

# Lenalidomide Pregnancy Prevention Programme

## And

### Information for Healthcare Professionals Prescribing or Dispensing Lenalidomide

## Ireland

#### Important Safety Information:

This is risk minimisation material and is provided as a collaborative project between Accord Healthcare Ltd., Clonmel Healthcare Ltd. Rowex Ltd. and Teva Pharmaceuticals Ireland. For further information, please refer to the Summary of Product Characteristics (SmPC) for the respective medicinal product from the relevant Marketing Authorisation Holder available at [www.hpra.ie](http://www.hpra.ie)

or [www.ema.europa.eu](http://www.ema.europa.eu)

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 precautions and make sure you know what to do before prescribing and dispensing lenalidomide.

## Lenalidomide Pregnancy Prevention Programme:

Lenalidomide is an immunomodulating medicinal product.

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 Risk Awareness Form (RAF), 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.hpra.ie](http://www.hpra.ie)/[www.ema.europa.eu](http://www.ema.europa.eu).

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## 1.0 Licensed Indication

Lenalidomide is an immunomodulating medicinal product.  
Lenalidomide Accord/Clonmel/Rowex/Teva indicated for the following:

- 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.

AN

- 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. Please refer to the SmPC for further information.

## 1.1 Newly Diagnosed

### 1.11 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.

### 1.12 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.

### 1.13 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/m<sup>2</sup> 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.

### 1.14 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.

## 1.2 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.

## 1.3 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.

## 1.4 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.

## 1.5 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/m<sup>2</sup> 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.

## 1.6 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 with 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 in humans. Therefore, lenalidomide is contraindicated in pregnancy and in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme described in this HCP guide are met.

## 1.7 Lenalidomide Accord/Clonmel/Rowex/Teva 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 pregnancy (this must be documented via a Risk Awareness Form which is available for this purpose). The patient should receive a copy of the Risk Awareness Form when completed.
- You must ensure that your patient continues to understand the need to avoid foetal exposure to lenalidomide

during pregnancy.

- 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 [www.patientsafetyhub.ie](http://www.patientsafetyhub.ie) 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 and handling of lenalidomide.
- Patients must be provided with the appropriate Patient Guide, Risk Awareness Form and Patient Pocket Information Card.

The lenalidomide Accord/ Clonmel/Rowex/Teva Pregnancy Prevention Programme materials are contained within the Patient Safety Hub ([patientsafetyhub.ie](http://patientsafetyhub.ie)) 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.hpra.ie](http://www.hpra.ie) (enter 'Lenalidomide' under 'Find a Medicine' and click 'EdM' under the 'Documents' column for the relevant Lenalidomide product).

For further information on the Patient Safety Hub please refer to Section 3 – Patient Safety Hub.

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

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 Lenalidomide Accord/Clonmel/Rowex/ Teva 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 access programme
- All healthcare professionals dispensing or prescribing lenalidomide must read and understand the Lenalidomide Healthcare Professional's Information Guide.
- All pharmacies who dispense lenalidomide from Accord/Clonmel/Rowex/Teva must agree to implement risk minimisation by registering with the Lenalidomide Accord/Clonmel/Rowex/Teva 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.

## 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  $\geq$  50 years and naturally amenorrhoeic for  $\geq$  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.

## 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 prior to issuing a prescription (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 before initiating in order that contraception to 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 IUSs 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 is 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.**

If your patient needs to change or stop her contraceptive method during her lenalidomide therapy, she must understand the need to discuss this first with:

- The prescriber prescribing her contraceptive method.
- The prescriber prescribing her lenalidomide.

If a woman of childbearing potential has sexual contact without using an effective contraceptive method while taking lenalidomide, or believes for any reason that she may be pregnant, she must stop treatment and immediately consult her prescriber.

**Requirements in the event of a suspected pregnancy while on treatment with lenalidomide Accord/ Clonmel/ Rowex/Teva:**

- **Stop treatment immediately**
- **Refer the female patient to a physician specialised or experienced in teratology for evaluation and advice.**
- **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 Health Products Regulatory Authority (HPRA) Pharmacovigilance website: [www.hpra.ie](http://www.hpra.ie)**

## 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 human semen. As a precaution, all male patients taking lenalidomide, including those who have had a vasectomy as seminal fluid may still contain lenalidomide in the absence of spermatozoa, 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 and has no contraception.

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 Accord/Clonmel/Rowex/Teva 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.**

**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 HPRA Pharmacovigilance website: [www.hpra.ie](http://www.hpra.ie)**

### Advice to all patients

All patients should be advised not to donate blood during treatment (including dose interruptions) and for at least 7 days after cessation of treatment with lenalidomide. If they discontinue therapy, or if there are any unused capsules at the end of their treatment, they must return any unused lenalidomide to the pharmacist.

They must also understand that their lenalidomide is only for them, and it:

- Must not be shared with anyone else, even if they have similar symptoms.
- Must be stored away safely so no one else could take the capsules by accident.
- Must be kept out of sight and reach of children.

### 2.4.1 Points to Consider for Handling the Medicinal Product: For 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. Do not share the medicinal product with anyone else, even if they have similar symptoms. Store them safely so that no-one else can take them by accident and keep them out of the reach of children.**

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. Dispose of any

unused medication in accordance with local regulation. 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 them according to local requirements
- Wash hands thoroughly with soap and water after removing gloves.
- Patients should be advised never to give the medicinal product to another person.

**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**

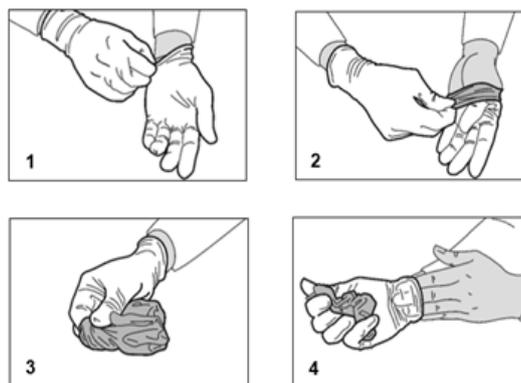
- If capsules are crushed or broken, dust containing drug substance may be released. Avoid dispersing the powder and avoid breathing and or inhaling the powder
- Wear disposable gloves to clean up the powder
- Place a damp cloth or towel over the powder area to minimise entry of powder into the air. 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. 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, being 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 (including dose interruptions) with lenalidomide.

## 2.4.3 Disposal of Unwanted Medicine

Patients must be advised never to give lenalidomide to another person and to return any unused capsules to their pharmacist at the end of treatment.

## 2.5 Prescribing and Dispensing Lenalidomide

**Lenalidomide treatment must be initiated and monitored under the supervision of physicians with expertise in managing immunomodulatory or chemotherapeutic agents.**

### 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.

### 2.5.2 Initial Prescription

Prescribe Lenalidomide using a High-tech Prescription.

Prescribers wishing to prescribe must read and understand the Healthcare Professionals' Information Guide.

Before issuing the initial prescription (High-tech Prescription), you must:

- Counsel the patient on the safe use of lenalidomide in accordance with the measures described in this guide and the SmPC.
- Provide educational materials (Patient Guide and Patient Information Pocket Card) to the patient.
- Obtain written confirmation (using the Risk Awareness Form for the appropriate patient category) that they have received and understood this information, and provide the patient with a copy
- Ensure that your patient is using an effective method of contraception, if appropriate
- Perform a pregnancy test (if appropriate) before initiating treatment.

### 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.

## 2.5.3 Subsequent Prescriptions

Before issuing subsequent prescriptions (High-tech Prescription) you must:

- Ensure your patient continues to understand the risks of lenalidomide therapy.
- Ensure that your patient is continuing to use the appropriate contraceptive measures, if relevant.
- Perform a pregnancy test, if relevant.
- Provide a 'Prescription Authorisation Form' to the patient or submit electronically to the pharmacy with each lenalidomide prescription.

**All prescribers must have read and understood the information contained within this Guide before prescribing lenalidomide.**

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

## 2.5.4 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:

- Patient initials, date of birth and the indication for which lenalidomide is being prescribed.
- Name of treating hospital, prescriber name, supervising physician name, signature and date.
- Confirmation that they have provided counselling on the teratogenic risk of lenalidomide and the required contraceptive measures for women of childbearing potential and male patients.
- 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.
- That the Risk Awareness Form has been completed and signed by the patient.
- That the prescriber has read and understood the contents of the Healthcare Professional's Information Guide.
- The information provided on this PAF is accurate, complete and in accordance with the requirements of the Pregnancy Prevention Programme for lenalidomide.
- Treatment has been initiated and is monitored under the supervision of a physician with expertise in managing immunomodulatory or chemotherapeutic agents.

The patient must present their 'Prescription Authorisation Form' to the pharmacy along with their prescription and the pharmacy will check this form prior to dispensing lenalidomide. The patient must return to their prescriber for every repeat prescription of lenalidomide.

When completing the Prescription Authorisation Form the pharmacist must confirm:

- 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

If any information is missing contact the prescriber for verification prior to dispensing.

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

For prescribers wishing to use the Patient Safety Hub for notifying nominated pharmacies and sending PAFs please refer to Section 3.0 – Patient Safety Hub.

The Prescription Authorisation Form should be retained with the High-tech Prescription in the pharmacy for a minimum of 2 years

## 2.6 Dispensing Lenalidomide Accord/Clonmel/Rowex/Teva

### Pharmacy notification and Registration

A pharmacy should receive a notification from the prescriber to advise the pharmacy that it has been nominated by the patient to dispense their lenalidomide and that it will soon be receiving a High-tech Prescription for lenalidomide. The pharmacy will need to register with the Lenalidomide PPP for the manufacturer of any products it will be dispensing prior to being able to order those lenalidomide products for the patient.

Notifications sent by the prescriber via the Patient Safety Hub will be received via Healthmail. Please refer to section 3.0 - Patient safety Hub

### Pharmacy registration

It is a requirement of the Lenalidomide Accord/Clonmel/ Rowex/Teva PPP 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 Accord/Clonmel/Rowex/Teva 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 and audit the use of a Prescription Authorisation Form.

**Dispensing of lenalidomide Accord/Clonmel/Rowex/ Teva products will only be allowed from pharmacies registered with the Lenalidomide Accord/Clonmel/Rowex/Teva PPP. The relevant distributor will not authorise purchase and supply of these lenalidomide products to pharmacies not registered with the Lenalidomide Accord/Clonmel/Rowex/ Teva PPP.**

**Lenalidomide is supplied to pharmacies registered with the Lenalidomide Accord/Clonmel/Rowex/ Teva PPP only for the purpose of dispensing the product by the PPP registered pharmacy to the patient.**

Pharmacies wishing to dispense Lenalidomide Accord/Clonmel/Rowex/ Teva must register via the Patient Safety Hub.

### Ordering of lenalidomide:

The pharmacy must be registered with the Marketing Authorisation Holder of the lenalidomide product it wishes to dispense before it can order lenalidomide from that Marketing Authorisation Holder. To order a lenalidomide product the pharmacy must use a lenalidomide order form specific to the lenalidomide product it wishes to order.

All orders for lenalidomide Accord/Clonmel/Rowex/ Teva must be placed through the Patient Safety Hub (refer to section 3.0).



## 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 a maximum duration of 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 Patient Safety Hub

The Patient Safety Hub (PSH) is an online platform which may be used by prescribers and pharmacies to support fulfillment of the requirements of the lenalidomide Accord/Clonmel/ Rowex/Teva Pregnancy prevention programme.

It is available at [patientsafetyhub.ie](http://patientsafetyhub.ie).

### **The prescriber can use the PSH to:**

- Access Risk Awareness Forms for the relevant patient category. This form must be printed, completed by the prescriber and patient, a copy retained in the patient's medical record and a copy provided to the patient.
- Select the pharmacy the patient wishes to nominate at the time of initial prescription. The PSH will send an email to the nominated pharmacy to notify the pharmacy that they have been nominated by your patient to dispense their lenalidomide.
- Generate an electronic PAF to accompany each prescription. The hub will notify the nominated pharmacy that a new PAF is in the hub.
- Amend and reissue an electronic PAF if the PAF is rejected by the pharmacy.

### **The pharmacy must use the PSH to:**

- Complete pharmacy registration with the Lenalidomide PPP for Accord, Clonmel, Rowex and Teva.
- Receive an electronic PAF from a prescriber via the PSH\*.
- Approve or reject an electronic PAF. If there is missing or inaccurate information, the pharmacy may reject the PAF. If the PAF is rejected a notification will be sent to the prescriber asking them to amend and reissue to PAF.
- Order lenalidomide from Accord, Clonmel, Rowex or Teva using the electronic order form. The completed order form is then emailed automatically to the relevant distributor.

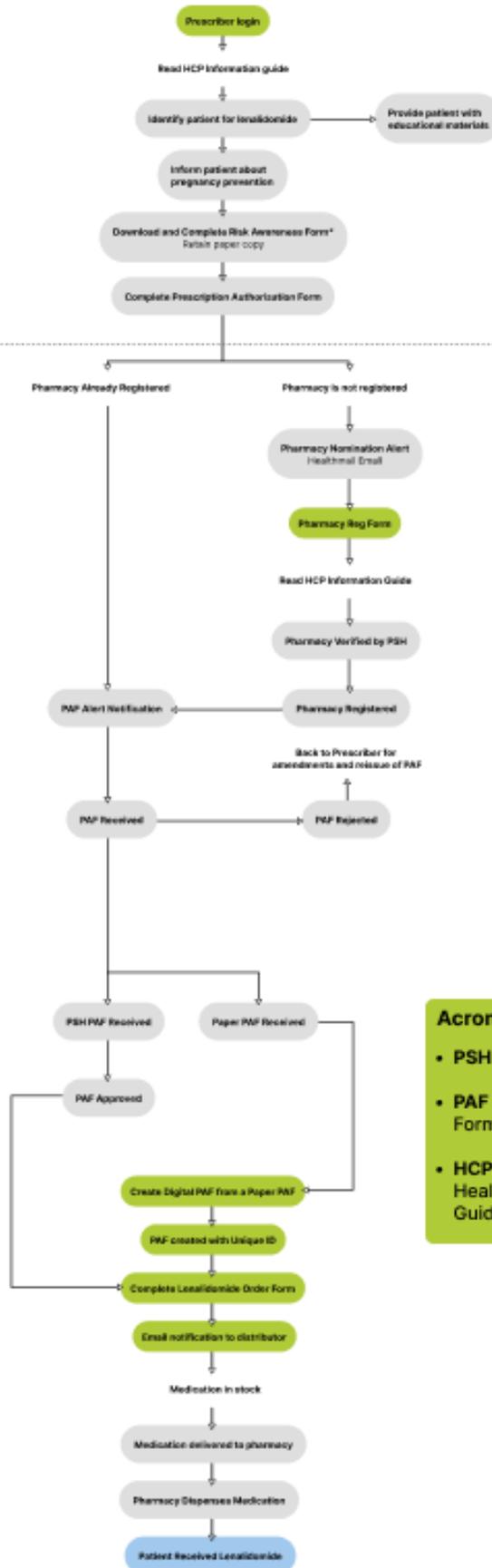
\*Notifications that you have been nominated or have received a new PAF in the PSH will be emailed to your pharmacy Healthmail address.

Please refer to the Patient Safety Hub User Manual for more detail on how to use the PSH.

### 3.1 The Prescribing and Dispensing of Lenalidomide using the Patient Safety Hub

#### Prescriber

#### Pharmacy



**Acronyms Key:**

- PSH - Patient Safety Hub
- PAF - Prescription Authorisation Forms
- HCP Information Guide - Healthcare Professional Information Guide

## 4.0 Follow-up Assessment of the Effectiveness of the Programme and monitoring of off-label use

The terms of the lenalidomide Marketing Authorisations require the respective Marketing Authorization 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 as well as to monitor for off-label use.

Accord Healthcare Ltd., Clonmel Healthcare Ltd. Rowex Ltd and Teva Pharmaceuticals Ireland., have agreed with the HPRA that each Marketing Authorization Holder can fulfil their obligations in this respect, by conducting a self-audit of the Patient Safety Hub.

This information will be provided in an anonymous and aggregated format to the HPRA.

It is therefore critical for prescribers and pharmacies to ensure that all documentation associated with the Pregnancy Prevention Programme is completed accurately, in the interest of patient safety.

## 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 autologous stem-cell transplantation (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. Please refer to SmPC for further details.

### 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 deletion (5q) abnormality. (see Section 4.4 of the SmPC).



## 6.0 Reporting Adverse Events, Suspected and Confirmed Pregnancies, and Foetal Exposures

The safe use of lenalidomide is of paramount importance.

Adverse Events (and cases of suspected or confirmed pregnancy or foetal exposure) should be reported. Adverse Event Report forms and Pregnancy Reporting forms can be found on [www.patientsafetyhub.ie](http://www.patientsafetyhub.ie) or can be obtained from the relevant Marketing Authorisation Holder and should be forwarded to the relevant Marketing Authorisation Holders as below:

### **Accord Healthcare Ltd**

Adverse Event Email: [safety.eu@lambda-cro.com](mailto:safety.eu@lambda-cro.com)

Medical Queries Email: [medinfo@accord-healthcare.com](mailto:medinfo@accord-healthcare.com)

Tel: 0044 1271 385257

### **Clonmel Healthcare Ltd**

Email: [medicalinformation@clonmel-health.ie](mailto:medicalinformation@clonmel-health.ie)

Tel: (052) 6177777

### **Rowex Ltd**

Email: [adverse.event.ireland@sandoz.net](mailto:adverse.event.ireland@sandoz.net)

Tel: 087 794 1968

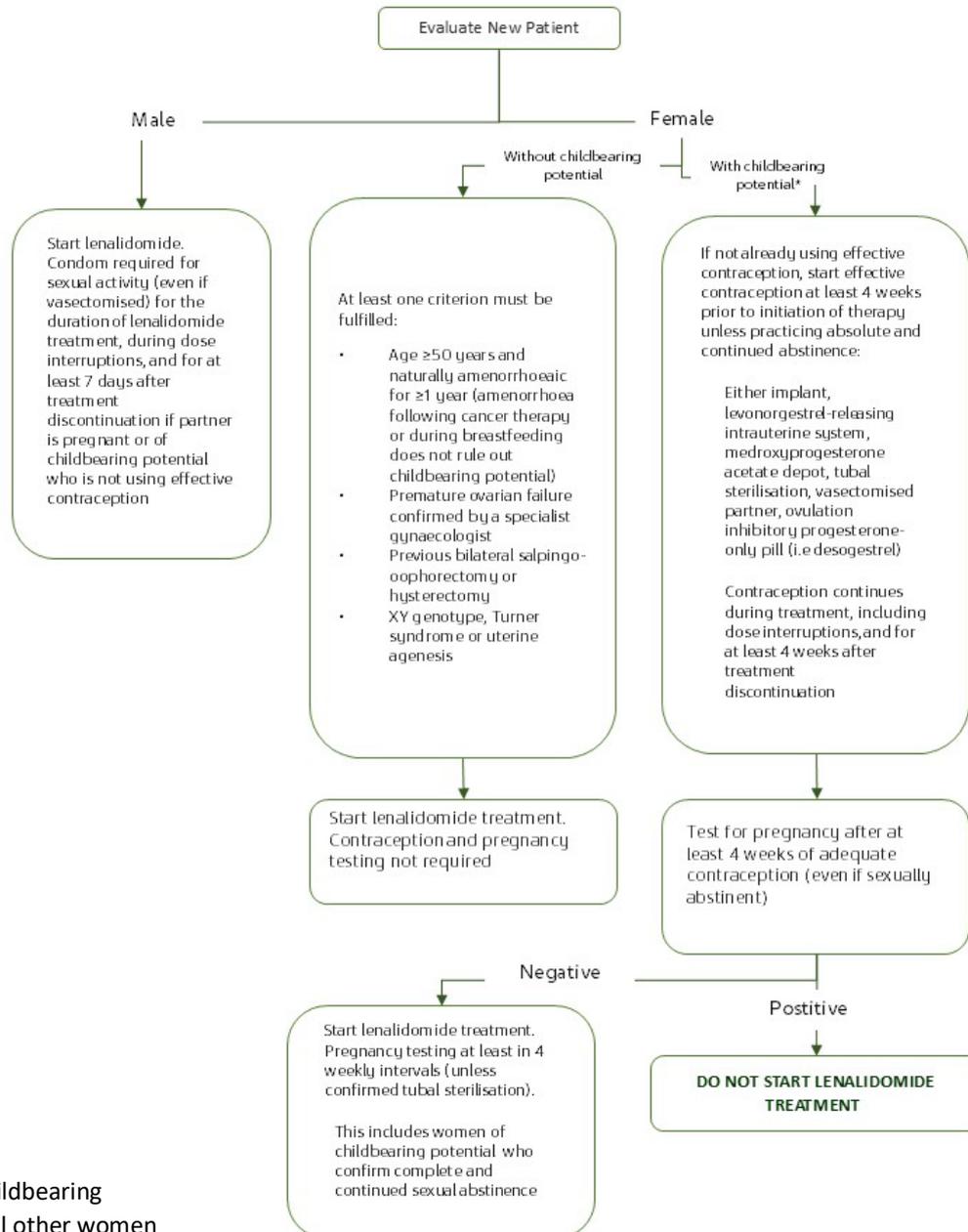
### **Teva Pharmaceuticals Ireland**

Email: [medinfo@tevauk.com](mailto:medinfo@tevauk.com)

Tel: 0044 207 540 7117

**Suspected adverse reactions can also be reported via the HPRA Pharmacovigilance website: [www.hpra.ie](http://www.hpra.ie)**

# 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 gynaecological opinion if at all unsure as to whether a woman meets the criteria for being of non-childbearing potential

## 8.0 Contact Details

### Digital Hub ([www.patientsafetyhub.ie](http://www.patientsafetyhub.ie)) Queries:

For technical information and questions on the Patient Safety Hub, prescriber registrations, pharmacy registrations and the use of the Prescription Authorisation Form, and the use of the Hub, please contact:

#### Patient Safety Hub

Email: [clientsupport@healthbeacon.com](mailto:clientsupport@healthbeacon.com)

Tel: +353 58 38 234

Fax: 01 902 0925

## Risk Management

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

#### Accord Healthcare Ltd

Email: [medinfo@accord-healthcare.com](mailto:medinfo@accord-healthcare.com)

Tel: 0044 1271 385257

#### Clonmel Healthcare Ltd

Email: [medicalinformation@clonmel-health.ie](mailto:medicalinformation@clonmel-health.ie)

Tel: 1800 932 902

#### Rowex Ltd

Email: [adverse.event.ireland@sandoz.net](mailto:adverse.event.ireland@sandoz.net)

Tel: 087 794 1968

#### Teva Pharmaceuticals Ireland

Email: [medinfo@tevauk.com](mailto:medinfo@tevauk.com)

Tel: 0044 207 540 7117

## 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.

### Accord Healthcare Ltd

Adverse Event Email: [safety.eu@lambda-cro.com](mailto:safety.eu@lambda-cro.com)

Medical Queries Email: [medinfo@accord-healthcare.com](mailto:medinfo@accord-healthcare.com)

Tel: 0044 1271 385257

### Clonmel Healthcare Ltd

Email: [medicalinformation@clonmel-health.ie](mailto:medicalinformation@clonmel-health.ie)

Tel: (052) 6177777

### Rowex Ltd

Email: [adverse.event.ireland@sandoz.net](mailto:adverse.event.ireland@sandoz.net)

Tel: 087 794 1968

### Teva Pharmaceuticals Ireland

Email: [medinfo@tevauk.com](mailto:medinfo@tevauk.com)

Tel: 0044 207 540 7117

**Suspected adverse reactions can also be reported via the HPRA Pharmacovigilance website: [www.hpra.ie](http://www.hpra.ie)**

## Data Protection Contact Details

Please see below contact details for data protection queries for the relevant Marketing Authorisation Holder.

### Accord Healthcare Ltd

Email: [emena\\_compliance@accord-healthcare.com](mailto:emena_compliance@accord-healthcare.com)

### Clonmel Healthcare Ltd

Email: [dpo@clonmel-health.ie](mailto:dpo@clonmel-health.ie)

### Rowex Ltd

Email: [adverse.event.ireland@sandoz.net](mailto:adverse.event.ireland@sandoz.net)

### Teva Pharmaceuticals Ireland

Email: [EUprivacy@tevaeu.com](mailto:EUprivacy@tevaeu.com)