Lenalidomide Rowex

Healthcare Professional's Information Guide

Ireland

Important Safety Information

Healthcare Professionals involved in the prescribing or dispensing of lenalidomide must read and understand the information contained in this guide.

For complete safety information please refer to the Summary of Product Characteristics (SmPC) for Lenalidomide Rowex available at the following website: HPRA www.hpra.ie

Lenalidomide Pregnancy Prevention Programme and Information for Healthcare Professionals involved in the prescribing or dispensing of lenalidomide.

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

Lenalidomide Rowex Pregnancy Prevention Programme:

If lenalidomide is taken during pregnancy it is expected to cause severe birth defects or death to an unborn baby. This Programme is designed to make sure that unborn babies are not exposed to lenalidomide. It will provide you with information about how to follow the programme and explain your responsibilities.
It is a requirement of the Pregnancy Prevention Programme that all Healthcare Professionals (HCPs) ensure that they have read and understood this 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 refer to the Lenalidomide Rowex Summary of Product Characteristics (SmPC). This can be found on the following website: www.hpra.ie

Contents

1. Introduction

1.1. Licenced indication and posology

Lenalidomide is an immunomodulating medicinal product.

Lenalidomide Rowex 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 Rowex 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 Rowex 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 Rowex 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.

1.2 Posology

Newly Diagnosed Multiple Myeloma
Lenalidomide Maintenance in Patients who have Undergone Autologous Stem Cell Transplantation (ASCT) 2022
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.

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/m2 body surface area subcutaneously twice weekly on Days 1, 4, 8 and 11 of each 21-day cycle. Up to eight 21-day treatment cycles (24 weeks of initial treatment) are recommended. Continue lenalidomide 25 mg orally once daily on Days 1 to 21 of repeated 28-day

cycles in combination with dexamethasone. Treatment should be continued until disease progression or unacceptable toxicity. Dose reduction steps are provided in Section 4.2 of the SmPC.

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.

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.

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

Lenalidomide – Risk of Teratogenicity

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

2. Lenalidomide Rowex Pregnancy Prevention Programme

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

• All men and all women of childbearing potential should undergo, at treatment initiation, counselling regarding the need to avoid foetal exposure to lenalidomide during pregnancy (this must be documented via a Treatment Initiation Form and checklists for counselling which are available for this purpose).

• The description of the Pregnancy Prevention Programme and the categorisation of patients based on sex and childbearing potential is set out in the Algorithm contained within this guide.

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

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

All of the lenalidomide Rowex Pregnancy Prevention Programme materials are available electronically on the HPRA website: www.HPRA.ie (enter 'Lenalidomide Rowex' under 'Find a Medicine' and click 'EdM' under the 'Documents' column). Additional hard copies can be obtained from Rowex 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 Rowex will only be allowed from pharmacies registered with Rowex Ltd.
Rowex Ltd. will not authorise supply of Lenalidomide Rowex to pharmacies that are not registered with Rowex.

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

- A controlled distributing system
- All HCPs dispensing or prescribing lenalidomide must read and understand the lenalidomide HCP's Information Guide
- All prescriptions for lenalidomide must be accompanied by a lenalidomide Prescription Authorisation Form, which must be completed by the prescriber and the pharmacist
- All pharmacies who dispense Lenalidomide Rowex must implement risk minimisation by registering with the Rowex Pregnancy Prevention Programme and in accordance with the measures described in this guide.

2.2 Safety advice to avoid foetal exposure

- **2.2.1 Women of non-childbearing potential**

Women in the following group 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. Please note amenorrhea following cancer therapy or during lactation 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.

➢ 2.2.2 Women of child-bearing 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 amenorrhea) must:

- Use one effective method of contraception (see below) for 4 weeks before therapy, during therapy, and until 4 weeks after lenalidomide therapy, and even in case of dose interruption

or

- Commit to absolute and continuous sexual abstinence

and

- Have a medically supervised negative pregnancy test (with a minimum sensitivity of 25 mIU/ml) once established on contraception for 4 weeks, at 4-weekly intervals during therapy and 4 weeks after the end of therapy (unless confirmed tubal sterilisation). This also 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 HCP 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 sterilization
- 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 Rowex, she must immediately stop treatment and inform her physician.

Refer the woman to a physician specialised or experienced in teratology for evaluation and advice.

Notify Rowex Ltd. immediately of all such occurrences by contacting Rowex Ltd. Drug Safety Department (Tel: 02750077) or email: pv@rowa-pharma.ie Please also complete the Pregnancy Reporting Form. Rowex Ltd. will wish to follow-up with you the progress of all pregnancies.

Suspected pregnancies can also be reported via the HPRA Pharmacovigilance website: www.hpra.ie

- **2.2.3 Men**

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

Pharmacokinetic data has demonstrated that lenalidomide is present in human semen at extremely low levels during treatment and is undetectable in human semen 3 days after stopping the drug in the healthy subject.

As a precaution, all male patients taking lenalidomide should be informed of the following:

- The effective contraceptive methods that his female partner can use.
- If their partner is pregnant or of childbearing potential and not using effective contraception, that the male patients should use condoms throughout the duration of treatment, during dose interruption and for 1 week after cessation of treatment, even if the male patient has undergone a vasectomy.
- If pregnancy occurs in a partner of a male patient 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 prescriber 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 taking Lenalidomide Rowex becomes pregnant, he must inform his physician immediately. Then refer the female partner to a physician specialised or experienced in teratology for evaluation and advice.

Notify Rowex Ltd. immediately of all such occurrences by contacting Rowex Ltd. Drug Safety Department (Tel: 02750077) Please also complete the Pregnancy Reporting Form. Rowex Ltd. will wish to follow-up with you the progress of all pregnancies.

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

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.

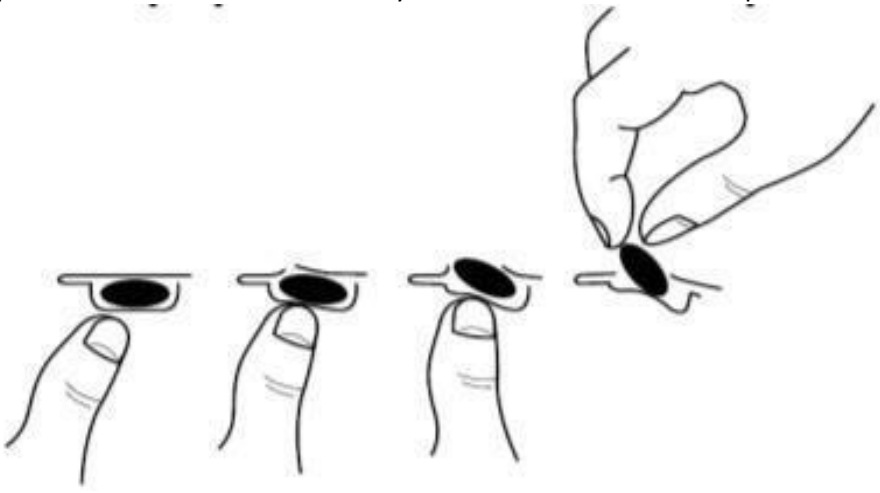
Keep the blisters with the capsules in the original pack.

Capsules can occasionally become damaged when pressing them out of the blister, especially when the pressure is put onto the middle of the capsule. Capsules should not be pressed out of the blister by putting pressure on the middle nor by putting pressure on both ends as this can result in deformation and breaking of the capsule.

Healthcare professionals and caregivers should wear disposable gloves when handling the blister or capsule. Gloves should then be removed carefully to prevent skin exposure, placed in a sealable plastic polyethylene bag and disposed of in accordance with local requirements. Hands should then be washed thoroughly with soap and water.

Women who are pregnant or suspect they may be pregnant should not handle the blister or capsule.

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



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

- If you are a woman who is pregnant or suspect that you may be pregnant, you should not handle the blister or capsule
- Wear disposable gloves when handling product and/or packaging (i.e. blister or capsule)
- Use proper technique when removing gloves to prevent potential skin exposure (see below)

- Place gloves in sealable plastic polyethylene bag and dispose according to local requirements
- Wash hands thoroughly with soap and water after removing gloves.

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

- If outer carton is visibly damaged – Do Not Open
- If blister strips are damaged or leaking or capsules are noted to be damaged or leaking – Close Outer Carton Immediately
- Place the product inside a sealable plastic polyethylene bag
- Return unused pack to the pharmacist for safe disposal as soon as possible.

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

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

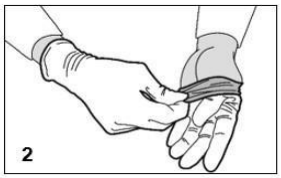
If the contents of the capsule are attached to the skin or mucous membranes

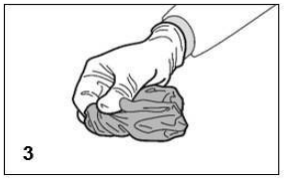
- If you touch the drug powder, please wash exposed area thoroughly with running water and soap
- If the powder gets in contact with your eye, if worn and if easy to do, remove contact lenses and discard them. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation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

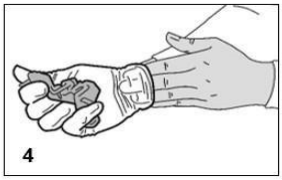
Proper Technique for Removing Gloves:

- Grasp outside edge near wrist (1)
- Peel away from hand, turning glove inside-out (2)
- Hold in opposite gloved hand (3)
- Slide ungloved finger under the wrist of the remaining glove, be careful not to touch the outside of the glove (4)
- Peel off from inside, creating a bag for both gloves
- Discard in appropriate container

Wash your hands with soap and water thoroughly.







2.3 Prescribing and Dispensing lenalidomide

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

➢ 2.3.1 Maximum prescription lengths

You may prescribe a maximum of four weeks of therapy for women of childbearing potential, or twelve weeks of therapy for all other patients and continuation of treatment requires a new prescription.

➢ 2.3.2 Initial prescription

Before issuing the initial prescription you must:

- Counsel the patient on the safe use of lenalidomide in accordance with the measures described in this guide and the SmPC.
- Obtain their 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.

➢ 2.3.3 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.

– 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 the Healthcare Professional Information Guide before prescribing lenalidomide Rowex.

➢ 2.3.4 Prescription Authorisation Form

A completed Prescription Authorisation Form must accompany every prescription.

The patient must present their 'Prescription Authorization Form' to the pharmacy for each 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 Prescriber must confirm 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.
- 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.
- 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.
- 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 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 chemotherapy.

The Pharmacist must confirm on the Prescription Authorisation Form:

- That the Prescription Authorization Form has been completed in full by the prescriber
- That dispensing 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 this guide.

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

The Prescription Authorisation From should be retained with the High-Tech Prescription in the pharmacy.

2.4 Dispensing Lenalidomide

It is a requirement of the Pregnancy Prevention Programme that pharmacies wishing to purchase and dispense Lenalidomide Rowex are registered with Rowex Ltd. Registration involves reading and understanding the Healthcare Professional's Information Guide, completing and signing the Pharmacy Registration Form and e-mailing or posting the completed form to Rowex Ltd. to indicate agreement and compliance with the content.
In order to be registered, the Chief Pharmacist/Superintendent 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 Rowex will only be allowed from pharmacies registered with Rowex Ltd.
Rowex Ltd. will not authorise purchase and supply of Lenalidomide Rowex to pharmacies not registered with Rowex Ltd.

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

2.4.1 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 Rowex, it must first contact Rowex to register with them using the **Lenalidomide Rowex Pharmacy Registration Form**. Rowex will then send the pharmacy the relevant documentation if not already received.

2.4.2 Ordering lenalidomide

The pharmacy must be registered with Rowex Ltd. to order lenalidomide Rowex. To order Lenalidomide Rowex the pharmacy must use a specific lenalidomide Rowex order form (available on request from Rowex 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.

2.4.3 Dispensing Advice

2.4.3.1 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.

2.4.3.2 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.

2.4.2.3 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 to the pharmacy. Pharmacies must accept any unused lenalidomide 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 of the PPP and the dispensing procedures for lenalidomide.

3. Follow-up

3.1 Follow-up assessment of the effectiveness of the Programme and monitoring of off-label use

The terms of the Lenalidomide Rowex Marketing Authorization require Rowex Ltd. 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 pregnancy in patients treated with lenalidomide as well as to monitor for off- label use.
Pharmacies can therefore fulfill their obligations in this respect, by conducting a n annual self- audit of the prescription authorization forms, against which the pharmacy has dispensed lenalidomide Rowex and reporting appropriately anonymised and aggregated results to Rowex Ltd. This information will be provided in an anonymous and aggregated format to the HPRA. Rowex Ltd. will supply pharmacists with a self-audit pack, such that self-auditing of pharmacies and feedback of the audit results to Rowex Ltd. can occur.
It is critical, therefore, that all documentation associated with the Pregnancy Prevention programme are completed accurately, and that the audit results are provided faithfully and diligently, in the interest of patient safety.

4. Other selected Risks of Lenalidomide

The following section contains advice to HCPs about how to minimise the risk of the principal adverse events associated with the use of lenalidomide. For a full list of the adverse events that may be associated with its use please refer to the Lenalidomide Rowex SmPC.

4.1 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 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.

4.2 Second primary malignancies

An increase of second primary malignancies (SPM) has been observed in clinical trials in previously treated myeloma patients receiving lenalidomide/dexamethasone (3.98 per 100 patient-years) compared to controls (1.38 per 100 patient-years). 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.
The risk of occurrence of SPM must be taken into account before initiating treatment with lenalidomide either in combination with melphalan or immediately following high dose melphalan and ASCT. Physicians should carefully evaluate patients before and during treatment using standard cancer screening for occurrence of SPM and institute treatment as indicated.

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).

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 the treatment.

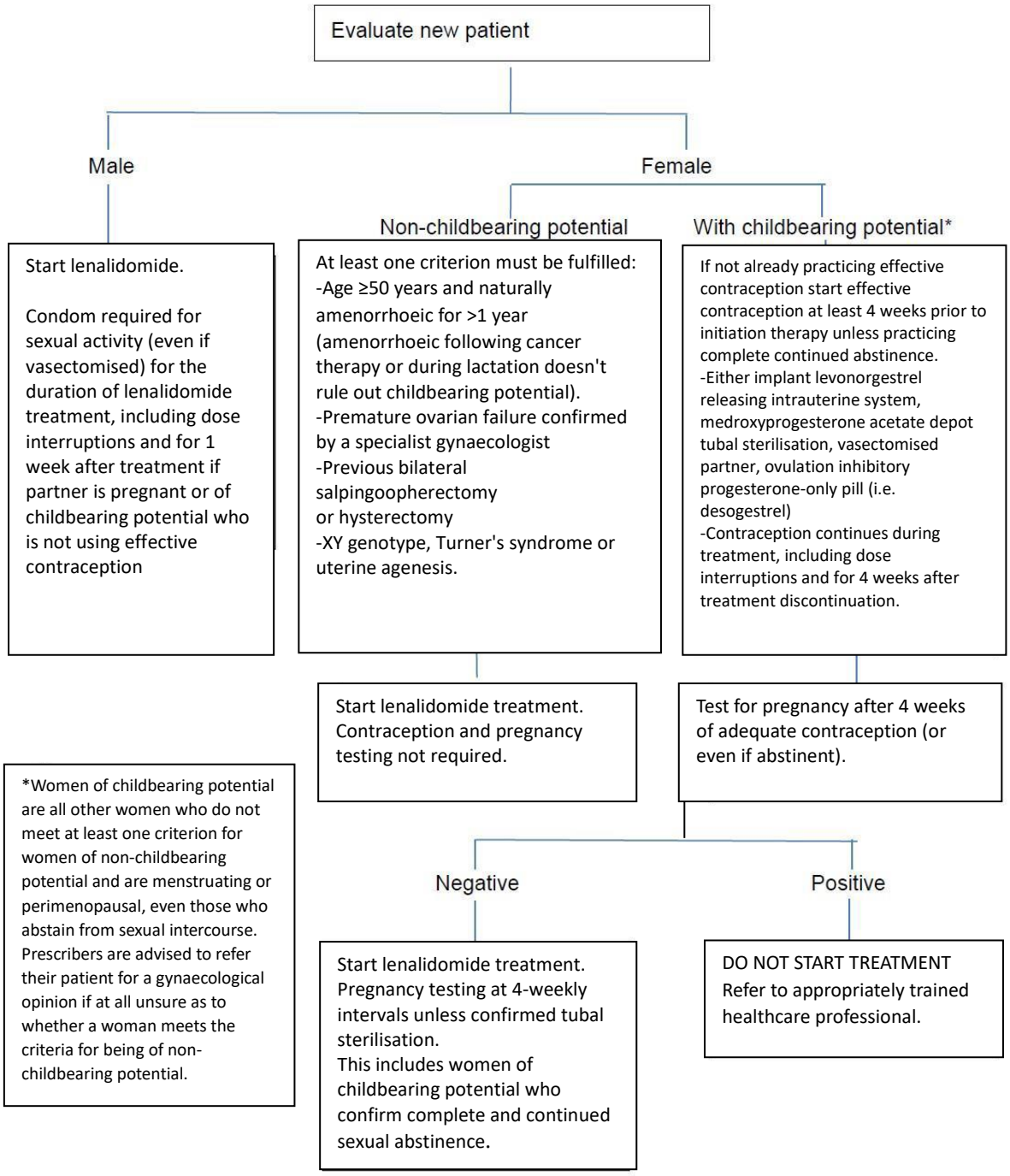
4.4 Blood donation

Patients should not donate blood during treatment, including during dose interruptions and for at least 1 week after cessation of treatment with lenalidomide.

5. Reporting of Adverse Reactions

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 should be forwarded to the Rowex Ltd. Drug Safety Department (See contact details) or to HPRA Pharmacovigilance www.hpra.ie

Lenalidomide
Description of the Pregnancy Prevention Programme (PPP) and Patient Categorisation.



Prescribers Guide to Prescribing lenalidomide

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 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 must read the Healthcare Professional's Information Guide.
2. Please complete a 'Community Pharmacy Dispensing Notification Form' to notify the nominated community pharmacy that their patient will be presenting with a prescription for lenalidomide. Fax 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'.

Pharmacist Guide to Dispensing lenalidomide

In order to dispense Lenalidomide Rowex:

As a nominated community pharmacy, you will receive a 'Community Pharmacy Dispensing Notification Form' from the prescriber / 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 Rowex Ltd.

1. Contact Rowex Risk Management on 1800 304 400 to obtain a Healthcare Professional's Information Guide which includes all relevant information, pharmacy registration forms and order forms.
2. Read the Guide.
3. Complete 'Pharmacy Registration Form' and fax to Rowex on 027 50417. Or email pv@rowa-pharma.ie You will be notified when you have been registered.
4. Once you are informed that you are registered with Rowex, complete a 'Lenalidomide Rowex Order Form'.
5. Fax or email UDD 'UDD Lenalidomide Rowex Order Form' to UDD on 01 463 2404 or **specialorders@united-drug.com**
   UDD aim to deliver complete orders placed before 13:30 Monday to Friday for the following working day.
6. For orders through Uniphar fax or email ' Uniphar Lenalidomide Rowex Order Form' to Rowex on 02750417 or email **specialorders@rowa-pharma.ie**

You are a Community Pharmacy that has previously registered with Rowex

1. Complete a 'Lenalidomide Rowex Order Form'.
2. For orders through UDD:
   Fax or email 'UDD Lenalidomide Rowex Order Form' to UDD on 01 463 2404 or specialorders@united-drug.com.
   UDD aim to deliver complete orders placed before 13:30 Monday - Friday for the following working day.

Or

3. For orders through Uniphar:
   Fax or email 'Uniphar Lenalidomide Order Form' to Rowex on 02750417 or specialorders@rowa-pharma.ie

NB. 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 Prescription Authorisation Form. The form is used within the Pregnancy Prevention Programme and must be completed each time you prescribe lenalidomide.

Prescription Authorisation Form

1	Name of treating hospital			Both signatures must be present prior to dispensing lenalidomide
2	Patient date of birth DD MM YYYY	Patient ID number/Initials:		**Prescriber's declaration** As the Prescriber, I have read and understood the 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.
3	Prescriber: (print) Supervising physician name (print)		8	Sign / Print Date / Bleep
4	Indication (tick)	Multiple myeloma □ Mantle cell lymphoma relapsed and/or refractory □ Myelodysplastic syndromes with isolated del5qcytogenetic abnormality □ Follicular lymphoma □ Other (please specify) □	A	**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, the dispensing will be taking place within 7 days of the date of prescription. I am dispensing no more than a 4 week supply to women of childbearing potential and 12 weeks for males and women of non- childbearing potential
5	Capsule strength prescribed: (tick) 2.5mg□ 5mg□ 7.5mg□ 10mg□ 15mg□ 20mg□ 25mg□		B	Sign / Print Date / Bleep
	Quantity of **Capsules** prescribed: * * Do **NOT** enter number of packs			Name and postcode of dispensing pharmacy
	Enter the cycle number(s) prescribed for this patient			
	Please tick all boxes that apply			
	Woman of non-childbearing potential Yes □ No □			
	Male Yes □ No □			
6	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). Yes □ No □		E	Lenalidomide brand dispensed
Note to pharmacist – Do not dispense unless ticked YES for Male patients □				
	Woman of childbearing potential Yes □ No □ 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. Yes □ No □			
7	Date of last negative pregnancy test:			
Note to pharmacist – Do not dispense unless ticked yes and a negative test has been conducted within 3 days prior to the prescription date and dispensing is taking place within 7 days of the prescription date				

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.

Instructions for pharmacists

A. Check that all relevant sections of the form have been fully completed by the prescriber, including:
a. That counselling and contraceptive measures have been confirmed by the prescriber as appropriate.
b. That for woman of childbearing potential a negative pregnancy test date is provided within 3 days of the prescription date.
c. The indication, capsule strength, capsule quantity and number of cycles have been provided.
B. Check the form does not contain confidential information

5. Print the diagnosis/indications – this is for purpose of monitoring off label use.
6. Enter the capsule strength, quantity of capsules prescribed and the number of cycles prescribed.
7. Complete this section appropriately to indicate that counselling has occurred and appropriate contraception measures ae 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 3days prior to prescribing). If this is not the case 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.

(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.
i. Dispense only a maximum of 4 weeks supply for women of childbearing potential at any one time.
ii. Dispense only a maximum of 12 weeks supply for Males and Women of Non-childbearing Potential.
E. Record the brand of lenalidomide dispensed for each dispensing cycle the PAF was used for. This will assist in completion of the pharmacy self-audit for the particular lenalidomide brand.

Further information and materials are available from:
Rowex Ltd.
Tel 027 50077
Email: pv@rowa-pharma.ie

Mandatory Lenalidomide Rowex Order Forms

Following discussions with the Health Products Regulatory Authority (HPRA) compliance with the PPP will also be monitored through Lenalidomide Rowex 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 Distributor (UDD) to Rowex who will then compile anonymised and aggregated data reports to provide to the HPRA on an annual basis.

Rowex will keep the order forms for orders through Uniphar and will provide Uniphar with a copy.

Prescribing and dispensing of lenalidomide

Pharmacist

Prescriber

Identify patients for lenalidomide, obtain **Healthcare Professional's Information Guide** from Rowex

Read Guide, fax Pharmacy Registration Form to Rowex

Read and understand the Guide

Patient presents at pharmacy, pharmacist:

- Cross-checks Prescription Authorisation Form
- Signs Prescription Authorisation Form
- Orders lenalidomide Rowex via the Lenalidomide Rowex order form
- Dispenses lenalidomide Rowex to patient
- Retains Prescription Authorisation Form for a minimum of two years.
- Sends self-audit/ reconciliation to Rowex as arranged.

Pharmacies must undertake the mandatory annual self-audit of the Prescription Authorisation Forms and provide feedback of the audit results to Rowex.

Identify patient for lenalidomide:

- Inform patient about pregnancy prevention
- Complete 'Treatment Initiation form'
- Complete 'Prescription authorisation form'
- Provide patient educational materials
- For first prescription, notify the pharmacy of an incoming prescription via the 'Community pharmacy Dispensing Notification form'.

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

6. Contact Details

Risk Management:
For information and questions on the risk management of the Rowex Ltd. products, the Pregnancy Prevention Programme, pharmacy registrations and the use and submission of the Prescription Authorisation Form:
Tel: 027 50077 Email: pv@rowa-pharma.ie

Drug Safety:
To report any adverse events to Rowex Ltd.
Tel: 027 50077 Email: pv@rowa-pharma.ie
You can also report side effect directly via the HPRA Pharmacovigilance website:
www.hpra.ie

Medical Information:
To obtain Medical Information
Tel: 027 50077 Email: pv@rowa-pharma.ie

Data Protection:
Any queries regarding Data Protection
Tel: 027 50077 Email: rowex@rowa-pharma.ie

Distributor:
United Drug Distribution (UDD) Tel: 01 463 2478
United Drug House Fax: 01 463 2404
Magna Business Park Email: specialorders@united-drug.com
Citywest Road
Dublin 2

Or

Uniphar Group Reception 01 428 7777
4045 Kingswood Road Customer Service 01 4687501
Citywest Business Park Email: info@uniphar.ie
Co. Dublin Orders: specialorders@rowa-pharma.ie
D24 VO6K Orders fax: Tel 027 50417