POMALIDOMIDE S.K.®

Pregnancy Prevention Programme (PPP)

Risk management plan (RMP)

Information for Healthcare Professionals Prescribing or Dispensing Pomalidomide

SK-PHARMA

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

POMALIDOMIDE S.K. Pregnancy Prevention Programme:
If pomalidomide is taken during pregnancy, it can cause severe birth defects or death to an unborn baby. This programme is designed to make sure that unborn babies are not exposed to pomalidomide. It will provide you with information about how to follow the programme, the controlled distribution and explain your responsibilities, before prescribing and dispensing POMALIDOMIDE S.K.

For your patients' health and safety, please read this brochure carefully. You must ensure that your patients fully understand what you have told them about pomalidomide and that they have provided written confirmation on the patient registration Form, before starting treatment.

Contents

1.0 Introduction

This Brochure contains the information needed for prescribing and dispensing POMALIDOMIDE S.K.® (pomalidomide), including information about the Pregnancy Prevention Programme (PPP). For full details, please refer to the SMPC. When pomalidomide is given in combination with other medicinal products, the corresponding SMPC must be consulted prior to treatment.

1.1 Summary of the POMALIDOMIDE S.K. Pregnancy Prevention Programme

Pomalidomide is structurally related to thalidomide, 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 POMALIDOMIDE S.K.® (pomalidomide) is taken during pregnancy, a teratogenic effect of pomalidomide in humans is expected. Pomalidomide is therefore contraindicated in pregnancy and in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are met (please refer to sections 4.4 and 4.6 of the SmPC for further details).
Pomalidomide K.S Pregnancy Prevention Programme and controlled distribution program. Due to the potential toxicity of Pomalidomide and to avoid fetal exposure, Pomalidomide K.S is only available under a special controlled distribution program. 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 a copy of the Patient Brochure.

In order to obtain pomalidomide, it is a requirement of the Pregnancy Prevention Programme that all healthcare professionals ensure that they have read and understood the Additional Risk Minimisation Materials before prescribing or dispensing pomalidomide for any patient.

- Prescribers must complete the appropriate patient registration Form with every patient before the first prescription is issued.
- Pharmacies must register with S.K. PHARMA to be able order and dispense pomalidomide.

All patients should be given a Patient Brochure to take home – these materials remind patients of the key educational information and risks of treatment.

For women of childbearing potential, prescriptions of pomalidomide should be limited to a maximum duration of 4 weeks of treatment and continuation of treatment requires a new prescription. Ideally, pregnancy testing, issuing a prescription and dispensing should occur on the same day. Dispensing pomalidomide should occur within a maximum of 7 days of the prescription and the date of the last negative pregnancy test must be within the 3 days prior to the date of the prescription.

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

1.2 Overview of the Healthcare Professionals' Information Pack

All of the POMALIDOMIDE S.K. Pregnancy Prevention Programme materials are contained within this pack and, the Additional Risk Minimisation Materials (ARMMs) are also available as individual materials. Additional hard copies can be obtained by contacting S.K. PHARMA Risk Management using the contact details displayed on the front of this brochure.

You must ensure that your patients fully understand what you have told them about pomalidomide before starting treatment.

This brochure contains key information for healthcare professionals and contains the following:

- educational information
- therapy management advice to avoid foetal exposure to pomalidomide
- a controlled distribution system
- Safety advice of relevance to all patients.
- Process for reporting adverse events and pregnancy in patients treated with pomalidomide.

This Healthcare Professionals' Information Pack also contains an Algorithm and and checklist for physicians, reports on pregnancy during treatment with pomalidomide and data privacy policy.
The description of the Pregnancy Prevention Programme and the categorisation of patients based on sex and childbearing potential are set out in the attached Algorithm.

1.3 Teratogenicity: Potential or Actual Foetal Exposure to Pomalidomide

Pomalidomide must never be used by women who are able to become pregnant unless they follow the POMALIDOMIDE S.K. Pregnancy Prevention Programme described in this pack (Section 2.0).
Since pomalidomide may be present in the semen of male patients, all male and female patients must both follow effective contraceptive measures. Female patients must use two Contraceptive measures.

If a female patient or female partner of a male patient misses, or is suspected to have missed her period, or has any abnormality in menstrual bleeding, or suspects she is pregnant, then the patient must contact the doctor.
If she becomes pregnant whilst taking Pomalidomide, she must stop therapy immediately and inform her treating physician immediately. The woman should be referred to a physician experienced in teratology for further evaluation and counselling.

2.0 Therapeutic Management Advice to Avoid Foetal Exposure

2.1 Women of Non-Childbearing Potential (WNCBP)

Women in the following groups are considered not to have childbearing potential

- Patient is ≥ 50 years and naturally amenorrhoeic for ≥12 consecutive months *
- Has previously undergone a hysterectomy or bilateral oophorectomy.
- Premature ovarian failure confirmed by a specialist gynaecologist.
- XY genotype, Turner syndrome, uterine agenesis.
- Any other case which will be determined by the prescriber

*Amenorrhoea following cancer therapy or during breastfeeding does not rule out childbearing potential.

A female patient is considered to have childbearing potential unless she meets at least one of the above criteria. Prescribers are advised to refer their patient for a gynaecological opinion if at all unsure as to whether a woman meets the criteria for being of non-childbearing potential.

2.2 Women of Childbearing Potential (WCBP)

Women of childbearing potential must never take pomalidomide if:

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

In view of the teratogenic risk of pomalidomide, foetal exposure should be avoided. Women of childbearing potential must understand the need to avoid pregnancy, and these patients must be adequately informed regarding the use of effective contraceptive measures every time a prescription is issued.

Women of childbearing potential (even if they have amenorrhoea) must use two effective methods 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. This must be followed unless the patient commits to absolute and continuous abstinence confirmed to her prescriber on a monthly basis.

If your patient is not established on effective contraception, she must be referred to an appropriately trained healthcare professional for contraceptive advice before initiating contraception.

Contraceptive methods must include at least 1 highly effective method AND 1 additional effective barrier method.

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

- 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).

The following are Additional effective barrier methods :

- 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 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 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 immediately inform her physician.

If your patient needs to change or stop her method of contraception during her pomalidomide therapy, she must understand the need toinform the physician prescribing her pomalidomide.

Pregnancy Testing

For women of childbearing potential a pregnancy test must be performed prior to issuing a prescription. A pregnancy test is required even if the patient has not had heterosexual intercourse since her last pregnancy test.

Women of childbearing potential (even if they have amenorrhoea) must have a medically supervised negative pregnancy test prior to issuing a prescription (with a minimum sensitivity of 25 mIU/ml).

A medically supervised pregnancy test should be repeated every 4 weeks, including 4 weeks after the end of treatment. These pregnancy tests should be performed on the day of the prescribing visit or in the 3 days prior to the visit to the prescriber.

A pregnancy test must be performed immediately if a patient misses her period, if there is any abnormality in menstrual bleeding, if she has heterosexual intercourse without using a contraceptive method, or if she suspects she is pregnant.

Ideally, pregnancy testing, issuing a prescription and dispensing should occur on the same day. Dispensing of Pomalidomide to women of childbearing potential should occur within 7 days of the prescription.

If a female patient has a positive pregnancy test, then:

- Stop treatment immediately.
- Refer the patient to a physician specialised or experienced in dealing with teratology for advice and evaluation.
- Notify S.K. PHARMA immediately.

2.3 Men

In view of the expected teratogenic risk of pomalidomide, foetal exposure should be avoided. Therefore your male patients must be counselled at treatment initiation on the risks and benefits of pomalidomide therapy including the risk of birth defects, other side effects and important precautions associated with pomalidomide therapy. Inform your patient which are the effective contraceptive methods that his female partner can use.

Pomalidomide is present in human semen. As a precaution, and taking into account special populations with potentially prolonged elimination time such as renal impairment, 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 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 their physician 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 4 weeks following discontinuation of pomalidomide.

2.4 Advice for all Patients

Your patient must be informed not to donate blood during or within 4 weeks after stopping treatment.
If your patient discontinues therapy, they must return any unused pomalidomide to the pharmacy.

3.0 Information for Prescribers

3.0.1 Patient and Healthcare Professional Education

As the prescriber, you play a central role in ensuring that pomalidomide is used safely and correctly.

Most importantly, you will be helping to ensure that your patients understand the risks involved in taking pomalidomide and that they are aware of their responsibilities in preventing foetal exposure to the drug. In addition, you may need to help your patients understand the processes involved in the POMALIDOMIDE S.K. Pregnancy Prevention Programme. This will help to prevent any delays in your patients receiving their treatment.

3.0.2 Educational materials and controlled distribution system

Because of the different levels of risk, you will need to communicate different information to men, women and children. You must ensure that your patient Understands the information before they complete their section of the patient enrollment Form.

Please make use of the Patient Brochure to help explain the relevant information.

A national controlled distribution system has been implemented in collaboration with the Ministry Of Health. The controlled distribution system includes the use of a patient brochure, a prescribing and health care professional brochure and dispensing controls.

3.0.3 Prescribing pomalidomide

3.0.3.1 Maximum Prescription Lengths

- Prescriptions for women of childbearing potential can be for a maximum duration of treatment of 4 weeks according to the approved indications dosing regimens, and prescriptions for all other patients can be for a maximum duration of 12 weeks.
- 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.

3.1 Information for Pharmacists

As a pharmacist you play an important role in ensuring that pomalidomide is used safely and correctly. Pomalidomide will only be supplied to pharmacies that have completed a 'pomalidomide' Pharmacy Registration Form'

3.1.1 Dispensing Pomalidomide S.K

- The dispensing for women of childbearing potential is taking place within 7 days of the prescription date, and the date of the last negative pregnancy test must be within the 3 days prior to the date of the prescription.
- The pharmacist must read and understood the contents of this Healthcare Professionals' Information Pack.

3.1.2 Dispensing Advice

- Please ensure that you dispense pomalidomide blisters intact; capsules must not be removed from blisters and packaged into bottles.
- For each prescription, dispense a maximum of a 4 week supply for women of childbearing potential or maximum of a 12 week supply for all other patients.
- Please educate all pharmacists within your pharmacy about the dispensing procedures for pomalidomide.
- Instruct patients to return any unused pomalidomide to the pharmacy. Pharmacies must accept any unused pomalidomide returned by patients for destruction and follow Good Pharmacy Practice guidelines for destruction of dangerous medicines.

4.0 Safety Advice Relevant to all Parties

The following section contains advice to Healthcare Professionals about how to minimise the risk of thrombocytopenia and cardiac failure associated with the use of pomalidomide. Please refer also to SmPC (Sections 4.2 Posology and method of administration, 4.3 Contraindications, 4.4 Special warnings and precautions for use and 4.8 Undesirable effects) for complete information on all the risks associated with pomalidomide.

In general, most adverse reactions occurred more frequently during the first 2 to 3 months of treatment. Please note that the posology, adverse event profile and recommendations outlined herein, particularly in respect of neutropenia and thrombocytopenia, relate to the use of pomalidomide within its licensed indication. There is currently insufficient evidence regarding safety and efficacy in any other indication.

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

4.1 Risk of Thrombocytopenia and Cardiac Failure with pomalidomide

4.1.1 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 pomalidomide are outlined in the table below:

Dose Modification or Interruption Instructions

Toxicity	Dose Modification
<u>Thrombocytopenia</u> • Platelet Count <25 x 10^9/L •	Interrupt pomalidomide treatment, follow CBC weekly.
<u>Platelet Count return to ≥50 x 109/L</u>	Resume pomalidomide treatment at one dose lower than previous dose.
• 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.

4.1.2 Cardiac Failure

Cardiac events, including congestive cardiac failure, pulmonary oedema and atrial fibrillation (see Section 4.8 of the SmPC), 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 SmPC).

4.2 Points to Consider for Handling the Medicinal Product: For Healthcare Professionals and Caregivers

Capsules should not be opened or crushed. If powder from pomalidomide makes contact with the skin, the skin should be washed immediately and thoroughly with soap and water. If pomalidomide makes contact with the mucous membranes, they should be thoroughly flushed with water.

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.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements. Unused medicinal product should be returned to the pharmacist at the end of treatment.

For full details, please refer to the SmPC.

5.0 Reporting Adverse Events, Suspected and Confirmed Pregnancies, and Foetal Exposures

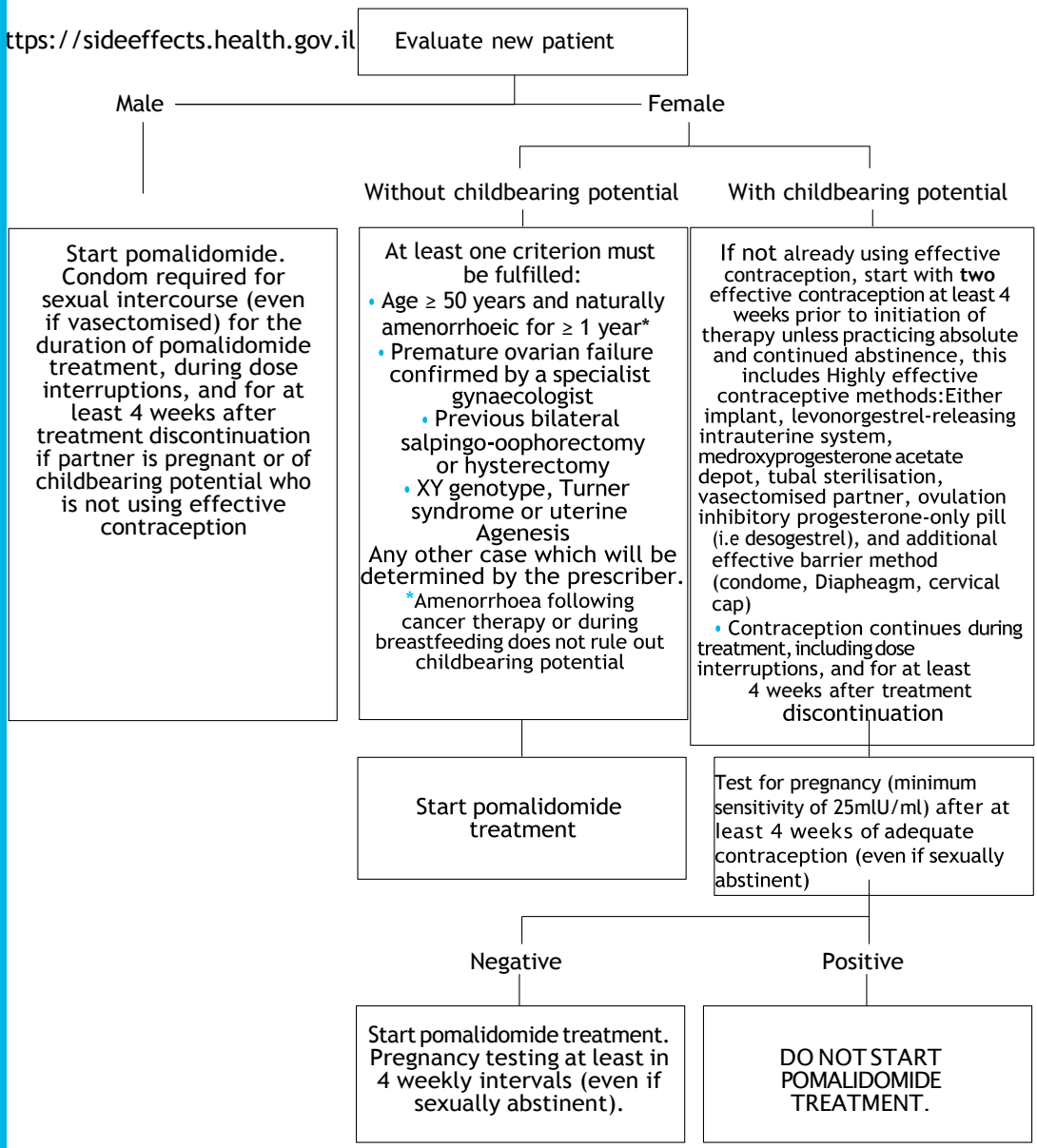
The safe use of pomalidomide is of paramount importance.
Adverse events (and cases of suspected or confirmed pregnancy or foetal exposure) should be reported to S.K. PHARMA Medical Information

(Tel: 03-6114543 or report@sk-pharma.com / pomalidomide@sk-pharma.com). Pregnancy Reporting forms are included in the Healthcare Professional Information Pack. These should be forwarded to S.K. PHARMA Medical Information using the aforementioned details.

Side effects and pregnancy cases can be reported to the Ministry of health by clicking the link “Reporting side effects due medication treatment” on the Ministry of Health homepage (www.health.gov.il) that refers to the online form for reporting side effects - https://sideeffects.health.gov.il.

This document was last approved in Oct-2024 by the Israeli ministry of health (MOH)

6.0 Description of the Pregnancy Prevention Programme and Patient Categorisation Algorithm



7.0 Contact Details

Risk Management Operations:
For questions about the eRMP:
Tel: 03-611-4543
Fax: 077-3181051
Email: pomalidomide@sk-pharma.com

Risk Management:
For information and questions on the Risk Management of S.K. PHARMA products, the Pregnancy Prevention Programme, pharmacy registrations and the use of the paper PAFs.
Tel: 03-611-4543
Fax: 077-3181051
Email: pomalidomide@sk-pharma.com
Distributor: K.S KIM International (SK-Pharma) Ltd.

Information Security:
K.S. Kim International, as the holder of the registration for the drug Pomalidomide S.K., is responsible for implementing the Privacy Protection Law and the information security regulations. This includes the proper safeguarding and securing of personal information, with an emphasis on transparency, consent, and the protection of individual rights.

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Annex A- checklist for prescribing doctors

☐ Pomalidomide S.K prescribed to the patient in line with its approved indication

☐ **The patient was explained** that Pomalidomide is a derivative of thalidomide known to cause severe birth defects and that they must not get pregnant whilst taking it.

☐ **For male patients:** the patient was explained that he must use condoms during Pomalidomide therapy until 4 weeks after stopping therapy, even if they have undergone a successful vasectomy

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

☐ **For female patients:** She must consistently and correctly use two effective methods of contraception

☐ The patient, were explained that the risk persists even after the medication is stopped and that they must not get pregnant within 4 weeks after stopping treatment.

☐ **For women of child- beraing potential:**

- ☐ The patient has received advice on contraception which is appropriate for her and has committed to using it throughout the risk period.
- ☐ The patient is aware of the risk of contraceptive failure.
- ☐ The first prescription for Pomalidomide can only be given after the patient has had medically supervised pregnancy test and four weeks of contraceptive use. This is to make sure she is not already pregnant before starting treatment.
- ☐ The patient was explained that in order to support regular follow up, including pregnancy testing and monitoring, the prescription should be limited to 28 days.
- ☐ The patient was explained the need for and agrees to pregnancy testing before, during and after treatment.

throughout treatment and for a period of 4 weeks after stopping treatment.

☐ Patient was explained that Pomalidomide prescription should be signed no later than 3 days from the negative pregnancy test. Dispensing of Pomalidomide to women of childbearing potential should occur within 7 days of the prescription.

☐ The patient has received a copy of the Patient Information Booklet.

☐ The patient was explained that, according to Israeli ministry of health requirements, Pomalidomide S.K. is under controlled distribution program and that information regarding all patients and prescriptions is collected by K.S. Kim International. The information might be shared with the ministry of health and other applicable bodies, per regulatory requirements.

☐ The patient was explained to contact the doctor if they have unprotected sex, miss their period, become pregnant, or suspect that they have become pregnant during the risk period.

☐ If pregnancy occurs, treatment must be stopped and the patient should be referred to an expert physician specialised or experienced in teratology for advice.

☐ The patient was explained that Pomalidomide S.K. has been prescribed to her only and must not be shared with others, and that they should always return any unused capsules to the pharmacist for safe disposal as soon as possible

☐ The patient was explained that they must not donate blood during treatment with Pomalidomide and for 4 weeks after discontinuation.