Lenalidomide Krka (lenalidomide)

Healthcare Professionals Information Guide

IRELAND

Version 02

Important Safety Information:
Healthcare Professionals involved in the prescribing or dispensing of lenalidomide must read and understand the information contained within this Guide

For complete safety information, please refer to the Summary of Product Characteristics (SmPC) for Lenalidomide Krka available via the HPRA website: **www.hpra.ie** or on the EMA Website: **www.ema.europa.eu**

Risk Management contact details:
Telephone : +353 1 413 3710
Email : Info.IE@krka.biz *or* pharmacovigilance.IE@krka.biz

Medical Information Queries:
Telephone : +353 1 413 3710
Email : pharmacovigilance.IE@krka.biz

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Lenalidomide Krka (lenalidomide)

Pregnancy Prevention Programme

and

Information for Healthcare Professionals

Prescribing or Dispensing Lenalidomide

IRELAND

This Guide contains the information and materials 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.

Lenalidomide Krka 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 (HCP) ensure that they have read and understood the HCP 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 PPP, as well as safety information, side effects and recommended precautions please also refer to the Lenalidomide Krka Summary of Product Characteristics (SmPC), which is available at the following websites: www.hpra.ie/www.ema.europa.eu.

Contents

Introduction

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 4 mg/kg/day. Findings from this study showed that lenalidomide produced external malformations (short limbs, bent fingers/toes, wrist and/or tail, supernumerary or absent fingers/toes) 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 can be expected. Therefore, lenalidomide is contraindicated in pregnancy and in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are met.

Licensed Indication

Lenalidomide is an immunomodulating medicinal poduct.

- 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 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 initiation of treatment.

Posology

Newly Diagnosed Multiple Myeloma

Lenalidomide maintenance in patients who have undergone autologous stem cell transplantation (ASCT)

The recommended starting dose is lenalidomide 10 mg orally once daily continuously (on Days 1 to 28 of repeated 28-day cycles) given until disease progression or intolerance. After 3 cycles of lenalidomide maintenance, the dose can be increased to 15 mg orally once daily if tolerated. Dose reduction steps are provided in Section 4.2 of the SmPC.

Lenalidomide in combination with dexamethasone until disease progression in patients who are not eligible for transplant

The recommended starting dose of lenalidomide is 25 mg orally once daily on Days 1 to 21 of repeated 28-day cycles. The recommended dose of dexamethasone is 40 mg orally once daily on Days 1, 8, 15 and 22 of repeated 28-day cycles. Patients may continue lenalidomide and dexamethasone therapy until disease progression or intolerance. Dose reduction steps are provided in Section 4.2 of the SmPC.

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^2 body surface area subcutaneously twice weekly on Days 1, 4, 8 and 11 of each 21-day treatment cycles. 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.

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/day orally on Days 1-21 of repeated 28-day cycles for up to 9 cycles, melphalan 0.18 mg/kg orally on Days 1-4 of repeated 28 day cycles, prednisone 2 mg/kg orally on Days 1-4 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 alone as follows: 10 mg/day orally on Days 1-21 of repeated 28-day cycles given until disease progression. Dose reduction steps are provided in Section 4.2 of the SmPC.

Multiple Myeloma patients with at least one prior therapy

The recommended starting dose of lenalidomide is 25 mg orally once daily on Days 1-21 of repeated 28-day cycles. The recommended dose of dexamethasone is 40 mg orally once daily on Days 1-4, 9-12, and 17-20 of each 28-day cycle for the first 4 cycles of therapy and then 40 mg once daily on days 1-4 every 28 days. Dosing is continued or modified based upon clinical and laboratory findings. Prescribing physicians 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.

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.

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.

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^2 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.

Lenalidomide Krka Pregnancy Prevention Programme (PPP)

- It is a requirement of the Pregnancy Prevention Programme that all Healthcare Professionals read and understand this Guide before prescribing or dispensing Lenalidomide Krka 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 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 illustrated in the **Algorithm below**
- Patients should be capable of complying with the requirements of safe use of lenalidomide
- Patients must be provided with appropriate Patient Educational Guide (Patient Guide) and Patient Pocket Information Card

All of the Lenalidomide Krka Pregnancy Prevention Programme materials are available electronically on the website www.hpra.ie (enter 'Lenalidomide Krka' under 'Find a Medicine' and click 'EdM' under the 'Documents' column). Additional hard copies can be obtained from KRKA by using the contact details provided in this Guide.

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

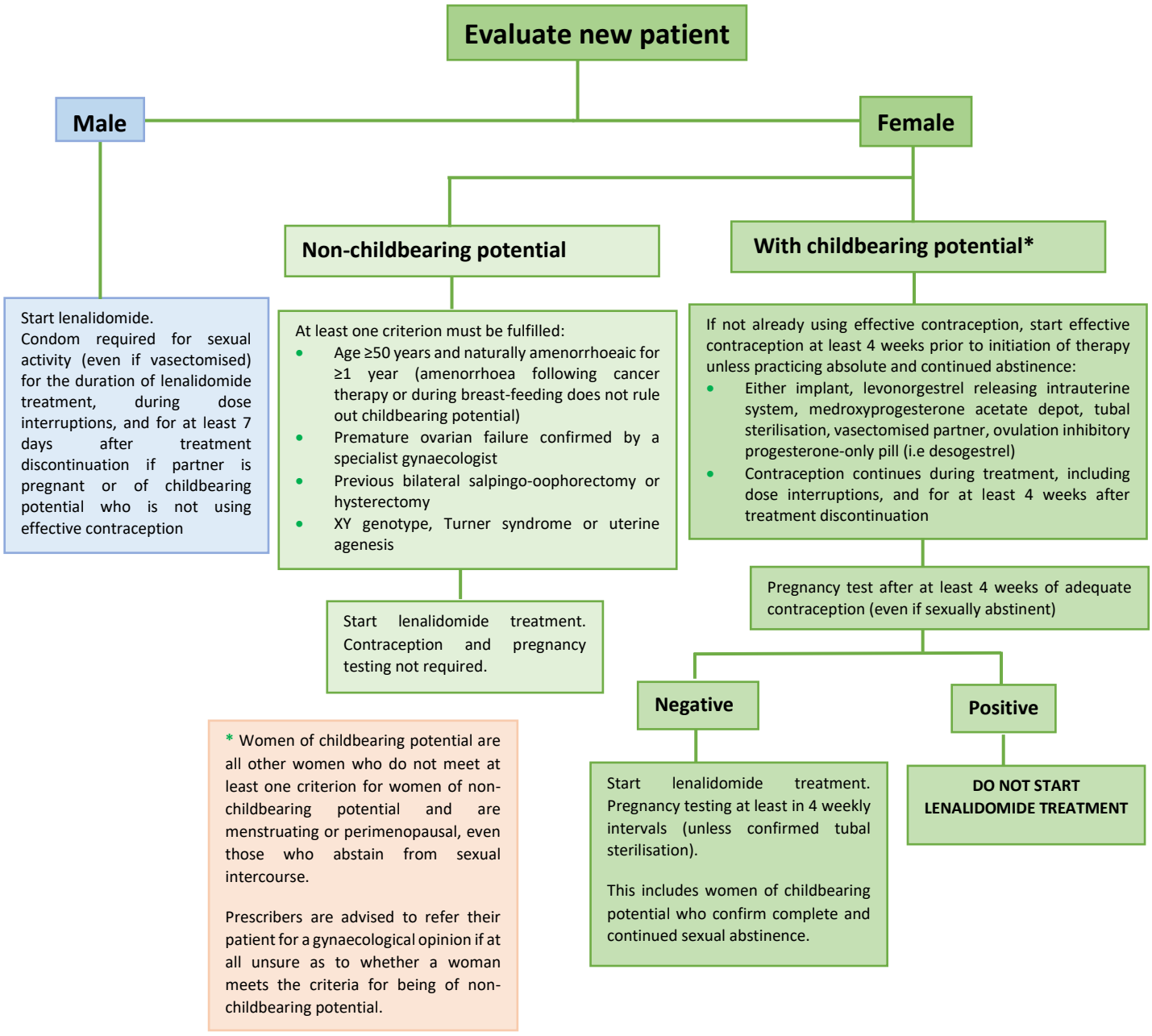
In order to ensure that the actions to minimise the risk of foetal exposure are carried out for all patients, dispensing of Lenalidomide Krka will only be allowed from pharmacies registered with KRKA. KRKA will not authorise supply of lenalidomide to pharmacies that are not registered with KRKA.

The following are core requirements of the Pregnancy Prevention Programme (PPP):

- A controlled distribution system
- All healthcare professionals who intend to prescribe or dispense lenalidomide must be provided with Lenalidomide Krka Healthcare Professional's Information Guide and other relevant materials as needed

- All healthcare professionals prescribing or dispensing lenalidomide must read and understand the Healthcare Professional's Information Guide
- Every prescription for lenalidomide must be accompanied by a Prescription Authorisation Form, which must be completed and signed by the prescriber and checked and counter-signed by the pharmacy
- All pharmacies who dispense Lenalidomide Krka must implement risk minimisation by registering with the KRKA Pregnancy Prevention Programme and in accordance with the measures described in this Guide

Description of Pregnancy Prevention Program and Patient Evaluation Algorithm



Safety Advice to Avoid Foetal Exposure

PPP Advice for Women of Non-Childbearing Potential

Determine if a woman is of 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 amenorrhoeic for ≥ 1 year (amenorrhoea following cancer therapy or during breast-feeding does not rule out childbearing potential)
- Confirmed premature ovarian failure if 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 unsure whether or not she meets the criteria for being of non-childbearing potential.

PPP Advice for Women of Childbearing Potential

Women of childbearing potential must never take lenalidomide if:

- 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 sexual abstinence, confirmed on 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 every 4 weeks 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 continuous 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 prescriber 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 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 inform her prescriber.

Requirements in the event of a suspected pregnancy while on treatment with Lenalidomide Krka:

- **Stop treatment immediately**
- **Refer the patient to a physician specialised or experienced in teratology for evaluation and advice**
- **Notify KRKA immediately of all such occurrences by contacting KRKA (Telephone❨: +353 1 413 3710; Email✉: pharmacovigilance.IE@krka.biz). Please also complete the Pregnancy Reporting Form. KRKA 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.**

PPP Advice for 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 becomes pregnant whilst he is taking lenalidomide or shortly after he has stopped taking lenalidomide he should inform his prescriber immediately. The partner should inform her docter 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 7 days following discontinuation of lenalidomide.

If the partner of a male taking Lenalidomide Krka becomes pregnant, 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 KRKA immediately of all such occurrences by contacting KRKA (Telephone❨: +353 1 413 3710; Email✉: pharmacovigilance.IE@krka.biz). Please also complete the Pregnancy Reporting Form. KRKA 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.

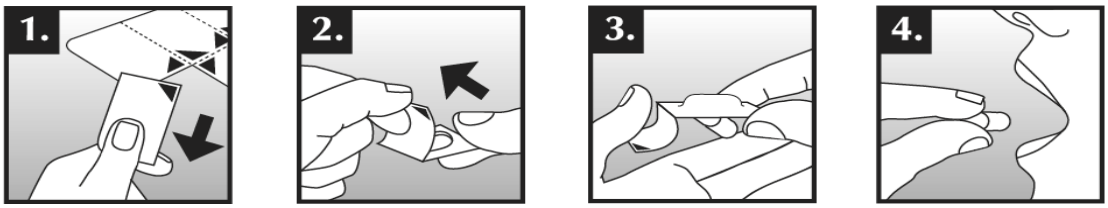
Points to consider for handling the medicinal product: for patients, healthcare professionals and caregivers

Taking this medicine

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.

To remove the Lenalidomide Krka capsule from the blister:

1. Hold the blister at the edges and separate one blister cell from the rest of the blister by gently tearing along the perforations around it.
2. Pull up the edge of the foil and peel the foil off completely.
3. Tip the capsule out onto your hand.
4. Swallow the capsule whole, preferably with water.



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 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 tell your doctor and / or pharmacist immediately or please report to KRKA (Phone number: +353 1 413 3710; Email: pharmacovigilance.IE@krka.biz).

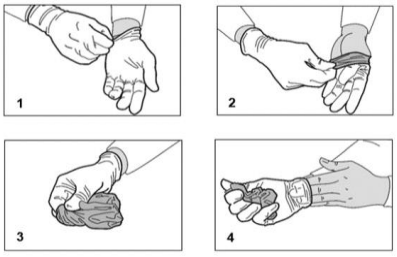
If the contents of the capsule are attached to the skin or mucous membranes

- If you touch the drug powder, please wash exposed area thoroughly with running water and soap.
- If your eye had contact with the powder, 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

Healthcare professionals and caregivers should wear disposable gloves when handling the blister or capsule. Gloves should then be removed carefully to prevent skin exposure 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.

- 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



Blood donations

Patients should not donate blood during treatment, including during dose interruptions and for at least 7 days after stopping of treatment with lenalidomide.

Prescribing and Dispensing Lenalidomide

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

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 (women of non-childbearing potential or male)**, prescriptions of lenalidomide should be limited to a maximum duration of 12 weeks and continuation of treatment requires a new prescription.

Initial Prescription

Before issuing the initial prescription, you must:

- Counsel the patient on the safe use of lenalidomide in accordance with the measures described in this 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
- Ensure that your patient is using an effective method of contraception, if appropriate
- Perform a pregnancy test (if appropriate) before initiating treatment

Community Pharmacy Notification

A lenalidomide Community Pharmacy Dispensing Notification Form should be used to advise the community pharmacy that it has been nominated by the patient and of the need to be registered with the manufacturer in order to dispense lenalidomide. The lenalidomide Community Pharmacy Dispensing Notification Form must be completed by the prescriber and faxed/emailed to the patient's nominated pharmacy on the first occasion that the patient is being prescribed lenalidomide.

Subsequent Prescriptions

- Before issuing subsequent prescriptions, 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.
- Provide a 'Prescription Authorisation Form' to the patient or submit electronically to the pharmacy with each lenalidomide prescription.

Prescribers wishing to prescribe Lenalidomide Krka must read the Healthcare Professional's Information Guide provided by KRKA. This is available in hardcopy from KRKA or electronically via the website www.hpra.ie.

Prescription Authorisation Form

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 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 information provided on this Prescription Authorisation Form 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.

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

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

The Prescription Authorisation Form should be retained with the High Technology Prescription in the pharmacy.

Dispensing Lenalidomide

It is a requirement of the Pregnancy Prevention Programme that pharmacies wishing to purchase and dispense Lenalidomide Krka are registered with KRKA. Registration involves reading and understanding the Healthcare Professional's Information Guide, completing and signing the Pharmacy Registration Form, and emailing the completed form to indicate agreement and compliance with the content.

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 Krka will only be allowed from pharmacies registered with KRKA. KRKA will not authorise purchase and supply of lenalidomide to pharmacies not registered with KRKA.

Lenalidomide Krka is supplied to pharmacies registered with KRKA's Pregnancy Prevention Programme (PPP) only for the purpose of dispensing the product by the PPP registered pharmacy to the patient.

Community Pharmacy Notification and Registration

A lenalidomide Community Pharmacy Dispensing Notification Form should be received from the prescriber/hospital pharmacy to advise the community pharmacy that it has been nominated by the patient and that it will soon be receiving a High-Tech Prescription for lenalidomide for your patient. The community pharmacy will need to register with the Lenalidomide Pregnancy Prevention Programme for the manufacturer of any products it will be dispensing prior to being able to order those lenalidomide product for your patient and dispense them. If the nominated pharmacy is not already authorised to supply Lenalidomide Krka, it must first contact KRKA to register with them using the **Lenalidomide Krka (lenalidomide) Pharmacy Registration Form**. KRKA will then send the pharmacy the relevant documentation if not already received.

Ordering of lenalidomide

The pharmacy must be registered with KRKA to order Lenalidomide Krka. To order Lenalidomide Krka the pharmacy must use a specific Lenalidomide Krka (lenalidomide) Order Form (available on request from KRKA and electronically for download on the HPRA website: www.hpra.ie). The pharmacy must write the name of the prescriber on their Order Form when placing an order for lenalidomide.

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.
- ideally, pregnancy testing, issuing a prescription and dispensing should occur on the same day.
- prescriptions for lenalidomide should be limited to 4 weeks of treatment and continuation of treatment requires a new prescription.

For males and women of non-childbearing potential

- prescriptions of lenalidomide should be limited to 12 weeks and continuation of treatment requires a new prescription.

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 PPP and the dispensing procedures for lenalidomide.

Monitoring the Effectiveness of the Programme and Monitoring of Off-Label Use

The terms of the Lenalidomide Krka Marketing Authorisation require KRKA to assess the effectiveness of the Pregnancy Prevention Programme (PPP) 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 off-label use.

KRKA have agreed with the HPRA that pharmacies can fulfil their obligations in this respect, by conducting a manual self-audit of the Prescription Authorisation Forms, against which the pharmacy has dispensed Lenalidomide Krka and reporting the results to KRKA. This information will be provided in an anonymous and aggregated format to the HPRA. KRKA will supply pharmacies who are registered with KRKA with an Audit Form, such that annual self-auditing of the pharmacies and feedback of the audit results to KRKA can occur.

It is therefore critical for pharmacies to ensure that all documentation associated with the PPP is completed accurately and that audit results are provided faithfully and diligently, in the interest of patient safety.

Other Selected Risks of Lenalidomide

The following section contains advice to Healthcare Professionals about how to minimise the main risks associated with the use of lenalidomide. Please refer also to the 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).

Tumour flare reaction in mantle cell lymphoma and follicular lymphoma patients

Tumour flare reaction (TFR) has commonly been observed in patients with mantle cell lymphoma, who were treated with lenalidomide or 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 practiced when introducing these patients to lenalidomide. These patients should be monitored closely, especially during the first cycle or dose-escalation and appropriate precautions taken.

At the physician's discretion, lenalidomide may be continued in patients with Grade 1 or 2 TFR without interruption or modification. At the physician'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.

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.

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).

Reporting Adverse Events, Suspected and Confirmed Pregnancies, and Foetal Exposure

The safe use of lenalidomide is of paramount importance.
Adverse Events (and cases of Suspected or Confirmed Pregnancy or Foetal Exposure) should be reported to the manufacturer. Adverse Event Report Forms and Pregnancy Reporting Forms for Lenalidomide Krka should be forwarded to KRKA Medical Information (Telephone❫: +353 1 413 3710; Email✉: pharmacovigilance.IE@krka.biz)

Suspected Adverse reaction reports can also be reported via the HPRA Pharmacovigilance website: www.hpra.ie.

Prescribers Guide to Prescribing Lenalidomide Schematic

In order to initiate therapy with lenalidomide:

1. Read the Lenalidomide Healthcare Professional's Information Guide
2. Evaluate childbearing potential of patient and implement the Pregnancy Prevention Programme as required
3. Evaluate risks relevant to all patients, take relevant precautions and provide counselling as appropriate
   a. Provide Educational Materials (Patient Guide and Patient Pocket Information Card) to the patient.
   b. Obtain patient's signature for the Treatment Initiation Form and provide patient with a copy.

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

For the FIRST prescription of lenalidomide Follow steps 1 to 4

1. Prescribers wishing to prescribe lenalidomide must read the Healthcare Professional's Information Guide
2. Please complete **a Lenalidomide Community Pharmacy Dispensing Notification Form** to notify the nominated community pharmacy that their patient will be presenting with a prescription for lenalidomide. Fax/E-mail this form to the Nominated Community Pharmacy.

For SUBSEQUENT prescriptions of lenalidomide Follow steps 3 to 4

3. Prescribe lenalidomide using High Technology Medicines prescription. Only a maximum of 4 weeks can be dispensed per prescription for a woman of childbearing potential. Up to a maximum of 12 weeks can be dispensed per prescription for a woman not of childbearing potential and male patients.
4. All prescriptions for lenalidomide must be accompanied by a **Lenalidomide Prescription Authorisation Form.**

Pharmacists Guide to Dispensing Lenalidomide Schematic

In order to dispense Lenalidomide Krka:

As a nominated community pharmacy, you will receive a ***'Community Pharmacy Dispensing Notification Form'*** from the Hospital or Clinic informing you that a patient will soon be presenting with a High Technology Prescription for lenalidomide.

You are a Community Pharmacy that has NOT previously registered with KRKA

1. Contact KRKA on Info.IE@krka.biz/ pharmacovigilance.IE@krka.biz to obtain a Healthcare Professional's Information Guide which includes all relevant information, Pharmacy Registration Form and Order Form (if you have not already received these materials).
2. Read the Guide.
3. Complete **Pharmacy Registration Form** and Email to KRKA on Info.IE@krka.biz/ pharmacovigilance.IE@krka.biz. You will be notified when you have been registered.
4. Once you are informed that you are registered with KRKA, complete a **'Lenalidomide Krka (lenalidomide) Order Form'.**
5. Fax/Email **'Lenalidomide Krka (lenalidomide) Order Form'** to UDD on 01 463 2404/SpecialOrders@united-drug.com. UDD aim to deliver complete orders placed before 13:30 Monday - Friday on the customers' next available route as per customers' current delivery arrangements with United Drug Wholesale.
6. For orders through Uniphar, email 'Lenalidomide Krka (lenalidomide) Order Form' to KRKA on Info.IE@krka.biz

You are a Community Pharmacy that has previously registered with KRKA

1. Complete a '**Lenalidomide Krka (lenalidomide) Order Form'**.
2. Fax/Email **'Lenalidomide Krka (lenalidomide) Order Form'** to UDD on 01 463 2404/SpecialOrders@united-drug.com. UDD aim to deliver complete orders placed before 13:30 Monday - Friday on the customers' next available route as per customers' current delivery arrangements with United Drug Wholesale.

Or

3. For orders through Uniphar, email'Lenalidomide Krka (lenalidomide) Order Form' to KRKA on Info.IE@krka.biz

Note. Please ensure that all details are completed on this Order Form in full to ensure your order is processed appropriately and in a timely manner.

Complete Pharmacist's declaration section of the '**Prescription Authorisation Form'**. This form is retained with the High Technology Prescription in the pharmacy. Dispense lenalidomide from High Technology Prescription

A Guide to Completing the Prescription Authorisation Form (PAF)

This guide will help you complete the lenalidomide Prescription Authorisation Form. The form is used within the Pregnancy Prevention Programme (PPP) and must be completed each time you prescribe or dispense lenalidomide.

Instructions for prescribers

1. Print the full hospital name where the patient is treated.
2. Print the patient's date of birth and initials. If the middle initial is not known please use an underscore (e.g. J_S for John Smith). Do not provide confidential information (e.g. Patient Name and Hospital Number).
3. Print your name clearly.
4. Clearly print the name of the Supervising Physician (if you are not the supervising physician) i.e. the Physician experienced in managing immunomodulatory drugs and supervising treatment.
5. Tick the indication for which lenalidomide is being prescribed – this is for the purposes of monitoring off-label use.
6. Enter the capsule strength, quantity of capsules prescribed and the number of cycles precribed.
7. Complete this section appropriately to indicate that counselling has occurred and appropriate contraceptive measures are in place. This is a requirement of the Pregnancy Prevention Programme.
8. For women of childbearing potential you must provide a valid negative pregnancy test date (within 3 days prior to prescribing). If this is not included lenalidomide must not be dispensed.
9. You must sign, date and print your name to declare that all steps have been observed and that you authorise the Prescription Authorisation Form.

Instructions for pharmacists

A. Check that all relevant sections of the form have been fully completed by the prescriber, including that:
   - counselling and contraceptive measures have been confirmed by the prescriber as appropriate
   - indication, capsule strength, quantity or capsules and number of cycles prescribed have been provided
   - for women of childbearing potential a negative pregnancy test date is provided and is within 3 days of the prescription date

B. Check the form does not contain confidential information (e.g. Patient Name and Hospital Number).

C. Check the form is complete and legible.

D. You must sign, date and print your name to declare that the form has been completed fully and dispensing is taking place within 7 days of the date of prescription for women of childbearing potential.
   - dispense only a maximum of 4 weeks supply for Women of childbearing potential at any one time
   - dispense only a maximum of 12 weeks supply for Males and Women of non-childbearing potential

E. Ensure you record the brand of lenalidomide dispensed for each dispensing cycle the PAF was used for. You will need this for completion of the pharmacy self-audit for the particular lenalidomide brand.

Further information and materials are available from KRKA

Phone number✆: +353 1 413 3710

Email✉: Info.IE@krka.biz **or** pharmacovigilance.IE@krka.biz

Lenalidomide Prescription Authorisation Form (PAF)

A newly completed copy of this form MUST accompany EVERY lenalidomide prescription. Completion of this information is mandatory for ALL patients. The completed form should be retained in the pharmacy.

Name of treating Hospital:						
Patient date of birth: DD/MM/YYYY		**Patient ID number/Initials:**				
Prescriber (PRINT):						
Supervising Physician:						
Indication (tick)						
☐ Multiple Myeloma						
☐ Myelodysplastic Syndromes with isolated del5q cytogenetic abnormality						
☐ Mantle Cell Lymphoma relapsed and/or refactory						
☐ Follicular Lymphoma						
☐ Other (please specify) _____						
Capsule strength prescribed (tick) / Quantity of capsules prescribed(*do not enter number of packs)						
☐ 2.5 mg	☐ 5 mg	☐ 7.5 mg	☐ 10 mg	☐ 15 mg	☐ 20 mg	☐ 25 mg
Quantity*	Quantity*	Quantity*	Quantity*	Quantity*	Quantity*	Quantity*
Number of cycles prescribed:						
Please tick all boxes that apply						
Woman of non-childbearing potential	TICK					
Male	TICK					
The patient has been counselled about the teratogenic risk of treatment with lenalidomide and understands the need to use a condom if involved in sexual activity with a woman of childbearing potential not using effective contraception or if their partner is pregnant (even if the patient has had a vasectomy).					Y	N
Note to pharmacists – do not dispense unless ticked 'Y' for male patients'						
Woman of childbearing potential	TICK					
The patient has been counselled about the teratogenic risk of treatment and the need to avoid pregnancy, and has been on effective contraception for at least 4 weeks or committed to absolute and continuous abstinence confirmed on a monthly basis.					Y	N
Date of last negative pregnancy test	DD	MM	YYYY			
Note to pharmacists – do not dispense unless ticked 'Y' and a negative test has been conducted within 3 days prior of the prescription date and dispensing is taking place within 7 days of the prescription date						

Both signatures must be present prior to dispensing lenalidomide.

Prescriber's declaration

As the Prescriber, I have read and understood the lenalidomide Healthcare Professional's Information Guide. I confirm the information provided on this PAF is accurate, complete and in accordance with the requirements of the Pregnancy Prevention Programme for lenalidomide. I confirm treatment has been initiated and is monitored under the supervision of a physician with expertise in managing immunomodulatory or chemotherapeutic agents.

Sign	Print
Date DD MM YYYY	Bleep number

Pharmacist's declaration

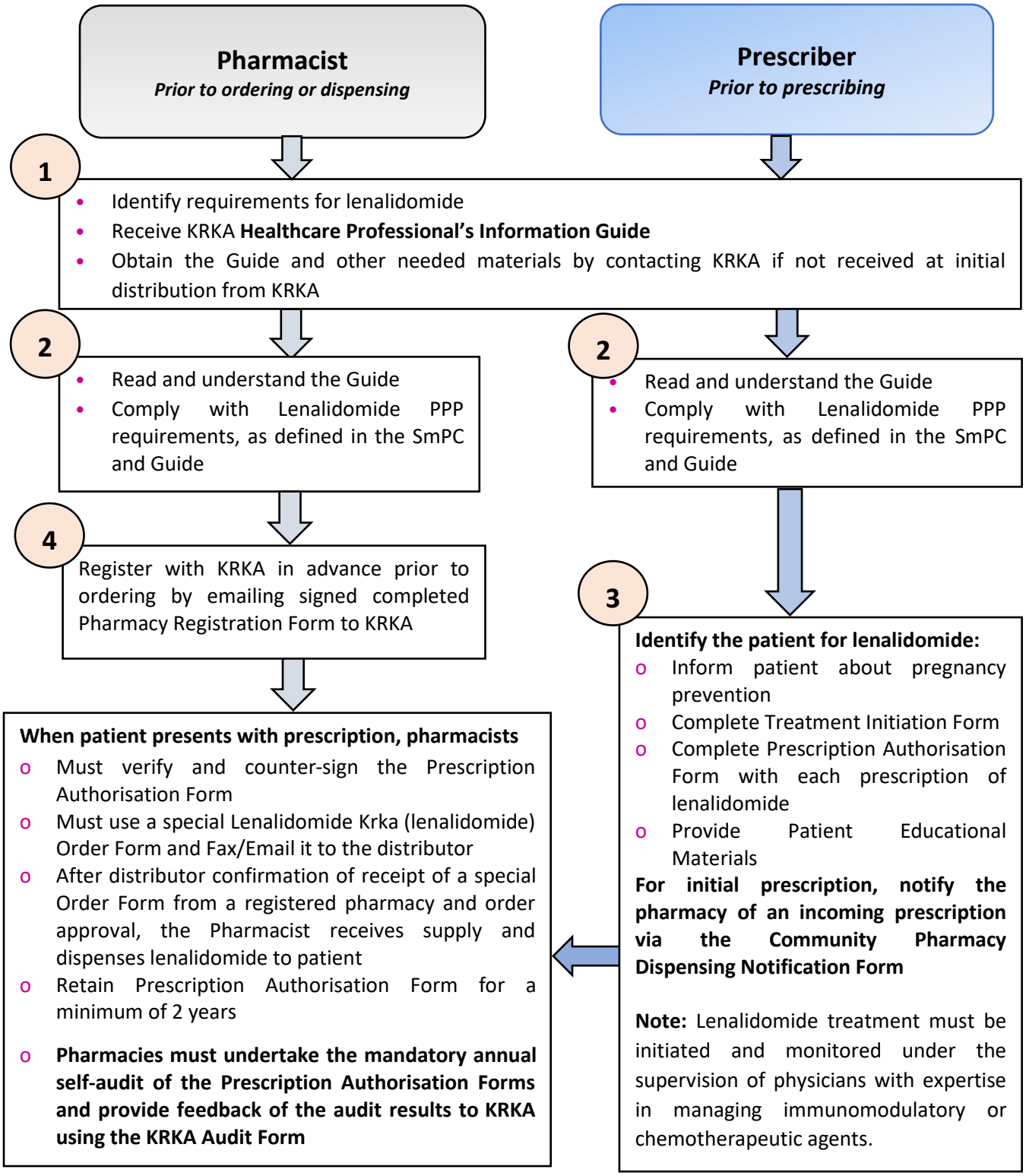
I am satisfied that this **Lenalidomide** Prescription Authorisation Form has been completed fully and that I have read and understood the **Lenalidomide** Healthcare Professional's Information Guide. For women of childbearing potential, dispensing will be taking place within 7 days of the date of prescription. I am dispensing no more than a 4 weeks supply to women of childbearing potential and 12 weeks for males and women of non-childbearing potential.

Sign	Print
Date	DD MM YYYY
Name of dispensing pharmacy	
Lenalidomide Brand dispensed	

Mandatory Lenalidomide Krka Order Forms

Following discussions with the Health Products Regulatory Authority (HPRA), compliance with the PPP will also be monitored through Lenalidomide Krka (lenalidomide) Order Forms to enable additional exposure data to be captured.
All information required to complete these Order Forms can be found on the Prescription Authorisation Form. Order Forms will be forwarded by United Drug Distribution (UDD) to KRKA who will then compile anonymised and aggregated data reports to provide to the HPRA on a annual basis.
KRKA will keep the Order Forms for orders through Uniphar and will provide Uniphar with a copy.

Prescribing and Dispensing of Lenalidomide Schematic



Contact Details

Risk Management:

For information and questions on the Risk Management of KRKA products, Lenalidomide Krka Pregnancy Prevention Programme, Pharmacy Registrations, and the use of the Prescription Authorisation Form and to order hard copies of any of the Lenalidomide Krka Pregnancy Prevention Plan materials:

Telephone 🕽: +353 1 413 3710
Email ✉: Info.IE@krka.biz *or* pharmacovigilance.IE@krka.biz

Medical Information:

To report any Adverse Events or Suspected Pregnancies, or to obtain Medical Information on Lenalidomide KRKA products.

Telephone 🕽: +353 1 413 3710
Email ✉: pharmacovigilance.IE@krka.biz

Suspected adverse reactions can also be reported via the HPRA Pharmacovigilance website: **www.hpra.ie.**

Data Protection:

Telephone 🕽: +353 1 413 3710
Email ✉: Info.IE@krka.biz

Distributor:

For product delivery enquiries.

United Drug Distribution (UDD)
United Drug House
Magna Business Park
Citywest Road, Dublin 24

Telephone🕽: 01 463 2478
Fax: 01 463 2404
Email✉: SpecialOrders@united-drug.com

Or

Uniphar Group
4045 Kingswood Road
Citywest Business Park
Co. Dublin, D24 VO6K

Reception Telephone🕽: 01 428 7777
Customer Service🕽: 01 468 7501
Email✉: RepsOrders@uniphar.ie
Orders Email✉: Info.IE@krka.biz

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