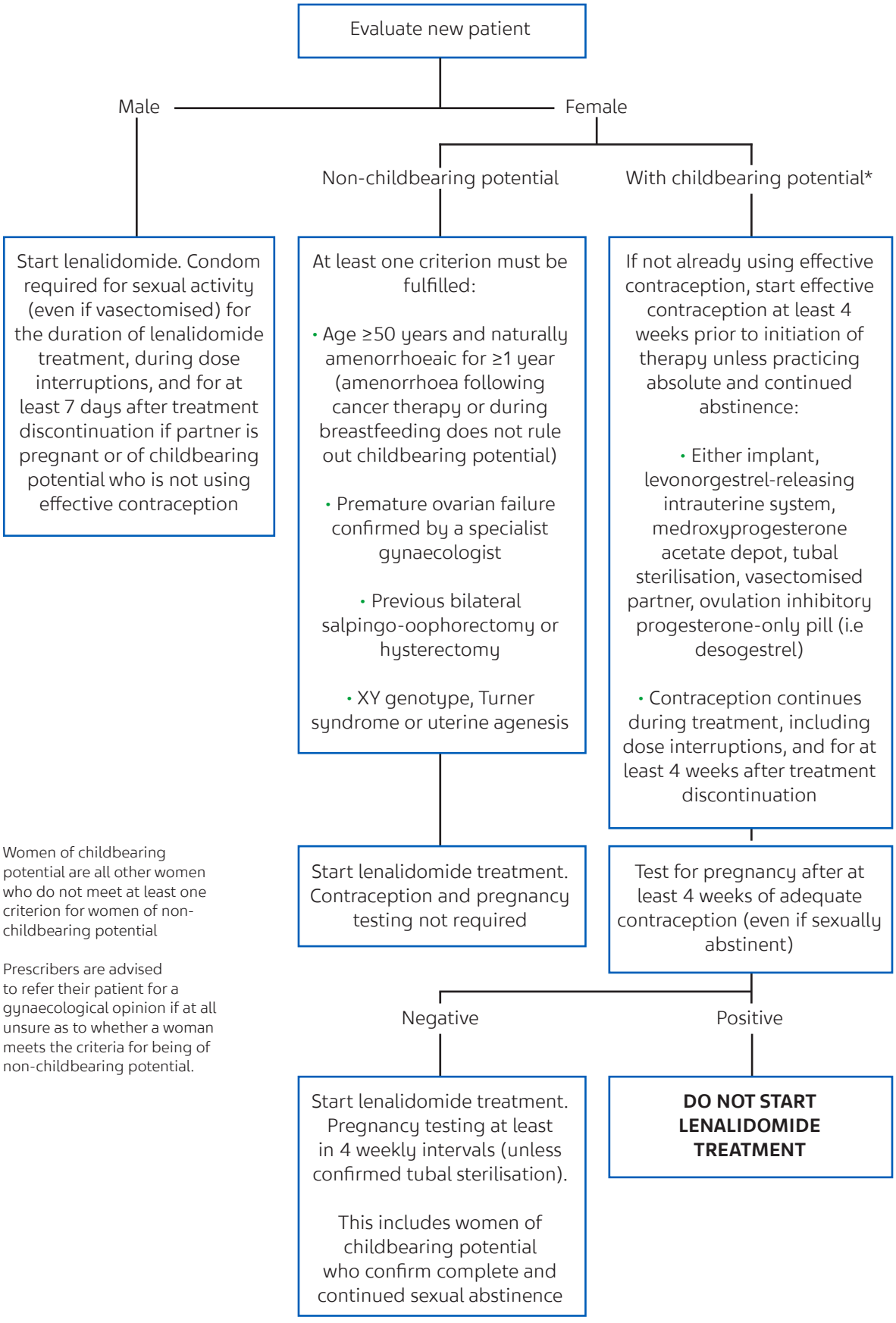
# 6.0 reporting of the Adverse Events, we will need to have contact details of all MAHs and also

Suspected pregnancies and adverse events can also be reported online via the Yellow Card Website https://yellowcard@mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store. Alternatively, prepaid Yellow Cards for reporting are available:

- By writing FREEPOST YELLOW CARD (no other address details necessary);
- By emailing yellowcard@mhra.gov.uk
- By telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- Or by downloading and printing a form from the Yellow Card section of the MHRA website

## List of MAH`s:

# 7.0 Description of the Pregnancy Prevention Programme and Patient Categorisation Algorithm




* Women of childbearing potential are all other women who do not meet at least one criterion for women of non-childbearing potential

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 non-childbearing potential.

# 8.0 Contact Details

**Pathfinder RMP Queries:**
For technical information and questions on the Pathfinder RMP, physician registrations, pharmacy registrations and the use of the Prescription Authorisation Form, and the use of the Portal, please contact:

### Pathfinder RMP - HealthBeacon

Email: support@pathfinderrmp.co.uk
Tel: +44 203 936 8807

Mon - Fri 9am - 5pm GMT

### Risk Management

For information and questions on the Risk Management of Lenalidomide, the Pregnancy Prevention Programme, please contact Pharmacare please see contact details below.

### Pathfinder RMP - Pharmacare Group

Email: support@pharmacaregroup.co.uk
Tel: 0330 043 0908

Mon - Fri 9am - 5pm GMT

### Medical Information and Adverse Event

To report any Adverse Events or suspected pregnancies, or to obtain Medical Information on the respective medicinal product from the relevant Marketing Authorisation Holder, please see contact details below.

**Sun Pharma UK Limited**
Email: medinfoeurope@sunpharma.com
Tel: +44 (0) 208 848 5052

**Advanz Pharma Services (UK) Limited**
Email: medicalinformation@advanzpharma.com
Tel: +44 (0) 208 588 9131

**Viatris UK Healthcare Limited**
Email: info.uk@viatris.com
Tel: +44 (0) 203 535 5790

**STADA**
Email: thorntonross@medinformation.co.uk
Tel: 01 484 848164

**Sandoz UK Ltd**
Email: sandozgb@EU.propharmgroup.com
Tel: +44 1276 698 101

**Amarox Limited**
Email: safety@amaroxpharma.com
Tel: 020 39720001

**Piramal Critical Care Ltd**
Email:medical.information@piramal.com
Tel: 0800 756 3979

## Data Protection Contact Details

Personal data is used solely for the purpose of entering you into the Pregnancy Prevention Programme and is processed by the relevant marketing authorisation holder, as marketing authorisation holder of pharmaceutical products and by the third-party service provider HealthBeacon and Pharmacare Group, to the extent and for as long as necessary, for the purposes of compliance with the Risk Management Plan legal obligations and for storage purposes. Should you have any queries in relation to the use of your personal data please contact support@pathfinderrmp.co.uk