Thalidomide
Pregnancy Prevention Programme

Information for Healthcare Professionals

Prescribing or Dispensing Thalidomide

This brochure is intended for healthcare professionals involved in prescribing or dispensing thalidomide, and contains information about:

- **Preventing harm to unborn babies:** If thalidomide is taken during pregnancy it can cause severe birth defects or death to an unborn baby.

- **Other side effects of thalidomide:** Ischaemic heart disease including myocardial infarction. Further information and recommended precautions can be found in the thalidomide Summary of Product Characteristics (SmPC).

- **Thalidomide Pregnancy Prevention Programme:** This Programme is designed to prevent unborn babies being exposed to thalidomide. 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 ensure that they have read and understood this brochure

To ensure your patients' safety, please read this brochure carefully. You must ensure that your patients fully understand what you have told them about thalidomide before starting treatment.

CONTENTS

Introduction

Thalidomide belongs to a group of medicines known as 'immunomodulatory' medicines. As the prescriber or pharmacist, you play a central role in ensuring that thalidomide is used safely and in accordance with the requirements of the Pregnancy Prevention Programme.

Thalidomide in combination with melphalan and prednisone is approved across Europe for the following indication:

- Thalidomide in combination with melphalan and prednisone as first line treatment of patients with untreated multiple myeloma, aged ≥ 65 years or ineligible for high dose chemotherapy.

Thalidomide is prescribed and dispensed according to the thalidomide Pregnancy Prevention Programme.

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

The recommended oral dose is 200 mg per day, and a maximum number of 12 cycles of 6 weeks should be used. Thalidomide should be taken as a single dose at bedtime, to reduce the impact of somnolence. Thalidomide can be taken with or without food.

This brochure is part of the 'Thalidomide Pregnancy Prevention Programme' because if thalidomide is taken during pregnancy it can cause severe birth defects or death to an unborn baby. In the 1950s and 1960s, approximately 12,000 children were born with severe birth defects caused by thalidomide, and approximately 5,000 are alive today.

This brochure will describe your responsibilities as a prescriber or a pharmacist, and will summarise the information that you need to tell your patient to ensure they are aware of the risks and their responsibilities.

All of the Thalidomide Pregnancy Prevention Programme materials are contained within the 'Educational Healthcare Professional's Kit', and additional copies can be obtained by contacting Celgene. These materials can be used for counselling patients on the risks of thalidomide and the precautions to be taken.

You must be sure that your patients fully understand what you have told them about thalidomide before starting treatment.

Special warnings and precautions for use:
Teratogenic effects. Thalidomide is a powerful human teratogen, inducing a high frequency of severe and life-threatening birth defects. Thalidomide must never be used by women who are pregnant or by women who could become pregnant unless all the conditions of the Thalidomide Pregnancy Prevention Programme are met. The conditions of the Thalidomide Pregnancy Prevention Programme must be fulfilled for all male and female patients.

Thalidomide must never be used by women who are pregnant, as just a single dose (one capsule) can induce a high frequency of severe and life-threatening birth defects. Thalidomide must never be used by women who are able to become pregnant unless they follow the Thalidomide Pregnancy Prevention Programme. Since thalidomide may be present in the seminal fluid of male patients, male patients must also follow contraceptive measures.

Requirements in the event of a suspected pregnancy:

- Stop treatment immediately, if female patient
- Refer patient to a physician specialised or experienced in teratology for evaluation and advice
- Notify Celgene *and the Medicines Authority*of such occurrences
    - Pregnancy Reporting Form is included in this pack

    Call AM Mangion Ltd on + 356 23976333

    -
    - Celgene will wish to follow-up with you on the progress of all pregnancies.

Thalidomide and Other Potential Side Effects

In addition to the teratogenic effects of thalidomide, other potential side effects your patients should be aware of include ischaemic heart disease, including myocardial infarction. Please refer to the **thalidomide SmPC** for full information about the side effects and recommended precautions.

Your patient should be encouraged to report any unusual reactions or side effects from their medication to their prescriber. The side effects are also described in the thalidomide product information leaflet, which patients should read thoroughly.

Healthcare Professionals' Obligations

Obligations of healthcare professionals who intend to prescribe or dispense thalidomide are:

- The need to provide comprehensive advice and counselling to patients
- To ensure their patients are capable of complying with the requirements for the safe use of thalidomide
- To provide patients with the appropriate patient educational materials
- To report any pregnancy, or adverse events to Celgene and the local health authority (if applicable to a Member State) using the forms provided in the 'Educational Healthcare Professional's Kit'

Information for Prescribers

Introduction

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

Most importantly, you will be helping to ensure that your patients understand the risks involved in taking thalidomide 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 thalidomide Pregnancy Prevention Programme.

If you refer your patient to a fertility expert (e.g. obstetrician or gynaecologist) for further contraceptive advice, it is your responsibility to ensure that the fertility expert is aware of the Thalidomide Pregnancy Prevention Programme requirements.

A summary of the Thalidomide Pregnancy Prevention Programme process is found on the last page of this brochure.

You must ensure that your patient understands the information before they complete their section of the *'Treatment Initiation Form'*

Please make use of the patient brochures to help explain the relevant information.

Specific advice for female patients

At treatment initiation, your female patients must be counselled on the risks of thalidomide therapy including the risk of birth defects, other side effects and important precautions associated with thalidomide therapy.

Childbearing and non–childbearing potential

In order to provide appropriate information to your female patients about the precautions they must follow when using thalidomide, it is important to determine whether your patient is or is not of childbearing potential.

• **Women not of childbearing potential** include women who fulfil at least one of the following criteria:

- 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's syndrome, uterine agenesis

Contraceptive methods

Women of childbearing potential must use at least one effective method of contraception for at least 4 weeks before start of treatment, during treatment, and until at least 4 weeks after thalidomide treatment and even in case of dose interruptions unless the patient commits to absolute and continuous abstinence confirmed on a monthly basis.

If your patient is not established on effective contraception, they must be referred preferably to an appropriately trained health care professional for contraceptive advice in order that contraception can be initiated.

The following are effective methods of contraception

- Implant
- Levonorgestrel-releasing intrauterine system (IUS)
- Medroxyprogesterone acetate depot
- Tubal sterilisation
- Sexual intercourse with a vasectomised male partner only; vasectomy must be confirmed by two negative semen analyses
- Ovulation inhibitory progesterone-only pills (i.e., desogestrel)

Because of the increased risk of venous thromboembolism in patients with multiple myeloma, combined oral contraceptive pills are not recommended. If a patient is currently using combined oral contraception they should switch to one of the effective method listed above. The risk of venous thromboembolism continues for 4−6 weeks after discontinuing combined oral contraception.

If your patient needs to change or stop using her method of contraception during her thalidomide therapy, she must understand the need to inform:

- The physician prescribing her contraception about the thalidomide treatment.
- You if a change or stop of method of contraception is needed.

Your patient should be advised that if she is a woman of childbearing potential and has heterosexual intercourse without using a method of contraception while taking thalidomide, or believes for any reason that she may be pregnant, she must stop treatment immediately and inform her physician immediately.

Pregnancy testing

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

The pregnancy test must have a minimum sensitivity of 25 mIU/ml. The test must be performed by a healthcare professional, and the result must be negative before thalidomide treatment can begin or continue.

The pregnancy test must be performed during the consultation when thalidomide is being prescribed, or in the 3 days prior to the visit to the prescriber once the patient had been using effective contraception for at least 4 weeks. Further pregnancy tests must then be performed at least every 4 weeks during thalidomide treatment, and a final test conducted at least 4 weeks after treatment ends.

Specific Advice for Male Patients

Your male patients must be counselled on the risks of thalidomide therapy including the risk of birth defects, other side effects and important precautions associated with thalidomide therapy.

Patients must be informed not to donate semen or sperm during treatment (including during dose interruptions) and for at least 7 days after stopping treatment.

Contraceptive methods

As thalidomide is present in seminal fluid, male patients must be instructed to use a condom every time they have sexual intercourse if their partner is pregnant or is of child-bearing potential and not using effective methods of contraception. Condoms must be used during treatment, during dose interruption and for at least 7 days after treatment has finished.

Advice for all Patients

Your patient must be informed not to donate blood during treatment (including during dose interruptions) and for at least 7 days after stopping treatment.
If they discontinue therapy, they must return any unused thalidomide to the pharmacy.

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

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

Patients should be advised that capsules should not be opened or crushed. If powder from thalidomide makes contact with the skin, the skin should be washed immediately and thoroughly with soap and water. If thalidomide makes contact with the mucous membranes, they should be thoroughly flushed with water.

Prescribing thalidomide

Before issuing the initial prescription, you must:

- Counsel the patient on the safe use of thalidomide in accordance with the measures described in this brochure and the SmPC
- Obtain their written confirmation (using the correct *'Treatment Initiation Form'* that they have received and understood this information
- Retain a copy of the written confirmation, and provide a copy to the patient.

A 'Patient Card' and/or equivalent tool must be provided to the patient with each thalidomide prescription, and this will contain:

- Confirmation that they have received counselling on the safe use of thalidomide
- Patient category (women of childbearing potential, women of non-childbearing potential, or male)
- For women of childbearing potential, the pregnancy test date and result.

For women of childbearing potential, prescriptions of thalidomide should be limited to 4 weeks of treatment and continuation of treatment requires a new prescription. Ideally, pregnancy testing, issuing a prescription and dispensing should occur on the same day. Dispensing of thalidomide should occur within a maximum of 7 days of the prescription.

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

• **Repeat or subsequent prescriptions:** the patient must return for every repeat prescription of thalidomide. You may prescribe a maximum of 4 weeks of therapy for women of childbearing potential, or 12 weeks of therapy for all other patients.

• **Pregnancy testing:** for women of childbearing potential, you will need to undertake a repeat pregnancy test even if the patient has not had heterosexual intercourse since the last test. Further information regarding pregnancy testing is provided in the pregnancy testing section.

Information for Pharmacists

Introduction

As a pharmacist you play an important role in ensuring that thalidomide is used safely and correctly.

Dispensing thalidomide

For women of childbearing potential, ideally pregnancy testing, issuing a prescription and dispensing should occur on the same day. Dispensing of thalidomide should occur within a maximum of 7 days of the prescription.

Dispensing advice

• Ensure the pack is sealed; 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 a 12 week supply for all other patients.

• Instruct patients to return any unused thalidomide to the pharmacy.

Patient education

At each supply of thalidomide, please ensure that you remind patients about the teratogenic risk and the safe use and handling of thalidomide.

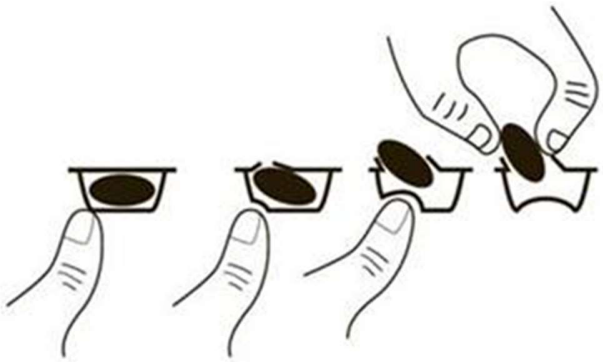
Points to consider for handling the medicinal product: for healthcare professionals and caregivers

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.

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.

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. Refer below for further guidance.



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.
- Patients should be advised never to give thalidomide to another person.

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

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

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

- If capsules are crushed or broken, dust containing drug substance may be released. Avoid dispersing the powder and avoid breathing 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 AM Mangion at

  Tel: + 356 23976333

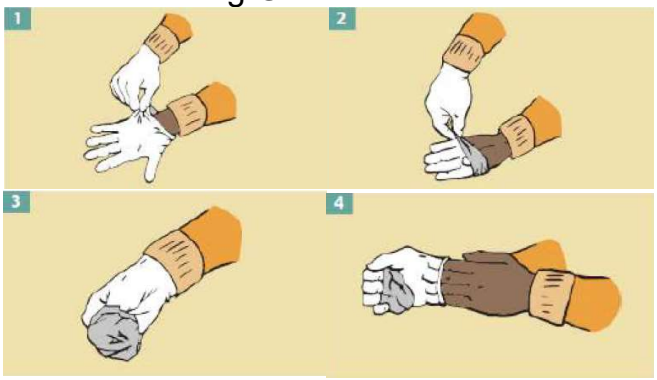
  Email: pv@ammangion.com

  .

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

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

Proper Technique for Removing Gloves



- 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.

The Thalidomide Pregnancy Prevention Programme at a Glance

Prescriber: You must

• Communicate the risks and benefits of thalidomide therapy to your patient.

• Complete a '*Treatment Initiation Form* along with your patient (this only needs to be done once). Retain a copy with your records, and provide a copy to the patient.

• Provide contraceptive counselling at treatment initiation.

• Perform a pregnancy test (if appropriate) prior to every prescription.

• Issue 'Patient Card' and/or equivalent tool to show:
  • confirmation that your patient has received counselling
  • patient category
  • pregnancy test date and result (if appropriate).

• Remind your patient of the safe use of thalidomide at each consultation.

Pharmacist: You must

• Remind your patient of the safe use of thalidomide, each time a prescription is dispensed.

▼ ***This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions via www.medicinesauthority.gov.mt/adrportal***

Description of the Pregnancy Prevention Programme and Patient Categorisation Algorithm