IMNOVID® (POMALIDOMIDE)

RMP- Risk Management Plan
PPP- Pregnancy Prevention Programme

INFORMATION FOR HEALTHCARE PROFESSIONALS

BROCHURE

1 INTRODUCTION

This Brochure contains the information needed for prescribing and dispensing Imnovid® (pomalidomide), including information about the Pregnancy Prevention Programme (PPP).

When pomalidomide is given in combination with other medicinal products, the corresponding Israeli approved Prescribing Information must be consulted prior to treatment. Please refer to Israeli approved Prescribing Information for the latest information.

2 PREGNANCY PREVENTION PROGRAMME

Pomalidomide is structurally related to thalidomide. Thalidomide is a known human teratogenic substance that causes severe life-threatening birth defects. Pomalidomide induced, in rats and rabbits, malformations similar to those described with thalidomide.

If Imnovid® (pomalidomide) is taken during pregnancy, a teratogenic effect in humans is expected. Pomalidomide is therefore contraindicated in pregnancy and in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme described in this HCP brochure are met.

Due to the teratogenic effect of pomalidomide, Imnovid is only available under a controlled distribution program. It is a requirement of the Pregnancy Prevention Programme that all Healthcare Professionals ensure that they have read and understood this brochure before prescribing or dispensing pomalidomide for any patient. Prescribers and pharmacists registered with the program can prescribe and dispense the product to patients who are registered and meet all the conditions of the Pregnancy Prevention Programme.

All men and all women of childbearing potential should undergo, at treatment initiation, counselling of the need to avoid pregnancy. This must be documented via a Patient Registration Form.

Patients should be capable of complying with the requirements of safe use and handling of pomalidomide.

Patients must be provided with the appropriate educational Patient Brochure.

The description of the Pregnancy Prevention Programme and the categorisation of patients based on sex and childbearing potential is set out in the attached Algorithm.

The Pregnancy Prevention Programme (PPP) includes the following elements: HCP brochure, HCP registration form, patient brochure, patient registration form, pharmacy registration form and pregnancy tests results report form.

The purpose of educating participants in the programme is to ensure that patients and healthcare providers involved in the PPP process understand how to minimise risk of foetal exposure and the resultant severe life-threatening congenital malformations.

The local educational materials contain information regarding the safety concern of teratogenicity (PPP), other relevant safety concerns and the PPP controlled distribution plan.

3 PRESCRIBING POMALIDOMIDE

3.1 Women of Childbearing Potential:

- Prescriptions for women of childbearing potential can be for a maximum duration of treatment of 4 weeks according to the approved indications dosing regimens.
- Do not dispense to a woman of childbearing potential unless the pregnancy test is negative and was performed within 3 days prior to the prescription.
- Dispensing to women of childbearing potential should occur within a maximum of 7 days from the prescription.

3.2 All Other Patients:

- For all other patients, prescriptions of pomalidomide should be limited to a maximum duration of 12 consecutive weeks and continuation of treatment requires a new prescription.

3.3 Female Patients:

Determine if a woman is not of childbearing potential.

The following are considered to not have childbearing potential:

- Age ≥ 50 years and naturally amenorrhoeic for ≥ 1 year (amenorrhoea following cancer therapy or during breast-feeding 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

You are advised to refer your patient for a gynaecological opinion if you are unsure whether or not she meets these criteria.

3.4 PPP Advice for Women of Childbearing Potential

Women of childbearing potential must never take pomalidomide if:

Pregnant

A woman who is 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 pomalidomide, foetal exposure should be avoided.

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

Use at least one highly effective method AND one additional effective barrier method of contraception for at least 4 weeks before therapy, during therapy, and until at least 4 weeks after pomalidomide therapy finished, and even in case of dose interruption or

commit to absolute and continuous abstinence confirmed on a monthly basis

AND

have a medically supervised negative pregnancy test prior to issuing a prescription (with a minimum sensitivity of 25 mIU/ml) once she has been established on contraception for at least 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 continued abstinence.

Patients should be advised to inform the physician prescribing her contraception about the pomalidomide treatment.

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

If not established on effective contraception, the patient must be referred to an appropriately trained health care professional for contraceptive advice before initiating contraception.

The following can be considered to be examples of highly effective suitable methods of contraception:

- Intrauterine device (IUD)
- Levonorgestrel-releasing intrauterine system (IUS)
- Medroxyprogesterone acetate depot
- Tubal ligation

- Sexual intercourse with a vasectomized male partner only; vasectomy must be confirmed by two negative semen analyses
- Ovulation inhibitory progesterone-only pills (i.e., desogestrel)

The following can be considered to be examples of Additional effective barrier methods of contraception:

- Condom
- Diaphragm
- Cervical cap

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

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

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

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

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 COMPLETE AND CONTINUED ABSTINENCE AND PREGNANCY TEST IS NEGATIVE!

3.5 PPP Advice for Men

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

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

Pomalidomide is present in human semen. As a precaution, all male patients taking pomalidomide, including those who have had a vasectomy as seminal fluid may still contain pomalidomide in the absence of spermatozoa, should use condoms throughout treatment

duration, during dose interruption and for at least 4 weeks after cessation of treatment if their partner is pregnant or of childbearing potential and has no effective contraception.

Patients should be instructed that if their partner does become pregnant whilst he is taking pomalidomide or within 4 weeks after he has stopped taking pomalidomide, he should inform his prescriber immediately. The partner should inform her physician immediately. It is recommended that she be referred to a physician specialized in teratology for evaluation and advice.

Male patients should not donate semen or sperm during treatment, including during dose interruptions and for at least 4 weeks following discontinuation of pomalidomide.

4 RISKS OF POMALIDOMIDE

4.1 Thrombocytopenia

Thrombocytopenia is one of the major dose-limiting toxicities of treatment with pomalidomide.

It is therefore encouraged to monitor complete blood counts (CBC) - including platelet count - weekly for the first 8 weeks and monthly thereafter.

A dose modification or interruption may be required. Patients may require use of blood product support and/or growth factors.

Thrombocytopenia can be managed with dose modifications and/or interruptions.

Recommended dose modifications during treatment and restart of treatment with Imnovid® (pomalidomide) are outlined in the table below:

4.1.1 Dose Modification or Interruption Instructions

Thrombocytopenia	**Dose Modification**
Platelet Count < 25 x 10^9/l	
Platelet Count return to ≥ 50 x 10^9/l	Interrupt pomalidomide treatment, follow CBC weekly. Resume pomalidomide treatment at one dose lower than previous dose.

Thrombocytopenia	**Dose Modification**
For each subsequent drop < 25 x 10^9/l	Interrupt pomalidomide treatment.
Platelet count return to ≥ 50 x 10^9/l	Resume pomalidomide treatment at one dose level lower than the previous dose.

CBC – Complete Blood Count.

To initiate a new cycle of pomalidomide, the platelet count must be ≥ 50 x 10^9/l.

For other Grade 3 or 4 adverse reactions judged to be related to pomalidomide, stop treatment and restart treatment at 1 mg less than the previous dose when an adverse reaction has resolved to ≤ Grade 2 at the physician's discretion. If adverse reactions occur after dose reductions to 1 mg, then the medicinal product should be discontinued (see Section 4.2 of the Israeli approved Prescribing Information). Please also refer to the local Israeli approved Prescribing Information for further information under section 4.4 and 4.8.

4.2 Cardiac Failure

Cardiac events, including congestive cardiac failure, pulmonary oedema and atrial fibrillation (see Section 4.8 of the Israeli approved Prescribing Information), have been reported, mainly in patients with pre-existing cardiac disease or cardiac risk factors. Appropriate caution should be exercised when considering the treatment of such patients with pomalidomide, including periodic monitoring for signs or symptoms of cardiac events (see Section 4.4 of the Israeli approved Prescribing Information).

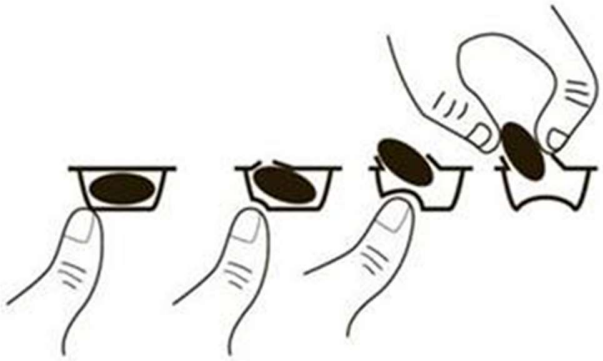
5 POINTS TO CONSIDER FOR HANDLING THE MEDICINAL PRODUCT: FOR HEALTHCARE PROFESSIONALS AND CAREGIVERS

Do not share the medicinal product with anyone else, even if they have similar symptoms. Store them safely so that no-one else can take them by accident and keep them out of the reach of children.

Keep the blisters with the capsules in the original pack.

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. The pressure should be located at one site only, which reduces the risk of the capsule deforming or breaking (see figure below).

Healthcare professionals and caregivers should wear disposable gloves when handling the blister or capsule. Remove gloves carefully to prevent skin exposure. Place in a sealable plastic polyethylene bag. Dispose of any unused medication in accordance with local regulations. Hands should then be washed thoroughly with soap and water. Women who are pregnant or suspect they may be pregnant should not handle the blister or capsule. Refer below for further guidance.



5.1 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 (ie, blister or capsule).
- Use proper technique when removing gloves to prevent potential skin exposure (see below).
- Place gloves in a sealable plastic polyethylene bag and dispose them according to local requirements.

- Wash hands thoroughly with soap and water after removing gloves.
- Patients should be advised never to give the medicinal product to another person.

5.2 If a Drug Product Package Appears Visibly Damaged, Use the Following Extra Precautions to Prevent Exposure

- If the outer carton is visibly damaged – **do not open.**
- If blister strips are damaged or leaking or capsules are noted to be damaged or leaking – **close the 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.

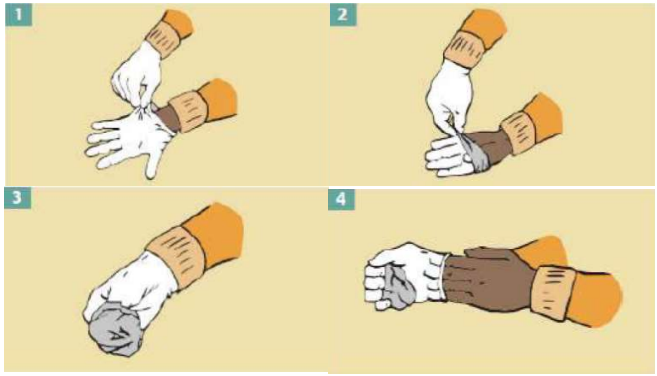
5.3 If Product is Released or Spilled, Take Proper Precautions to Minimize Exposure by Using Appropriate Personal Protection

- If capsules are crushed or broken, dust containing drug substance may be released. Avoid dispersing the powder and avoid breathing on or inhaling the powder.
- Wear disposable gloves to clean up the powder.
- Place a damp cloth or towel over the powder area to minimize entry of powder into the air. Add excess liquid to allow the material to enter the solution. After handling, clean the area thoroughly with soap and water, then dry it.
- Place all contaminated materials, including a damp cloth or towel, and gloves, into a sealable polyethylene plastic bag. Dispose of it according to local requirements for medicinal products.
- Wash your hands thoroughly with soap and water after removing the gloves.
- Please report to Neopharm by email: *drugsafety@neopharmisrael.com*, or by calling 03-9373796

5.4 If the Contents of the Capsule are Attached to the Skin or Mucous Membranes

- If you touch the drug powder, please wash the exposed area thoroughly with running water and soap.
- If drug powder makes contact with one or both of your eyes, remove and discard any contact lenses in use. Then, thoroughly flush eyes with water for at least 15 minutes. If irritation occurs, please contact an ophthalmologist.

5.5 Proper Technique for Removing Gloves



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

5.6 Blood Donation

- All patients should not donate blood during treatment (including dose interruptions) and for at least 4 weeks after cessation of treatment with pomalidomide.

5.7 Requirements in the Event of a Suspected Pregnancy

- Stop treatment if female patient.
- Refer female patient to a physician specialized or experienced in teratology for evaluation and advice.
- Notify the Israeli MoH of all suspected pregnancies in female patients or partners of male patients – please refer to "Reporting of adverse reactions".
- Notify Neopharm of all suspected pregnancies in female patients or partners of male patients – please refer to "Reporting of adverse reactions". Neopharm will wish to follow-up with you on the progress of all pregnancies.

6 REPORTING OF ADVERSE REACTIONS

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment that appears on the homepage of the Ministry of Health's website (www.health.gov.il) which links to a portal, or by the following link: https://sideeffects.health.gov.il
and by emailing the Registration Holder's Product Safety and Quality Department at:
drugsafety@neopharmgroup.com
Tel: 03-9373796

7 CONTACT DETAILS

For information and questions on the risk management of BMS's products, and the Pregnancy Prevention Programme, please refer to the Registration Holder's Product Safety and Quality Department at: RMP-Mishpuhe@NeopharmGroup.com
Tel: 03-9373796

For further information please refer to the local Israeli approved Prescribing Information.

8 PERSONAL DATA PRIVACY

Neopharm processes personal data relating to patients receiving this product and to health professionals involved in their therapeutic management, for the purposes of managing and reducing the risk linked to the use of this product as legally required. You may contact us at any time to ask what personal data we process about you. If such a request places Neopharm or its affiliates in breach of its obligations under applicable laws, regulations or codes of practice, then Neopharm may not be able to comply with your request. To exercise your rights: privacy@Neopharmgruop.com

Checklist for physicians

Please choose the applicable column for the risk category of the patient and refer to the counselling messages provided.

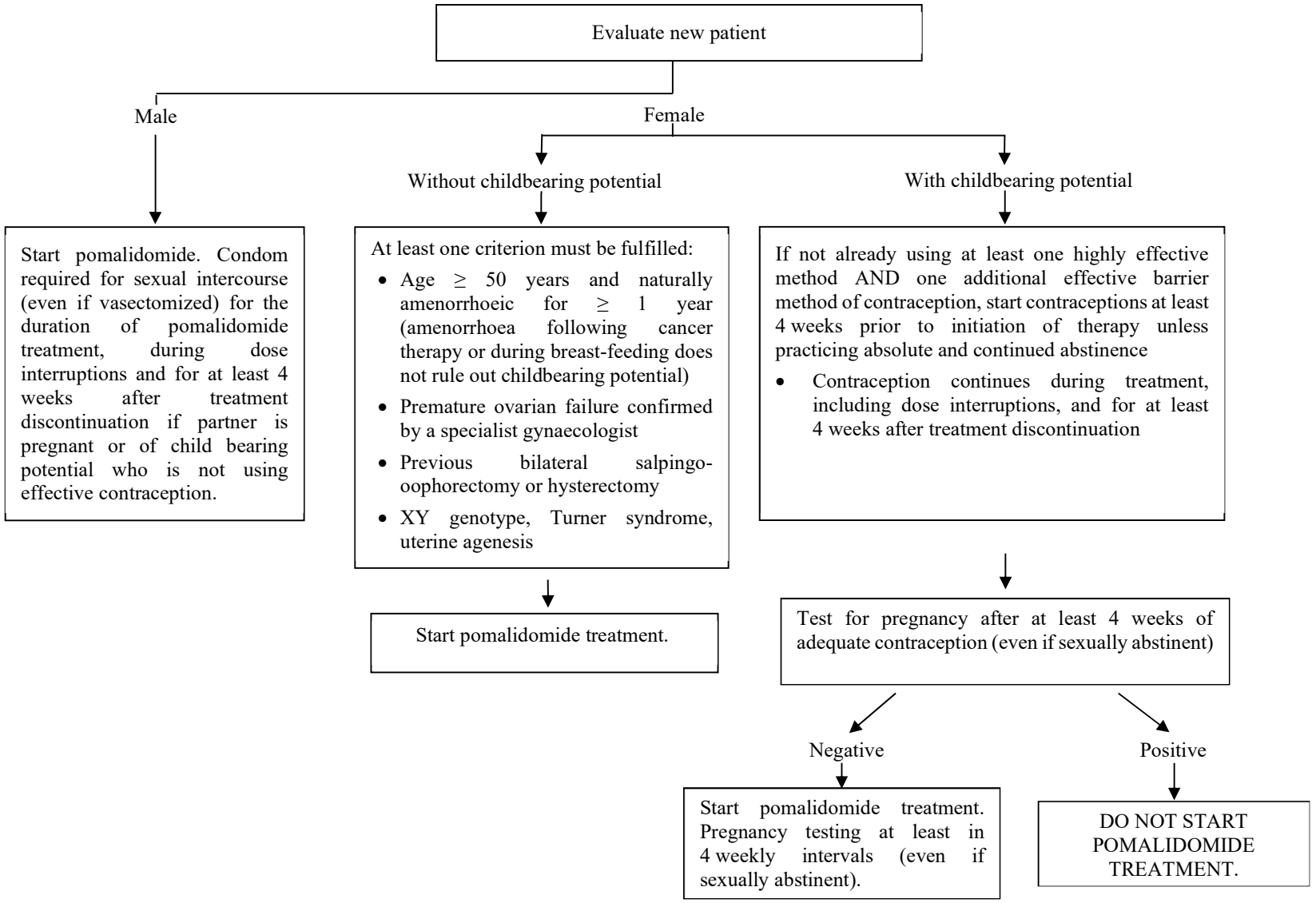
Did you inform your patient:	Male Patients	Women of Non-childbearing Potential*	Women of Childbearing Potential
• Pomalidomide is a derivative of Thalidomide known to cause severe birth defects and the need to avoid foetal exposure		N/A	
• That if she is pregnant or plans to be, she must not take Pomalidomide	N/A	N/A	
• That she understands the need to avoid Pomalidomide during pregnancy and to apply use simultaneously two reliable methods of contraception (One highly effective method [(i.e. an intra-uterine device or implant) and additional effective barrier methods (i.e. condom, Diaphragm, cervical cap)] without interruption, at least 4 weeks before starting treatment, throughout the entire duration of treatment, and at least 4 weeks after the end of treatment	N/A	N/A	
• That if she needs to change or stop using her method of contraception she should inform: a) the physician prescribing her contraception that she is taking Pomalidomide b) the physician prescribing Pomalidomide that she has stopped or changed her method of contraception	N/A	N/A	
• Of the need for pregnancy tests (i.e., before treatment) at least every 4 weeks during treatment and after treatment	N/A	N/A	
• Of the need to stop Pomalidomide immediately upon suspicion of pregnancy and the patient should be referred to an expert physician specialized or experienced in teratology for advice	N/A	N/A	
• Of the need to contact their doctor immediately upon suspicion of pregnancy	N/A	N/A	
• To not share the medicinal product with any other person			

• That they should not donate blood during treatment (including during dose interruptions) and for at least 4 weeks following discontinuation of Pomalidomide			
• That they should return the unused capsules to the pharmacist at the end of treatment			
• That Pomalidomide is found in semen, so there is a need to use condoms if the sexual partner is pregnant or is a WCBP, during Pomalidomide therapy and 4 weeks after stopping therapy (even if the man has had a vasectomy)		N/A	N/A
• That if his partner becomes pregnant, he should inform his treating doctor immediately and always use a condom		N/A	N/A
• That he should not donate semen during treatment (including during dose interruptions) and for at least 4 weeks following discontinuation of Pomalidomide		N/A	N/A
Can you confirm that your patient:	**Male Patients**	**Women of Non-childbearing Potential***	**Women of Childbearing Potential**
• Was referred to a contraceptive consultant, if required?	N/A	N/A	
• Is capable of complying with contraceptive measures?		N/A	
• The patient is aware of the risk of contraceptive failure.		N/A	
• Agreed to undergo pregnancy testing at least in 4 weekly intervals (including days intervals throughout treatment and also for a period of 4 weeks after stopping treatment) unless confirmed tubal sterilization? This includes women of childbearing potential who confirm absolute and continued abstinence.	N/A	N/A	
• Had a negative pregnancy test before starting treatment even if absolute and continued abstinence?	N/A	N/A	

* Refer to Prescribing Pomalidomide for criteria to determine if patient is a woman of non-childbearing potential.

This document was last approved in Oct/2025 by the Israeli Ministry of Health (MOH)

Description of the Pregnancy Prevention Programme and Patient Categorisation Algorithm



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