Thalidomide Celgene®

Healthcare Professional’s Information Pack

UK

Version 4
Thalidomide Celgene®
Healthcare Professional’s Information Pack
UK
Thalidomide Celgene®

Important Thalidomide Celgene forms

UK

CONTENT OF CD-ROM

Treatment Initiation Forms
Adverse Event Forms
Pregnancy Reporting Forms
Prescription Authorisation Form

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Version 4.0 April 2013
Your pack contains the information and materials needed for prescribing and dispensing Thalidomide Celgene®, including information about the Pregnancy Prevention Programme.

It is a requirement of the Pregnancy Prevention Programme that all healthcare professionals ensure that they have read and understood this pack before prescribing or dispensing Thalidomide Celgene® for ANY patient.

An easy reference guide is included at the back of your pack. This summarises the information for ongoing patient safety and the main steps in the Thalidomide Celgene® Pregnancy Prevention Programme process.

**Thalidomide Celgene® Warning**

*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 Celgene® Pregnancy Prevention Programme are met. The conditions of the Thalidomide Celgene® Pregnancy Prevention Programme must be fulfilled for all male and female patients.

**Version 4.0**

*Date of preparation of text: 24th September, 2013*
Contents

Information for Healthcare Professionals
Contains a booklet for prescribing physicians and pharmacists, providing an overview of the Thalidomide Celgene® Pregnancy Prevention Programme and summarising the safety information you will need to communicate to your patients. This section also contains the Pharmacy Registration Form.

Information for Patients
Contains booklets for your patients to take home and read, to reinforce the safety information you will provide to them during consultations.

Treatment Initiation Forms
There are three versions of this form, depending on whether your patient is a woman of childbearing potential, woman of non-childbearing potential, or male. Complete these forms before prescribing Thalidomide Celgene® to your patients.

Prescription Tools
Contains prescription authorisation forms to document that safety measures have been performed prior to prescribing Thalidomide Celgene®. Also contains patient health cards that your patients may present to other healthcare professionals to inform them about core information regarding their Thalidomide Celgene® treatment.

Adverse Events and Pregnancy Reporting Forms
Complete these forms if your patient experiences an adverse event or becomes pregnant while being treated with Thalidomide Celgene®, and send the information to the Celgene Drug Safety department.

Treatment checklists and algorithms

Frequently asked questions

Important contact information
Contact Details

Risk Management:
For information and questions on the risk management of Celgene’s products, the Pregnancy Prevention Programme and pharmacy registrations.
Tel: 0808 156 3059
Fax: 0808 156 3058
Email: rmp.uk.ire@celgene.com

Drug Safety:
To report any adverse events to Celgene.
Tel: 0808 238 9908
Fax: 0844 801 0466
Email: drugsafetyuk@celgene.com
Adverse events can also be reported to the MHRA using a ‘Yellow Card’ – reporting forms and information can be found at www.mhra.gov.uk/yellowcard.

Medical Information:
To obtain Medical Information on Celgene’s products.
Tel: 0844 801 0045
Fax: 0844 801 0046
Email: medinfo.uk.ire@celgene.com

Website:
Reference safety information (including the summary of product characteristics) and educational materials for all of Celgene’s products are available from our website - www.celgene.co.uk

Distributor:
For product delivery enquiries.
In Great Britain and Northern Ireland
Tel: 0208 831 8483
Fax: 0208 831 8792
Email: orders-uk@celgene.com

Thalidomide Celgene® (thalidomide)

Pregnancy Prevention Programme

Information for Healthcare Professionals
Prescribing orDispensing Thalidomide Celgene®

UK
This booklet is intended for healthcare professionals involved in prescribing or dispensing Thalidomide Celgene®, and contains information about:

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

- **Other side effects of Thalidomide Celgene®:**
  Some of the most commonly observed adverse reactions associated with the use of Thalidomide Celgene® in combination with melphalan and prednisone include: venous and arterial thromboembolic events, neutropenia, leukopenia, constipation, somnolence, paraesthesia, peripheral neuropathy, anaemia, lymphopenia, thrombocytopenia, dizziness, dysaesthesia, tremor and peripheral oedema. A full list of all side effects, further information and recommended precautions can be found in the Thalidomide Celgene® Summary of Product Characteristics (SmPC), which can be found on the Celgene website: www.celgene.co.uk.

- **Thalidomide Celgene® Pregnancy Prevention Programme:**
  This Programme is designed to make sure that unborn babies are not exposed to Thalidomide Celgene®. It will provide you with information about how to follow the programme and explain your responsibilities.

This booklet will help you understand these problems and make sure you know what to do before prescribing and dispensing Thalidomide Celgene®.

For your patients’ health and safety, please read this booklet carefully. You must ensure that your patients fully understand what you have told them about Thalidomide Celgene® before starting treatment.

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1.0 Introduction

1.1 Licensed indication and posology
Thalidomide Celgene® is licensed for use 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. The recommended oral dose is 200 mg per day, and a maximum number of 12 cycles of 6 weeks should be used. Thalidomide Celgene® should be taken as a single dose at bedtime, to reduce the impact of somnolence. Thalidomide Celgene® can be taken with or without food. For full details, please refer to the Summary of Product Characteristics (SmPC), which can be found on the Celgene website: www.celgene.co.uk.

1.2 The Thalidomide Celgene® Pregnancy Prevention Programme
Thalidomide Celgene® must be prescribed and dispensed according to the Thalidomide Celgene® Pregnancy Prevention Programme, which is necessary because if Thalidomide Celgene® 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.

Thalidomide Celgene® warning:
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 Celgene® Pregnancy Prevention Programme are met. The conditions of the Thalidomide Celgene® Pregnancy Prevention Programme must be fulfilled for all male and female patients.

1.3 Overview of the Healthcare Professional’s Information Pack
All of the Thalidomide Celgene® Pregnancy Prevention Programme materials are contained within the ‘Healthcare Professional’s Information Pack’, and additional copies can be obtained by using the contact details displayed on the front of this booklet. These materials can be used for counselling patients on the risks of Thalidomide Celgene® and the precautions to be taken.

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

Contained in this booklet is key information for Thalidomide Celgene® of relevance to healthcare professionals and contains the following:

- Thalidomide Celgene® Pregnancy Prevention Programme
  - educational information
  - therapy management advice to avoid foetal exposure to Thalidomide Celgene®
  - a distribution control system
- safety advice of relevance to all patients
- process for follow-up of effectiveness of the measures described in this pack
- process for reporting adverse events in patients treated with Thalidomide Celgene®

In order to obtain Thalidomide Celgene®, it is a requirement of the Pregnancy Prevention Programme that all healthcare professionals ensure that they have read and understood this pack before prescribing or dispensing Thalidomide Celgene® for any patient.

- Pharmacies must register with Celgene using the Pharmacy Registration Form, to be able to order and dispense Thalidomide Celgene®.
- Prescribers must complete the appropriate Treatment Initiation Form with every patient before the first prescription is issued
- Every prescription for Thalidomide Celgene® must be accompanied by a Prescription Authorisation Form
  - this form must be signed by prescriber and pharmacist and retained for a minimum of 2 years
  - this includes instances where Thalidomide Celgene® is prescribed to in-patients or if a prescription has to be dispensed in two parts due to the unavailability of sufficient stock to fulfill the prescription.
- The Pharmacy Registration Form and Prescription Authorisation Form are in subsequent sections of this pack.
All patients should be given a Patient Booklet and Health Card to take home — these materials remind patients of the key educational information and risks of treatment, and can be found in the Information for Patients section of this pack.

For women of childbearing potential, prescriptions of Thalidomide Celgene® 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, 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 Thalidomide Celgene® should be limited to 12 weeks and continuation of treatment requires a new prescription.

This Healthcare Professional’s Information Pack also contains adverse event reporting forms, treatment checklists and algorithms, example information and forms for obtaining informed consent and an example letter to notify a general practitioner that their patient is receiving Thalidomide Celgene®.

1.4 Teratogenicity: Potential or Actual Foetal Exposure to Thalidomide Celgene®

Thalidomide Celgene® 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 Celgene® must never be used by women who are able to become pregnant unless they follow the Thalidomide Celgene® Pregnancy Prevention Programme described in this pack (Section 2.0). Since thalidomide may be present in the semen of male patients, all male and female patients must both follow pregnancy prevention 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:

- Thalidomide Celgene® must be discontinued immediately
- The woman must have a pregnancy test
- If the pregnancy test is positive, the woman should be referred to a physician experienced in teratology for further evaluation and counselling.

Any positive pregnancy test or suspected foetal exposure to Thalidomide Celgene® must be reported immediately to the Medicines and Healthcare products Regulatory Agency (MHRA) and to the Celgene Drug Safety department. In this instance you must:

- Notify Celgene immediately by contacting the Celgene Drug Safety Department (Tel: 0808 238 9908). Please also complete the Pregnancy Reporting Form included in this pack. Celgene will wish to follow-up with you the progress of all pregnancies.
- Report the event to the Medicines and Healthcare products Regulatory Agency (MHRA) using the “Yellow Card” Scheme. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.

1.5 Safety advice relevant to all patients

In addition to information about the Pregnancy Prevention Programme, this booklet contains important advice for healthcare professionals about how to minimise the risk of adverse events during treatment with Thalidomide Celgene®.

For further information about the appropriate use and safety profile of Thalidomide Celgene® please refer to the SmPC, which can be found on the Celgene website: www.celgene.co.uk.
2.0 Therapeutic management advice to avoid foetal exposure

Patients must be counselled on the risks and benefits of Thalidomide Celgene® therapy, including the risk of birth defects, other side effects and important precautions associated with Thalidomide Celgene® therapy.

Animal studies have shown excretion of Thalidomide Celgene® in breast milk, but it is not known if this occurs in humans. Therefore breast-feeding should be discontinued during Thalidomide Celgene® therapy.

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

Thalidomide Celgene® is not recommended for use in children below 18 years of age as safety and efficacy have not been established, and any such use would be outside the approved indication. If you decide to treat a child or adolescent with Thalidomide Celgene® then all of the conditions of the Pregnancy Prevention Programme apply. Based on the age of the patient you must carefully consider how to proceed with education and counselling regarding pregnancy prevention measures, and evaluate when to involve the patient’s parent or guardian. The possibility of female patients becoming pregnant from the age of 8 years (the accepted lower age of menarche) should be considered

2.1 Women of non-childbearing potential

Women in the following groups are considered not to have childbearing potential and do not need to undergo pregnancy testing or receive contraceptive advice.

- Age ≥50 years and naturally amenorrhoeic for ≥1 year. Please note amenorrhoea following cancer therapy 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. Treating physicians 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.

If a patient does not meet at least one of above criteria, but the treating physician considers the patient to be of non-childbearing potential, then prior approval of any deviation from these stipulated criteria should be sought from the

Celgene Medical Director. This is a mandatory requirement. If there is a need for a deviation, then you should contact Celgene Risk Management (Tel: 0808 156 3059 Email: rmp.uk.ire@celgene.com). The following information is required to assess whether a patient, who does not meet at least one of the above criteria, can be treated as a women of non-childbearing potential:

- DOB and Initials of the Patient
- Details of why the physician considers the patient to be of non-childbearing potential
- Background to why a deviation has been requested.

2.2 Women of childbearing potential

Women of childbearing potential must understand the need to avoid pregnancy, and these patients must be adequately counselled regarding the use of pregnancy prevention measures every time a prescription is issued.

Women of childbearing potential must use one effective method of pregnancy prevention at least 4 weeks before therapy, during therapy and even in the case of dose interruptions, and for at least a further 4 weeks after stopping Thalidomide Celgene® therapy. This must be followed unless the patient commits to absolute and continuous abstinence confirmed to her physician on a monthly basis.

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

The following are effective methods of pregnancy prevention

- Subcutaneous hormonal 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 methods 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 her pregnancy prevention method during her Thalidomide Celgene® therapy, she must understand the need to discuss this first with:

- The physician prescribing her pregnancy prevention method
- The physician prescribing her Thalidomide Celgene®.

If a woman of childbearing potential has sexual contact without using a pregnancy prevention method while taking Thalidomide Celgene®, or believes for any reason that she may be pregnant, she must stop treatment and consult her doctor immediately.

Pregnancy testing

For women of childbearing potential a pregnancy test must be performed prior to issuing a prescription. This may be embarrassing for some patients and may need to be handled sensitively. A pregnancy test is required even if the patient has not had heterosexual intercourse since her last pregnancy test. Special consideration must be given when communicating such advice to female children.

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 Celgene® treatment can begin or continue. An inconclusive urine pregnancy test must be confirmed with a serum pregnancy test.

The pregnancy test must be performed during the consultation when Thalidomide Celgene® is being prescribed, or in the 3 days prior. Further pregnancy tests must then be performed every 4 weeks during Thalidomide Celgene® treatment, and a final test conducted at least 4 weeks after treatment ends.

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 pregnancy prevention method, or if she suspects she is pregnant.

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 Celgene immediately by contacting the Celgene Drug Safety Department (Tel: 0808 238 9908). Please also complete the Pregnancy Reporting Form included in this pack. Celgene will wish to follow-up with you the progress of all pregnancies.

- Report the event to the Medicines and Healthcare products Regulatory Agency (MHRA) using the “Yellow Card” Scheme. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.

2.3 Men

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

Patients must be informed not to donate semen during or within 1 week after stopping treatment.

Pregnancy prevention

As thalidomide is found in semen, male patients must use condoms during treatment and for 1 week after dose interruption and/or cessation of treatment if their partner is pregnant or is of childbearing potential potential and not using an effective pregnancy prevention method.

Thalidomide Celgene® is not recommended for use in children below 18 years of age as safety and efficacy have not been established, and any such use would be outside the approved indication. If you decide to treat a child or adolescent with Thalidomide Celgene® then all of the conditions of the Pregnancy Prevention Programme apply. Based on the age of the patient you must carefully consider how to proceed with education and counselling regarding pregnancy prevention measures, and evaluate when to involve the patient’s parent or guardian.

If the partner of a male patient becomes pregnant, then he must inform his doctor immediately, then:

- Refer the female partner to a physician specialised or experienced in dealing with teratology for advice and evaluation
- Notify Celgene immediately by contacting the Celgene Drug Safety Department (Tel: 0808 238 9908). Please also complete the Pregnancy Reporting Form included in this pack. Celgene will wish to follow-up with you the progress of all pregnancies.

- Report the event to the Medicines and Healthcare products Regulatory Agency (MHRA) using the “Yellow Card” Scheme. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.
### 2.4 Advice for all Patients

Your patient must be informed not to donate blood during or within one week after stopping treatment. If they discontinue therapy, they must return any unused Thalidomide Celgene® to the pharmacy.

They must also understand that their Thalidomide Celgene® 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 and sight of children.

### 3.0 Healthcare Professional Obligations

Healthcare professionals have specific obligations that must be followed when prescribing or dispensing Thalidomide Celgene®, which are:

**Prescriber: You must ensure that**

- Your patient is fully educated on the risks of Thalidomide Celgene®
- You complete the appropriate ‘Treatment Initiation Form’ with your patient before the first prescription is issued
- You provide the patient with a ‘Health Card and Patient Booklet’
- If relevant, your patient is using the appropriate pregnancy prevention measures
- Female patients of childbearing potential receive a pregnancy test, which must be negative, before every prescription that you issue
- You complete a ‘Prescription Authorisation Form’ with every prescription – this includes instances where Thalidomide Celgene® is prescribed to in-patients or if a prescription has to be dispensed in two parts due to the unavailability of sufficient stock to fulfill the prescription.
- You prescribe Thalidomide Celgene® in accordance with the measures described in this booklet and the SmPC, which can be found on the Celgene website: www.celgene.co.uk.

**Pharmacist: You must ensure that**

- Your Pharmacy is registered with the Thalidomide Celgene® Pregnancy Prevention Programme. Registration will be valid for 2 years.
- Thalidomide Celgene® is only dispensed if the prescription is accompanied by a Prescription Authorisation Form – this includes instances where Thalidomide Celgene® is prescribed to in-patients or if a prescription has to be dispensed in two parts due to the unavailability of sufficient stock to fulfill the prescription.
- You check and validate the ‘Prescription Authorisation Form’ prior to dispensing Thalidomide Celgene®
- You dispense Thalidomide Celgene® in accordance with the measures described in this booklet
- You remind patients of key education messages each time Thalidomide Celgene® is dispensed.
3.1 Information for Prescribers

3.1.1 Patient and healthcare professional education

As the prescribing physician, you play a central role in ensuring that Thalidomide Celgene® is used safely and correctly.

Most importantly, you will be helping to ensure that your patients understand the risks involved in taking Thalidomide Celgene® 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 Celgene® Pregnancy Prevention Programme. This will help to prevent any delays in your patients receiving their treatment.

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

A summary of the Thalidomide Celgene® Pregnancy Prevention Programme process can be found on the last page of this booklet.

3.1.2 Patient counselling and education

Because of the different levels of risk, you will need to communicate different things to men, women and children. 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 Booklet and Health Card to help explain the relevant information. Copies of the booklet are contained in your ‘Healthcare Professional’s Information Pack’, and your patient may wish to take these materials home to read in their own time or with a relative. Further copies can be obtained by using the contact details displayed on the front of this booklet.

3.1.3 Prescribing Thalidomide Celgene®

3.1.3.1 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. Thalidomide Celgene® treatment must be initiated and monitored under the supervision of physicians with expertise in managing immunomodulatory or chemotherapeutic agents and a full understanding of the risks of thalidomide therapy and monitoring requirements.

Approval from the Celgene Medical Director is a mandatory requirement prior to any deviation from these stipulated prescription lengths. If there is a need for an exception to the maximum prescription lengths, then you should contact Celgene Risk Management (Tel: 0808 156 3059 Email: rmp.uk.ire@celgene.com). The following information is required to assess whether a deviation to the maximum prescription length can be approved:

- DOB and initials of the patient
- Sex and childbearing potential
- Background to why a deviation has been requested.

3.1.3.2 Initial prescription

Before issuing the initial prescription, you must:

- Counsel the patient on the safe use of Thalidomide Celgene® in accordance with the measures described in this booklet and the SmPC, which can be found on the Celgene website: www.celgene.co.uk.
- Obtain their written confirmation (using the correct Treatment Initiation Form) that they have received and understood this information, and provide the patient with a copy
- Provide the patient with a Patient Booklet and Health Card
- A ‘Prescription Authorisation Form’ must be provided to the patient with each Thalidomide Celgene® prescription, and this will contain:
  - Patient name, date of birth and diagnosis
  - Prescriber name, signature and date
  - Patient category (women of childbearing potential, women of non-childbearing potential, or male)
3.1.3.3 Repeat of subsequent prescriptions

The patient must return to the initial prescriber for every repeat prescription of Thalidomide Celgene®. If a patient is transferred or consulted by another prescriber, the initial prescriber must remind them to contact Celgene and obtain a Thalidomide Celgene® ‘Healthcare Professional’s Information Pack’.

3.2 Information for Pharmacists

As a pharmacist you play an important role in ensuring that Thalidomide Celgene® is used safely and correctly. Thalidomide Celgene® will only be supplied to pharmacies, who have completed a ‘Thalidomide Celgene® Pregnancy Prevention Programme, Pharmacy Registration Form’ and returned this form to Celgene.

3.2.1 Dispensing Thalidomide Celgene®

Along with each Thalidomide Celgene® prescription, prescribers must complete a Prescription Authorisation Form and instruct the patient to provide this to their pharmacy. You must only dispense Thalidomide Celgene® if the prescriber has annotated this form correctly, and it must contain:

- Confirmation that the patient has received counselling on the safe use of Thalidomide Celgene®
- The patient category (women of childbearing potential, women of non-childbearing potential or male)
- For women of childbearing potential, the negative pregnancy test date.

If any information is missing, contact the doctor for verification prior to dispense. For women of childbearing potential, ideally pregnancy testing, issuing a prescription and dispensing should occur on the same day. Dispensing of Thalidomide Celgene® should occur within a maximum of 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.

Please retain the ‘Prescription Authorisation Form’ for 2 years.

- Every prescription for Thalidomide Celgene® must be accompanied by a Prescription Authorisation Form
- This form must be signed by prescriber and pharmacist and retained for a minimum of 2 years
- This includes instances where Thalidomide Celgene® is prescribed to in-patients or if a prescription has to be dispensed in two parts due to the unavailability of sufficient stock to fulfill the prescription.

3.2.2 Dispensing Advice

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

The terms of the Thalidomide Celgene® Marketing Authorisation require Celgene 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 Thalidomide Celgene®.

Celgene have agreed with the MHRA that pharmacies can fulfill their obligations in this respect, by conducting a manual self-audit and reporting the results to Celgene. This information will be provided, in an anonymised and aggregated format, to the MHRA and the European Medicines Agency (EMA). Celgene will supply pharmacies with an audit pack, such that annual self-auditing of pharmacies and feedback of the audit results to Celgene can occur.

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

5.0 Safety Advice Relevant to all Patients

The following section contains advice to healthcare professionals about how to minimise the risk of the principal adverse events associated with the use of Thalidomide Celgene®. For a full list of the adverse events that may be associated with its use please refer to the Summary of Product Characteristics (SmPC), which can be found on the Celgene website: www.celgene.co.uk.

5.1 Venous and arterial thromboembolic events

Patients treated with thalidomide have an increased risk of venous thromboembolism (such as deep vein thrombosis and pulmonary embolism) and arterial thromboembolism (such as myocardial infarction and cerebrovascular event). The risk appears to be greatest during the first 5 months of therapy. Thromboprophylaxis should be administered for at least the first 5 months of treatment, especially in patients with additional thrombotic risk factors. Prophylactic antithrombotic medicines, such as low molecular weight heparins or warfarin, are recommended. The decision to take antithrombotic prophylactic measures should be made after careful assessment of an individual patient’s underlying risk factors.

Previous history of thromboembolic events or concomitant administration of erythropoietic agents or other agents such as hormone replacement therapy, may also increase thrombotic risk in these patients. Therefore, these agents should be used with caution in multiple myeloma patients receiving thalidomide with prednisone and melphalan. Particulary, a haemoglobin concentration above 12g/dl should lead to discontinuation of erythropoietic agents.

Patients and physicians are advised to be observant for the signs and symptoms of thromboembolism. Patients should be instructed to seek medical care if they develop symptoms such as shortness of breath, chest pain, arm or leg swelling.

5.2 Severe Infections

Patients should be monitored for severe infections including sepsis and septic shock.

5.3 Peripheral neuropathy

This is a very common, potentially severe, adverse reaction of treatment with thalidomide that may result in irreversible damage. Peripheral neuropathy generally occurs following chronic use over a period of months and in a Phase 3 study the median time to first neuropathy event was 42.3 weeks. However, there are reports of neuropathy following relatively short-term use.
5.4 Syncope and bradycardia

Patients should be monitored for syncope and bradycardia and dose reduction or discontinuation may be required.

5.5 Skin reactions

If at anytime the patient experiences a toxic skin reaction e.g. Stevens-Johnson Syndrome, the treatment should be discontinued permanently.

5.6 Somnolence

Thalidomide frequently causes somnolence. Therefore, Thalidomide Celgene® should be taken as a single dose at bedtime. Patients should be instructed to avoid situations where somnolence may be a problem and to seek medical advice before taking other medicinal products known to cause somnolence. Patients should be monitored and dose reduction may be required.

Patients should be advised as to the possible impairment of mental and/or physical abilities required for the performance of hazardous tasks.

5.7 Tumour lysis syndrome

The patients at risk of tumour lysis syndrome are those with high tumour burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.

5.8 Patients with renal or hepatic impairment

Patients with severe renal or hepatic impairment should be carefully monitored for adverse effects.

Table 1: Recommended dose modifications for Thalidomide Celgene® 50mg hard capsule-related neuropathy.

<table>
<thead>
<tr>
<th>Severity of neuropathy</th>
<th>Modification of dose and regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (paraesthesia, weakness and/or loss of reflexes) with no loss of function</td>
<td>Continue to monitor the patient with clinical examination. Consider reducing dose if symptoms worsen. However, dose reduction is not necessarily followed by the improvement of symptoms.</td>
</tr>
<tr>
<td>Grade 2 (interfering with function but not with activities of daily living)</td>
<td>Reduce dose or interrupt treatment and continue to monitor the patient with clinical and neurological examination. If no improvement or continued worsening of the neuropathy, discontinue treatment. If the neuropathy resolves to Grade 1 or better, the treatment may be restarted, if the benefit/risk is favourable.</td>
</tr>
<tr>
<td>Grade 3 (interfering with activities of daily living)</td>
<td>Discontinue treatment</td>
</tr>
<tr>
<td>Grade 4 (neuropathy which is disabling)</td>
<td>Discontinue treatment</td>
</tr>
</tbody>
</table>
5.9 Safety and off-label use

Please note that the posology, adverse event profile and recommendations outlined above, relate to the use of Thalidomide Celgene® within its licensed indication.

Thalidomide Celgene® must always be used according to the Pregnancy Prevention Programme described in this pack – these precautions must be followed, irrespective of the treatment setting, including the indication for treatment.

It is essential that the patient’s diagnosis is entered on the Prescription Authorisation Form - this will allow an assessment of the clinical usage of Thalidomide Celgene®, which is important for ongoing monitoring of safety.

5.10 Disposal of unwanted medicine

Patients must be advised never to give Thalidomide Celgene® to another person and to return any unused capsules to their pharmacist at the end of the treatment.

5.11 Blood donation

Patients should not donate blood during treatment and for 1 week after cessation of treatment with Thalidomide Celgene®.

6.0 Reporting Adverse Events

The safe use of Thalidomide Celgene® 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 are included in this pack and should be forwarded to the Celgene Drug Safety Department (Tel: 0808 238 9908 Fax: 0844 801 0468; Email: drugsafetyuk@celgene.com).

The event should also be reported to the MHRA via the ‘Yellow Card’ scheme. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.
Thalidomide Celgene® Pharmacy Registration Form – Part 1

To be completed by the Chief Pharmacist or appointed deputy.

<table>
<thead>
<tr>
<th>Institution name:</th>
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</thead>
<tbody>
<tr>
<td>Chief Pharmacist (or appointed deputy):</td>
</tr>
<tr>
<td>Contact telephone number:</td>
</tr>
<tr>
<td>Email:</td>
</tr>
<tr>
<td>Pharmacy purchasing contact:</td>
</tr>
<tr>
<td>Delivery Address:</td>
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<td>Tel:</td>
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<td>Fax:</td>
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<td>Email:</td>
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</tbody>
</table>

On behalf of .................................................. [institution name], I will ensure the following procedures - as detailed in the Thalidomide Celgene Healthcare Professional’s Information Pack - are instigated when handling prescriptions for Thalidomide Celgene.

1. I have read and understood the Thalidomide Celgene Healthcare Professional’s Information Pack. **TICK**

2. All pharmacists within my pharmacy will read and understand the 'Thalidomide Celgene Healthcare Professional’s Information Pack' before dispensing Thalidomide Celgene. **TICK**

3. Dispensing will only occur if the prescription is accompanied by a fully completed ‘Prescription Authorisation Form’. **TICK**

4. Review and countersigning of the ‘Prescription Authorisation Form’ will occur prior to dispensing Thalidomide Celgene. **TICK**

5. Dispensing will only occur within 7 days of the prescription date. **TICK**

6. Dispensing will be limited to no more than a 4-week supply for women of childbearing potential, and 12 weeks for all other patients. **TICK**

7. The ‘Prescription Authorisation Form’ will be retained for a minimum of 2 years. **TICK**

8. Compliance with these procedures will be audited by the chief pharmacist or appointed deputy at least annually. Audit results will be made available to Celgene so that their obligation to report to the regulatory agencies on the overall effectiveness of the programme can be met. **TICK**

I understand that pharmacy registration is valid for two years, dependent upon implementation of the Thalidomide Celgene Pregnancy Prevention Programme and the procedures set out in the Thalidomide Celgene Healthcare Professional’s Information Pack.

Sign: ____________________________
Print: ____________________________
Date: DD MM YYYY

Fax the completed forms to Celgene on 0808 156 3058

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Thalidomide Celgene® Pharmacy Registration Form – Part 2

If you would like to register additional pharmacy sites to be covered by your registration please provide details below.

<table>
<thead>
<tr>
<th>Institution name:</th>
</tr>
</thead>
</table>

**Additional pharmacy sites covered by registration with Celgene to supply Thalidomide Celgene**

<table>
<thead>
<tr>
<th>Name of Hospital/Pharmacy:</th>
<th>Pharmacy purchasing contact:</th>
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<tr>
<th>Delivery Address:</th>
<th>Invoice Address (if different):</th>
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</table>
Information for Patients
Contains booklets for your patients to take home and read, to reinforce the safety information you will provide to them during consultations.
Thalidomide Celgene®
Pregnancy Prevention Programme

Information for Patients Taking
Thalidomide Celgene®

UK
This booklet contains information about:

• Preventing harm to unborn babies: If Thalidomide Celgene® is taken during pregnancy it can cause severe birth defects or death to an unborn baby.

• Other side effects of Thalidomide Celgene®: These include nerve damage, blood clots in your veins and arteries and, severe skin problems.

• Thalidomide Celgene® Pregnancy Prevention Programme: This Programme is designed to make sure that unborn babies are not exposed to Thalidomide Celgene®. It will provide you with information about what to expect from your treatment, and explain the risks and your responsibilities.

This booklet will help you understand these problems and make sure you know what to do before, during and after taking Thalidomide Celgene®.

This booklet will not give you information about multiple myeloma, you should ask your Doctor if you have any questions regarding myeloma.

Warning: Severe life-threatening birth defects. If Thalidomide Celgene® is taken during pregnancy it can cause severe birth defects or death to an unborn baby. Thalidomide Celgene® must never be used by women who are pregnant, as just one capsule can cause severe birth defects. Thalidomide Celgene® must never be used by women who are able to become pregnant unless they follow the Thalidomide Celgene® Pregnancy Prevention Programme.

For your own health and safety, please read this booklet carefully. If you do not understand something, please ask your doctor to explain it again.
Introduction

Thalidomide Celgene® belongs to a group of medicines known as ‘immunomodulatory’ medicines. These work by acting on the cells involved in your immune system. The immune system is part of the body’s defence which helps to fight illness and infection. Thalidomide Celgene® also has anti-angiogenic properties. This means that it prevents the development of new blood vessels (angiogenesis). Angiogenesis is important for cancers because they need to produce new blood vessels in order to grow.

Thalidomide Celgene® is now approved in the European Union for the treatment of multiple myeloma in combination with melphalan and prednisone.

The information leaflet which came with your medicine tells you more about Thalidomide Celgene®.

This booklet is part of the “Thalidomide Celgene® Pregnancy Prevention Programme”, which is necessary because if Thalidomide Celgene® is taken during pregnancy it can cause severe birth defects or death to an unborn baby. In the 1950s and 1960s thalidomide was prescribed to pregnant women as a sedative and to relieve morning sickness. As a result approximately 12,000 children were born with severe birth defects caused by thalidomide, approximately 5,000 survive today.
Thalidomide Celgene® and Birth Defects

All medicines can cause unwanted effects or ‘side effects’. An extremely important side effect of Thalidomide Celgene® is that if taken during pregnancy, it can cause severe birth defects or death to an unborn baby. The birth defects include shortened arms or legs, malformed hands or feet, eye or ear defects, and internal organ problems. This means Thalidomide Celgene® must never be taken by:

- Women who are pregnant
- Women who could become pregnant, unless they follow the Thalidomide Celgene® Pregnancy Prevention Programme.

Advice for Women of Childbearing Potential

During treatment if you miss or think you have missed a period, or you have any unusual menstrual bleeding, or suspect you are pregnant or if you have heterosexual intercourse without using an effective method of contraception, you must stop treatment and tell your doctor straight away.

Advice for Males

Thalidomide is present in semen. This means that men taking Thalidomide Celgene® must use pregnancy prevention measures every time they have intercourse with a woman who is able to become pregnant.

If you have a female partner who is able to become pregnant, then during your treatment if they miss or think they have missed a period, or have any unusual menstrual bleeding, or suspect they may be pregnant, you must tell your doctor straight away. Your partner must also tell her doctor straight away.

Thalidomide Celgene® and Other Possible Side Effects

Like all medicines, Thalidomide Celgene® can cause side effects although not everybody gets them. It is important that you talk to your doctor if you have any side effects from Thalidomide Celgene® treatment. You may also report any side effect to the UK Medicines and Healthcare Products Regulatory Agency via their “Yellow Card” scheme, by using their web site at www.mhra.gov.uk/yellowcard.

Stop taking Thalidomide Celgene® and see a doctor straight away if you notice the following serious side effect, as you may need urgent medical treatment:

- Severe skin reactions including rashes and blistering of the skin or inside of your mouth. You may have a high temperature (fever) at the same time.

Tell your doctor straight away if you notice any of the following serious side effects:

- Numbness, tingling, or pain in your hands and feet. This may be due to nerve damage (called ‘peripheral neuropathy’), which usually happens after you have been taking this medicine for several months but can happen sooner than this. It can also happen some time after treatment has stopped. It may not go away, or may go away slowly.

- Chest pain spreading to the arms, neck, jaw, back or stomach, feeling sweaty and breathless, feeling sick or vomiting. This may be due to blood clots in the arteries (which may be symptoms of a heart attack or "myocardial infarction”).

- Sudden pain in your chest or difficulty in breathing. This may be due to blood clots in the artery leading to your lungs (called ‘pulmonary embolism’), which can happen during treatment, or after treatment has stopped.

- Pain or swelling in your legs, especially in your lower leg or calves. This may be due to blood clots in the veins of your leg (deep vein thrombosis). These can happen during treatment, or after treatment has stopped.
Before Starting Your Treatment

Your doctor will talk to you about what to expect from your treatment, and explain the risks and your responsibilities. If there is anything you do not understand, please ask your doctor to explain it again.

Before starting treatment your doctor will ask you to read and sign a Treatment Initiation Form, which confirms that while taking Thalidomide Celgene®:

- You understand the risks of birth defects
- You agree not to become pregnant
- You understand the other important safety messages.

Your doctor will keep this form with your medical records.

Childbearing Potential Assessment

Female patients will be assessed by their doctors for childbearing potential, and unless you fall into one of the following categories you must follow the pregnancy prevention advice presented in the next section:

- You are at least 50 years old and it has been at least one year since your last period (if your periods have stopped because of cancer therapy, then there is still a chance you could become pregnant)
- Your womb has been removed (hysterectomy)
- Your fallopian tubes and both ovaries have been removed (bi-lateral salpingo oophorectomy)
- You have premature ovarian failure, confirmed by a specialist gynaecologist
• You have the XY genotype, Turner’s syndrome or uterine agenesis

• You are a child/adolescent who has not reached menstruation (started having periods), and cannot become pregnant.

Pregnancy Prevention Advice for Women of Childbearing Potential

Prior to starting treatment your doctor will talk to you about the pregnancy prevention measures that you must follow. If you could become pregnant you must use one effective method of pregnancy prevention:

• At least 4 weeks before starting Thalidomide Celgene® treatment

• During treatment, even if there are breaks in your treatment

• Until at least 4 weeks after stopping treatment.

Effective female pregnancy prevention methods are:

• Hormonal pregnancy prevention measures implanted under the skin

• Pregnancy prevention coil placed in the uterus

• Long acting pregnancy prevention hormonal injection

• Female sterilisation

• Progestogen-only pill that prevents release of an egg from the ovaries

• Male partner’s vasectomy, which must be confirmed by two negative semen tests

• Abstinence from heterosexual intercourse.

If you are pregnant or trying to become pregnant, you must not take Thalidomide Celgene®. If you are able to have children your doctor will perform regular pregnancy tests to confirm that you are not pregnant before taking Thalidomide Celgene®.

• You must have been using an effective pregnancy prevention method for at least 4 weeks before Thalidomide Celgene® can be prescribed

• A pregnancy test will take place every 4 weeks

• Your doctor will perform the pregnancy test during the consultation when Thalidomide Celgene® is prescribed, or in the previous three days

• Additional pregnancy tests must be performed if you miss your period or have any unusual menstrual bleeding

• A pregnancy test will take place at least 4 weeks after starting treatment.

It is important that you understand and follow the pregnancy prevention methods and pregnancy testing information described.

• Pregnancy tests must be performed every 4 weeks even if you think there is no chance you have become pregnant since your last test

• Pregnancy prevention methods must be followed 4 weeks before starting treatment, during treatment, and until at least 4 weeks after stopping treatment

• Talk to your doctor before changing any pregnancy prevention method

• If you have heterosexual intercourse without using an effective pregnancy prevention method, stop taking Thalidomide Celgene® and talk to your doctor straight away

• If you think you are pregnant, stop taking Thalidomide Celgene® and contact your doctor straight away.

It is important that you do not change pregnancy prevention methods without talking to your doctor first.
Pregnancy Prevention Advice for Males

Prior to starting treatment your doctor will talk to you about the pregnancy prevention measures that you must follow if you have a female partner who is pregnant or who is able to get pregnant, as you must protect her against any exposure to Thalidomide Celgene®. This means that if your partner is pregnant, or is not using an effective form of pregnancy prevention, you must use condoms every time you have intercourse:

- During treatment, even if there are breaks in your treatment
- Until 1 week after stopping treatment.

If you have a female partner who is pregnant or who is able to get pregnant, you must both tell your doctors immediately if:

- You have intercourse without using pregnancy prevention measures
- You think your male or female pregnancy prevention measure has failed
- Your partner misses a period or has any unusual menstrual bleeding during your treatment.

Safety Measures During Treatment

There are additional measures you must understand while taking Thalidomide Celgene®.

- Please remember that your Thalidomide Celgene® must only be used by you. Do not share your medicine with anyone else, even if they have similar symptoms to you.
- Store your Thalidomide Celgene® capsules safely, so no one else could take them by accident
- Keep Thalidomide Celgene® out of reach and sight of children

- You must not donate blood, and men must also not donate semen, while you are being treated with Thalidomide Celgene®, and for one week after stopping treatment
- If you are a woman who is breastfeeding, your doctor will advise you either to stop breastfeeding or to stop taking Thalidomide Celgene® while breastfeeding. It is not known if Thalidomide Celgene® is passed into human breast milk.

Receiving Your Prescription

When your doctor writes your prescription they will also provide you with a ‘Prescription Authorisation Form’ that must be provided to the pharmacist, which confirms that all of the Thalidomide Celgene® Pregnancy Prevention Programme measures have been followed. Your pharmacist will ask to review this documentation prior to dispensing your Thalidomide Celgene®.

For women of childbearing potential your doctor will write a prescription for no more than 4 weeks supply. Ideally, you should have the prescription dispensed within 7 days of the prescription date.

For women of non-childbearing potential and male patients your doctor will write a prescription for no more than 12 weeks supply.

You will need to see your doctor each time you need a repeat prescription.
End of Treatment Requirements

After completing your Thalidomide Celgene® treatment, it is important that:

- You return any unused Thalidomide Celgene® capsules to your pharmacist
- You do not donate blood for 1 week.

Additional advice for women of childbearing potential:

- Continue using your effective pregnancy prevention method for at least a further 4 weeks
- Your doctor will perform a final pregnancy test after at least 4 weeks.

Additional advice for male patients:

- If you have been using an effective pregnancy prevention method, you must continue doing so for 1 week
- If your female partner has been using an effective pregnancy prevention method, she must continue doing so for at least 4 weeks
- Do not donate blood or semen for 1 week.

Check List

Please use this check list to confirm that you have understood all of the important information regarding your Thalidomide Celgene® treatment.

- Yes, I have received and understood all the information on the risks of birth defects associated with taking Thalidomide Celgene®.
- Yes, I have received and understood all the information on the risks of other side effects associated with taking Thalidomide Celgene®.
- Yes, I understand that I need to sign the Treatment Initiation Form before starting treatment.
- Yes, I have received and understood the pregnancy prevention advice.
Treatment Initiation Forms
There are three versions of this form, depending on whether your patient is a woman of childbearing potential, woman of non-childbearing potential, or male. Complete these forms before prescribing Thalidomide Celgene® to your patients.
Thalidomide Celgene®
Pregnancy Prevention Programme

Woman of Childbearing Potential
Treatment Initiation Form

UK
I understand that I must use one effective method of pregnancy prevention without interruption, for at least 4 weeks before starting treatment, throughout the entire duration of treatment and even in the case of dose interruptions, and for at least 4 weeks after the end of treatment.

Warning: Severe life-threatening birth defects. If Thalidomide Celgene® is taken during pregnancy it can cause severe birth defects or death to an unborn baby.

Patient Details
- Patient First Name:
- Patient Last Name:
- Date of Birth: DD MM YYYY
- Counselling Date: DD MM YYYY

Pregnancy Prevention Referral
- Pregnancy prevention referral required: YES NO
- Pregnancy prevention referral made: DD MM YYYY
- Pregnancy prevention consultation conducted on: DD MM YYYY

Pregnancy Prevention
- The patient has been established on one of the following for at least 4 weeks
  - Implant
  - Levonorgestrel-releasing intrauterine system (LUS)
  - Medroxyprogesterone acetate depot
  - Tubal sterilisation
  - Sexual intercourse with a vasectomised male partner only, vasectomy must be confirmed by two negative semen analyses
  - Oral contraceptive pill (e.g., desogestrel)
  - Committed to complete and absolute abstinence

Pregnancy Test
- Date of last negative pregnancy test: DD MM YYYY

Thalidomide Celgene® treatment cannot start until the patient has been established on effective method of pregnancy prevention for 4 weeks, or commits to complete and continuous abstinence, and obtains a negative pregnancy test.

Prescriber Confirmation
- I have fully explained to the patient named above the nature, purpose and risks of the treatment associated with Thalidomide Celgene®, especially the risks to women of childbearing potential.

Patient: please read thoroughly and initial the adjacent box if you agree with the statement
- I understand that severe birth defects can occur with the use of Thalidomide. I have been warned by my doctor that any unborn baby has a high risk of birth defects and could even die if a woman is pregnant or becomes pregnant while taking Thalidomide Celgene®.
- I understand that I must not take Thalidomide if I am pregnant or plan to become pregnant.
- I understand that I must use one effective method of pregnancy prevention without interruption, for at least 4 weeks before starting treatment, throughout the entire duration of treatment and even in the case of dose interruptions, and for at least 4 weeks after the end of treatment.
- I understand that if I need to change or stop my method of pregnancy prevention I will discuss this first with the physician prescribing my pregnancy prevention method.
- I understand that if I need to change my method of pregnancy prevention I will discuss this first with the physician prescribing my Thalidomide Celgene®.
- I understand that before starting the Thalidomide Celgene® treatment I must have a pregnancy test. I will then have a pregnancy test every 4 weeks during treatment, and a test at least 4 weeks after the end of treatment.
- I understand that I must immediately stop taking Thalidomide Celgene® and inform my doctor if I become pregnant while taking this drug, or if I miss my menstrual period or experience any unusual menstrual bleeding, or think FOR ANY REASON that I may be pregnant.
- I understand that Thalidomide Celgene® will be prescribed ONLY for me. I must not share it with ANYONE.
- I have read the Thalidomide Celgene® Patient Information and understand the contents, including the information about other possible health problems (side effects) from Thalidomide.
- I know that I cannot donate blood while taking Thalidomide Celgene®, or for 1 week after stopping treatment.
- I understand that I must return any unused Thalidomide Celgene® to my pharmacy at the end of my treatment.

Patient Signature: Date: DD MM YYYY
Thalidomide Celgene®
Pregnancy Prevention Programme

Woman of Non-Childbearing Potential
Treatment Initiation Form

UK
Thalidomide Celgene®

Introduction
This Treatment Initiation Form must be completed for each female patient of non-childbearing potential prior to the initiation of their Thalidomide Celgene® treatment. Retain a copy of this form with their medical records, and provide a photocopy to the patient.

The aim of the Treatment Initiation Form is to protect patients and any possible unborn children by ensuring that patients are fully informed of and understand the risk of teratogenicity and other adverse effects associated with the use of thalidomide. It is not a contract and does not absolve anybody from his/her responsibilities with regard to the safe use of the product and prevention of foetal exposure.

Warning: Severe life-threatening birth defects. If Thalidomide Celgene® is taken during pregnancy it can cause severe birth defects or death to an unborn baby.

Prescriber Confirmation
I have fully explained to the patient named above the nature, purpose and risks of the treatment associated with Thalidomide Celgene®, especially the risks to women of childbearing potential.

| Prescriber First Name: |  |
| Prescriber Last Name: |  |
| Prescriber Signature: | Date: DD MM YYYY |

Patient Confirmation
I confirm that I understand and will comply with the requirements of the Thalidomide Celgene® Pregnancy Prevention Programme, and I agree that my doctor can initiate my treatment with Thalidomide Celgene®.

| Patient Signature: | Date: DD MM YYYY |

Patient Details

| Patient First Name: |  |
| Patient Last Name: |  |
| Date of Birth: DD MM YYYY | Counselling Date: DD MM YYYY |
Thalidomide Celgene®
Pregnancy Prevention Programme

Male Treatment Initiation Form

UK
Introduction
This Treatment Initiation Form must be completed for each male patient prior to the initiation of their Thalidomide Celgene® treatment. Retain a copy of this form with their medical records, and provide a photocopy to the patient.

The aim of the Treatment Initiation Form is to protect patients and any possible unborn children by ensuring that patients are fully informed of and understand the risk of teratogenicity and other adverse effects associated with the use of thalidomide. It is not a contract and does not absolve anybody from his/her responsibilities with regard to the safe use of the product and prevention of foetal exposure.

Warning: Severe life-threatening birth defects. If Thalidomide Celgene® is taken during pregnancy it can cause severe birth defects or death to an unborn baby.

Patient Details
- Patient First Name: 
- Patient Last Name: 
- Date of Birth: DD MM YYYY 
- Counselling Date: DD MM YYYY

Pregnancy Prevention
- The patient confirms that: 
  - They will use a condom during intercourse with a woman of childbearing potential 
  - Their female partner is using an effective method of pregnancy prevention
  - Their female partner is of non-childbearing potential
  - They are committed to complete and absolute abstinence

Prescriber Confirmation
I have fully explained to the patient named above the nature, purpose and risks of the treatment associated with Thalidomide Celgene®, especially the risks to women of childbearing potential.

- Prescriber First Name: 
- Prescriber Last Name: 
- Prescriber Signature: 
- Date: DD MM YYYY

Patient: please read thoroughly and initial the adjacent box if you agree with the statement

- I understand that severe birth defects can occur following exposure to Thalidomide Celgene®. I have been warned by my doctor that any unborn baby has a high risk of birth defects and could even die if a woman becomes pregnant following exposure to Thalidomide Celgene® or is exposed to Thalidomide Celgene® whilst pregnant.

- I have been told by my doctor that I must NEVER have unprotected sexual contact with women who are pregnant, or may become pregnant, while I am taking Thalidomide Celgene® and for 1 week after stopping treatment.

- I know that I must inform my doctor if I think that my sexual partner may be pregnant.

- I understand that Thalidomide Celgene® will be prescribed ONLY for me. I must not share it with ANYONE.

- I have read the Thalidomide Celgene® Patient Information and understand the contents, including the information about other possible health problems (side effects) from thalidomide.

- I understand that I cannot donate blood or semen while taking Thalidomide Celgene®, or for 1 week after stopping treatment.

- I understand that I must return any unused Thalidomide Celgene® to my pharmacy at the end of my treatment.

Patient Confirmation
I confirm that I understand and will comply with the requirements of the Thalidomide Celgene® Pregnancy Prevention Programme, and I agree that my doctor can initiate my treatment with Thalidomide Celgene®.

- Patient Signature: 
- Date: DD MM YYYY
Prescription Tools
Contains prescription authorisation forms to document that safety measures have been performed prior to prescribing Thalidomide Celgene®. Also contains patient health cards that your patients may present to other healthcare professionals to inform them about core information regarding their Thalidomide Celgene® treatment.
A guide to completing the Thalidomide Celgene® Prescription Authorisation Form (PAF) - UK

This guide will help you complete the Thalidomide Celgene Prescription Authorisation Form. The form is used within the Pregnancy Prevention Programme, and must be completed each time you prescribe Thalidomide Celgene.

Instructions for prescribers
1. Enter the patient’s name
2. Enter the hospital number and date of birth
3. Print your name
4. Provide the diagnosis – this is important for providing anonymous feedback to the MHRA, in the interests of patient safety
5. For males and women of childbearing potential, complete the appropriate section to indicate that counselling and appropriate pregnancy prevention has occurred.
6. For women of childbearing potential you must provide a valid negative pregnancy test date (within 3 days prior to prescribing). If this is not the case Thalidomide Celgene must not be dispensed.
7. You must sign, date and print your name to declare that all steps have been observed and you authorise the prescription.

Instructions for pharmacists
A. Check that all relevant sections of the form have been completed by the prescriber
   a. Counselling and pregnancy prevention measures must be in place
   b. The prescription and prescriber signature dates must be the same
   c. Thalidomide Celgene can only be dispensed within 7 days of the prescription date
   d. Only one month’s supply for women of childbearing potential, or three month’s supply for all other patients, of Thalidomide Celgene can be dispensed at any one time, without prior agreement from Celgene
B. Sign and date your declaration.
Thalidomide Celgene® Pregnancy Prevention Programme
Prescription Authorisation Form - UK

A newly completed copy of this form MUST accompany every Thalidomide Celgene® prescription. Completion of this form is mandatory for ALL patients and the completed form should be retained in pharmacy for 2 years as it will be required for review during a Thalidomide Celgene® Pregnancy Prevention Programme audit.

Patient Name: 
Hospital Number: 
Date of Birth: DD MM YYYY
Prescriber Name: 
Diagnosis: 

Please tick in the box next to the appropriate patient category, and enter the additional information requested for male and women of childbearing potential patients.

☐ Woman of non-childbearing potential
☐ Male

The patient has been counselled about the teratogenic risk of treatment with Thalidomide Celgene® and understands the need to use a condom if involved in sexual activity with a woman of childbearing potential who is not using an effective method of pregnancy prevention? Y N

Note to Pharmacist: do not dispense unless ‘Y’

☐ Woman of childbearing potential

The patient has been counselled about the teratogenic risk of treatment with Thalidomide Celgene®, the need to avoid pregnancy and has been using an effective method of pregnancy prevention for at least 4 weeks? Y N

Note to Pharmacist: do not dispense unless ‘Y’

Date of last negative pregnancy test: DD MM YYYY

Note to Pharmacist: Do not dispense unless a negative pregnancy test has been conducted within 3 days prior of the prescription date

Prescriber Confirmation
I have read and understood the Thalidomide Celgene® Healthcare Professional’s Information Pack, and confirm that the patient has signed a Treatment Initiation Form.

Prescriber First Name: 
Prescriber Last Name: 
Signature: Date: DD MM YYYY

Note to pharmacist: the date of the prescription must match the date on this prescription authorisation form.

Pharmacy Confirmation
I am satisfied that the Thalidomide Celgene® prescription authorisation form has been completed fully, confirm that dispensing is taking place within 7 days of the prescription date and that I have read and understood the Thalidomide Celgene® Healthcare Professional’s Information Pack

Pharmacist First Name: 
Pharmacist Last Name: 
Signature: Date: DD MM YYYY

Note to Pharmacist: do not dispense unless ‘Y’
You are taking Thalidomide Celgene®. You must contact your hospital doctor urgently if you develop any of the following:

- Severe skin reactions including rashes, which is a common side effect and blistering of the skin or inside of your mouth (Stevens Johnson Syndrome and toxic epidermal necrolysis, which are rare side effects). You may have a high temperature (fever) at the same time.
- Chest pain or difficulty breathing
- Pain or swelling in your arms or legs.

You must contact your doctor urgently if you suspect that you or your partner may be pregnant.

Further information for patients, carers, and healthcare professionals on Thalidomide Celgene®, its side effects, and pregnancy prevention, can be found at www.celgene.co.uk

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Emergency Contact Phone Numbers

Office hours:

Out of hours:

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Thalidomide Celgene® Information for Patients

You are taking Thalidomide Celgene®. You must contact your hospital doctor urgently if you develop any of the following:

- Severe skin reactions including rashes, which is a common side effect and blistering of the skin or inside of your mouth (Stevens Johnson Syndrome and toxic epidermal necrolysis, which are rare side effects). You may have a high temperature (fever) at the same time.
- Chest pain or difficulty breathing
- Pain or swelling in your arms or legs.

You must contact your doctor urgently if you suspect that you or your partner may be pregnant.
Information for Patients and Healthcare Professionals

Thalidomide Celgene® causes birth defects and death to the unborn child, therefore:

- Female patients of childbearing potential must always use adequate contraception
- Female patients of childbearing potential must have monthly pregnancy tests, prior to each prescription, to ensure that they are not pregnant
- Male patients with female partners of childbearing potential who are not using adequate contraception must always use a condom
- If a female patient, or female partner of a male patient, suspects they are pregnant they must contact their doctor immediately.

Information for Healthcare Professionals

This patient is receiving Thalidomide Celgene®, and is at risk of:

- Deep venous thrombosis and pulmonary embolus
- Peripheral neuropathy
- Syncope and bradycardia
- Skin reactions.
Adverse Events and Pregnancy Reporting Forms
Complete these forms if your patient experiences an adverse event or becomes pregnant while being treated with Thalidomide Celgene®, and send the information to the Celgene Drug Safety department.
**History and Start of Pregnancy**

This form must be returned to Celgene:

Celgene Limited · 1 Longwalk Road · Stockley Park · Uxbridge · UB11 1DB · United Kingdom

Phone: 0808 238 9908 · Fax: 0844 801 0468 · Email: drugsafetyuk@celgene.com

---

**Reporter**

- **Name:**
- **Address:**
- **Country:**
- **Phone:**
- **Fax:**
- **Email:**
- **Physician (Specialty):**
- **Nurse**
- **Pharmacist**
- **Other healthcare professional:**

**Female Patient Data**

- **Initials:**
- **Date of Birth:**
- **Age:**

---

**Type of Exposure**

- **Female patient:**
  - [ ] Yes
  - [ ] No
- **Female partner of male patient:**
  - [ ] Yes
  - [ ] No
- **Other:**

---

**Pregnancy Information**

- **Pregnancy tests:** dates and results of the three latest pregnancy tests including the test with confirmation of pregnancy:
  - N1: DD/MM/YYYY results: ____________
  - N2: DD/MM/YYYY results: ____________
  - N3: DD/MM/YYYY results: ____________
- **Date of last menstrual period:** DD/MM/YYYY
- **Start date of pregnancy:** DD/MM/YYYY
- **Echography:** date: DD/MM/YYYY
  - **Echographic age:** DD/MM/YYYY
  - **Results:**

---

**Monitoring of the Thalidomide Celgene® Pregnancy Prevention Program (PPP)**

**Childbearing Potential Category attributed to patient/partner at the beginning of treatment:**

- **With No Childbearing Potential**
  - [ ] please specify:
    - [ ] Age ≥ 50 years and naturally amenorrhoeic for ≥ 1 year
    - [ ] Premature ovarian failure confirmed by a specialist gynaecologist
    - [ ] XY genotype, Turner syndrome, uterine agenesis
    - [ ] Infertility in male (specify):
    - [ ] Other reasons (specify):

- **With Childbearing Potential**
  - [ ] please specify:

---

**Pregnancy testing:**

- performed before the start of therapy? 
  - [ ] Yes
  - [ ] No
- performed every 4 weeks during treatment?
  - [ ] Yes
  - [ ] No

**Contraception Use:**

- [ ] No contraception

- **Hormonal contraception:**
  - [ ] combined oral contraceptive pills (brand names to be specified):
  - [ ] progesterone only pills (brand name to be specified):
  - [ ] subcutaneous implants (brand name to be specified):
  - [ ] others (to be specified and brand name to be specified):

- [ ] Intratuterine device (IUD) (type to be specified):

---

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**Thalidomide Celgene® Pregnancy Exposure Form**

**History and Start of Pregnancy**

This form must be returned to Celgene: Celgene Limited · 1 Longwalk Road · Stockley Park · Uxbridge · UB11 1DB · United Kingdom

Phone: 0808 238 9908 · Fax: 0844 801 0468 · Email: drugsafetyuk@celgene.com

- Sterilisation:
  - male (type to be specified e.g. vasectomy):
  - female (type to be specified e.g. tubal ligation):

- Local contraception (type to be specified):

- Withdrawal method

- Other (specify):

**Reason for contraception failure:**

- Contraception missed

- Non recommended contraceptive method (e.g.: barrier methods, type to be specified):

If no contraception has been implemented specify the reason (e.g. abstinence):

---

**EDUCATIONAL MATERIAL**

Please specify if the patient:

- has been informed about the teratogenic risk of Thalidomide Celgene treatment
- has received the Patient Booklet
- has been informed about the need to follow the PPP measures

**ACTION TAKEN REGARDING PREGNANCY**

Has the pregnant patient or the pregnant partner of the patient been referred to a gynaecologist?  

<table>
<thead>
<tr>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
</table>

If yes, specify his/her name and contact details (address, phone number):

---

**Additional Information**

**Medical history:** Current or past relevant medical history (incl. concurrent illness, allergy, smoking, alcohol abuse):

<table>
<thead>
<tr>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
</table>

If yes please specify:

**Relevant obstetrical history:**

<table>
<thead>
<tr>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
</table>

If yes please specify:

**Thalidomide Celgene® Dosing Details**

**Indication for Thalidomide Use:**

Discontinued:  

<table>
<thead>
<tr>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
</table>

**Therapy start date:** (Day / Month / Year)

<p>| | |</p>
<table>
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</thead>
</table>

**Therapy stop date:** (Day / Month / Year)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
</table>

**Daily dose:**

<table>
<thead>
<tr>
<th>Type</th>
<th>mg</th>
</tr>
</thead>
</table>

**Batch No.**

200 mg  100 mg  Other: mg

**Concomitant Medication(s)**

<table>
<thead>
<tr>
<th>Generic Drug Name / Route</th>
<th>Dose &amp; frequency</th>
<th>Therapy start date: (Day / Month / Year)</th>
<th>Therapy stop date: (Day / Month / Year)</th>
<th>Indication for use of drug</th>
</tr>
</thead>
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</tr>
</tbody>
</table>

**Notification**

**Name:**

**Title:**

**Date:** DD MM YYYY

**Signature:**

---
Thalidomide Celgene®
Pregnancy Exposure Form
Outcome of Pregnancy

This form must be returned to Celgene: Celgene Limited · 1 Longwalk Road · Stockley Park · Uxbridge · UB11 1DB · United Kingdom
Phone: 0808 238 9908 · Fax: 0844 801 0468 · Email: drugsafetyuk@celgene.com

□ Initial report  □ Follow-up report  □ Final report  Date: DD MM YYYY

Reporter
Name:
Address:
Country: Phone:
Fax:
Physician (Specialty ____________)  Nurse  Pharmacist  Other healthcare professional: ____________

Female Patient Data
Initials: Date of Birth: DD MM YYYY Age:

Type of Exposure
Female patient: □ Yes □ No  Female partner of male patient: □ Yes □ No  Exposure of a pregnant female - not patient or partner: □ Yes □ No
Other: ________________________________

Outcome of Pregnancy
Is the newborn alive: □ No □ Yes
If no, please specify: __________________

Spontaneous abortion: □ No □ Yes Date: DD/MM/YYYY Term: _____ WA Histopathology: □ No □ Yes
Malformation: □ No □ Yes Details: __________________

Elective abortion: □ No □ Yes Date: DD/MM/YYYY Term: _____ WA Histopathology: □ No □ Yes
Malformation: □ No □ Yes Details: __________________
Reason for abortion (i.e. personal, medical, malformation diagnosis in foetus…): __________________

In utero death: □ No □ Yes Date: DD/MM/YYYY Term: _____ WA Histopathology: □ No □ Yes
Malformation: □ No □ Yes Details: __________________
Possible explanation (specify): __________________

Ectopic pregnancy: □ No □ Yes

Delivery (to be completed only if the newborn is alive)
Date: DD/MM/YYYY Term: _____ WA
Mode of Delivery: □ Normal  □ Induced  □ Caesarean
Foetal distress: □ No □ Yes  □ Chronic  □ Acute
Normal placenta: □ No □ Yes  □ Unknown
Comments:

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Thalidomide Celgene®
Pregnancy Exposure Form
Outcome of Pregnancy

This form must be returned to Celgene: Celgene Limited · 1 Longwalk Road · Stockley Park · Uxbridge · UB11 1DB · United Kingdom
Phone: 0808 238 9908 · Fax: 0844 801 0468 · Email: drugsafetyuk@celgene.com

New Born Condition

Sex: □ F □ M
Weight (g): __________  Height (cm): __________  H.C: __________
Premature: □ No □ Yes  Dysmature: □ No □ Yes  Apgar: __________  1 min __________  5 min __________
Malformation: □ No □ Yes
Neonatal pathology: □ No □ Yes  Specify:
Immediate outcome: Specify:
Breast-feeding: □ F □ M

Additional Information

Course of Pregnancy

Exposure(s): □ Tobacco ________ cig/day □ Alcohol ________ amount/day □ Drug addiction
Specify: ____________________________ Other: ____________________________
Illness(es) during pregnancy: □ High blood pressure □ Diabetes □ Infection
Specify: ____________________________ Other: ____________________________
Hospitalisation during pregnancy: □ No □ Yes  Reason(s): ____________________________
Antenatal diagnosis: □ No □ Yes
Echography: dates and results: ____________________________ Please enclose the results of the echography
Other specific tests – results: ____________________________
Retarded growth in utero: □ No □ Yes

Thalidomide Celgene® Dosing Details

Indication for Thalidomide Use: ____________________________

<table>
<thead>
<tr>
<th>Therapy start date: (Day / Month / Year)</th>
<th>Therapy stop date: (Day / Month / Year)</th>
<th>Daily dose:</th>
<th>Batch No.</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>/<strong>/</strong></em></td>
<td><em>/<strong>/</strong></em></td>
<td>□ 200 mg</td>
<td>□ Other: _______ mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>□ 100 mg</td>
<td></td>
</tr>
</tbody>
</table>

Medication(s) Taken During Pregnancy

<table>
<thead>
<tr>
<th>Generic Drug Name / Route</th>
<th>Dose &amp; frequency</th>
<th>Therapy start date: (Day / Month / Year)</th>
<th>Therapy stop date: (Day / Month / Year)</th>
<th>Indication for use of drug</th>
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<tr>
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<td><em>/<strong>/</strong></em></td>
<td><em>/<strong>/</strong></em></td>
<td><em>/<strong>/</strong></em></td>
</tr>
</tbody>
</table>

Notification

<table>
<thead>
<tr>
<th>Name:</th>
<th>Title:</th>
<th>Date: DD MM YYYY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Signature:</td>
</tr>
</tbody>
</table>
### CLINICAL SIGNS

1) **Extreme sensitivity** (diapason)
   - Lower limbs
     - Dorsiflexion of big toe (inter-phalangeal articulation)
     - Extensor hallucis longus
     - Dorsiflexion of foot (tibialis anterior)
     - Walking on heels
     - Step-on tips of toes
     - Proximal muscle strength (stool sign)
   - Upper limbs
     - Dorsal face of the 3rd metacarpophalangeal articulation
     - Radial styloid

2) **Superficial sensitivity**
   - Touch (the examiner touches the patient's limb with cotton wool, progressing from the distal to the proximal part of the limb)
   - Pin prick (the examiner pricks the skin with a needle, progressing from the distal to the proximal part of the limb)

   If an abnormality is detected, indicate the level of the sensory deficit:
   - Lower limbs
     - __________ __________ __________
   - Upper limbs
     - __________ __________ __________

3) **Muscle strength** (lower limbs)
   - Extensor hallucis longus
   - Dorsiflexion of foot (tibialis anterior)
   - Walking on heels
   - Step-on tips of toes
   - Proximal muscle strength (stool sign)

4) **Achilles reflexes** (patient kneeling on a chair with the sole of the foot lightly on the examiner's hand)
   - Dorsiflexion of big toe (inter-phalangeal articulation)

### Notification

<table>
<thead>
<tr>
<th>Name:</th>
<th>Title:</th>
<th>Signature:</th>
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<tbody>
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</table>

<table>
<thead>
<tr>
<th>Date:</th>
<th>DD-MM-YYYY</th>
</tr>
</thead>
</table>
**Indication for use of drug**

**History of prior neurological disturbance(s) prior to thalidomide therapy?**

- Yes
- No
- Not applicable
- Unknown

Did the neuropathy abate or improve after thalidomide was stopped or dose was reduced?

- Yes
- No
- Not applicable
- Unknown

Did neuropathy reappear after thalidomide was reintroduced?

- Yes
- No
- Not applicable
- Unknown

If neuropathy improved/resolved after any change in thalidomide treatment, specify new NCI CTCAE Grade:

- Grade 1
- Grade 2
- Grade 3
- Grade 4

Reasonable possibility neuropathy is related to thalidomide?

- Yes
- No

**Other alternative explanation of event:**

**MEDICAL HISTORY:** Please list all relevant medical history:

- History of prior neurological disturbance(s) prior to thalidomide therapy?
- Date of onset of prior neurological disturbance:
- Consumption of alcohol?

**Prior Exposure to Neurotoxic Drugs**

- Neurotoxic Drug
- Therapy start date:
- Therapy stop date:
- Therapy duration:

**Electrophysiological Examination**

- Electrophysiological examination before treatment:
- Electrophysiological examination during treatment:

**Clinical Examination**

- Time to onset/worsening of neuropathy after the start of thalidomide:
- Date of clinical examination:

**SUBJECTIVE SIGNS**

- Tingling of the extremities
- Burning sensation
- Restless legs

**Other Risk Factors for Neuropathy**

- History of amyloidosis:
- Diabetes:
- Renal failure:
- Dysglobulinemia:

**Other Concomitant Medication(s)**

- Includes medication(s) received during the past 3 months prior to the event

**Other Risk factors for neuropathy, specify:**

**Thalidomide Celgene® Adverse Event Report Form**

**Peripheral Neuropathy**

This form must be returned to Celgene:

- Celgene Limited · 1 Longwalk Road · Stockley Park · Uxbridge · UB11 1DB · United Kingdom
- Phone: 0808 238 9908 · Fax: 0844 801 0468 · Email: drugsafetyuk@celgene.com
Thalidomide Celgene®

ADVERSE EVENT REPORT FORM

This form must be returned to Celgene: Celgene Limited · 1 Longwalk Road · Stockley Park · Uxbridge · UB11 1DB · United Kingdom
Phone: 0808 238 9908 · Fax: 0844 801 0468 · Email: drugsafetyuk@celgene.com

CASE NO: ____________________

For company use only

Date of receipt: _______ / _______ / _______

Received by: _____________________________
(Name and organization – eg CRO, or company representative)

For Clinical Trials Enter:

Trial ID: ____________________________
Site Number: ____________________________ Patient Number: ____________________________

Reporter

Name: ____________________________
Job Title: ____________________________
Address: ____________________________
Country: ____________________________
Email: ____________________________
Fax: ____________________________
Phone: ____________________________

Patient Data

Initials: ____________________________
Weight (kg): ____________________________
Height (cm): ____________________________
Date of Birth: _______ / _______ / _______
Gender: □ Male □ Female Age: _______

Adverse Event

Overall diagnosis of the event: ____________________________

Description of Adverse Event – symptoms and treatment:

Event onset date: _______ / _______ / _______
Event stop date: _______ / _______ / _______

☐ or ongoing at the time of reporting
Duration (if < 24 hours) _______ Hours _______ Minutes _______

Outcome of adverse event:

☐ Recovered ☐ Recovered with sequelae ☐ Not recovered

☐ Unknown

Date of death: _______ / _______ / _______

Possible cause of death:

If autopsy is performed please forward report

Please attach relevant clinical laboratory assessments to confirm the event

Seriousness of the Event

(tick all that apply)

☐ Death ☐ Life-threatening ☐ Hospitalisation or prolonged hospitalisation

☐ Persistent or significant disability or incapacity event
☐ Congenital anomaly/birth defect ☐ Other medically important condition or
# Thalidomide Celgene®
## ADVERSE EVENT REPORT FORM

This form must be returned to Celgene: Celgene Limited • 1 Longwalk Road • Stockley Park • Uxbridge • UB11 1DB • United Kingdom
Phone: 0808 238 9908 • Fax: 0844 801 0468 • Email: drugsafetyuk@celgene.com

### Medical History

(May be supplied as a copy of Medical file if up to date)

Current or past relevant medical history (incl. concurrent illness, allergy, smoking, alcohol abuse)

- [ ] Yes
- [ ] No

If yes please specify:

### Suspect drug

<table>
<thead>
<tr>
<th>Drug, Dosage-form, Strength, Route (eg. Tab 5mg, oral)</th>
<th>Dose &amp; frequency</th>
<th>Batch No.</th>
<th>Therapy start date: (Day / Month / Year)</th>
<th>Therapy stop date: (Day / Month / Year)</th>
<th>Causal relationship</th>
<th>Indication for use of drug</th>
</tr>
</thead>
<tbody>
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</tbody>
</table>

### Other Medication

Medication taken during the past 3 months prior to the event

<table>
<thead>
<tr>
<th>Drug, Dosage-form, Strength, Route (eg. Tab 5mg, oral)</th>
<th>Dose &amp; frequency</th>
<th>Therapy start date: (Day / Month / Year)</th>
<th>Therapy stop date: (Day / Month / Year)</th>
<th>Causal relationship</th>
<th>Indication for use of drug</th>
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</thead>
<tbody>
<tr>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

### Action Taken, Suspect Drug

- [ ] Continued unchanged
- [ ] Continued, dose or dose regimen changed, specify:

  
- [ ] Withdrawn
- [ ] Not applicable

### Notification

- [ ] Initial report
- [ ] Final report
- [ ] Follow-up report

<table>
<thead>
<tr>
<th>Name:</th>
<th>Title:</th>
<th>Signature:</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>
Treatment checklists and algorithms
New Patient Evaluation

Male

Childbearing potential partner?

Yes or unknown

No

Yes to any

No to all

Female

Is patient ≥50 years and naturally amenorrhoeic for ≥1 year?

Amenorrhoea following cancer therapy does not rule out childbearing potential

Do they have:

Premature ovarian failure confirmed by a specialist gynaecologist?

Previous bilateral salpingo-oophorectomy, or hysterectomy?

XY genotype, Turner’s syndrome, uterine agenesis?

Has patient used one of the following pregnancy prevention methods for the last 4 weeks, or committed to complete and continuous abstinence?

Subcutaneous hormonal implant, Levonorgestrel-releasing intrauterine system, Medroxyprogesterone acetate depot, Tubal sterilisation, Sexual intercourse with a vasectomised male partner only, Ovulation inhibitory progesterone-only pills* (i.e. desogestrel)

* combined oral contraceptive pills are not recommended, patients using this method should switch to alternate method

No or unknown

Yes

Perform a pregnancy test 4 weeks after the patient has used a pregnancy prevention method, or if they are abstaining from sexual intercourse

Negative

Positive

START THALIDOMIDE CELGENE® TREATMENT

Must use a condom during sexual intercourse during treatment and for one week after treatment cessation

START THALIDOMIDE CELGENE® TREATMENT

Patient must use one effective pregnancy prevention method during treatment, even in case of dose interruptions and for at least 4 weeks after cessation, unless they commit to complete and continuous abstinence. Repeat pregnancy tests every 4 weeks, even if patient is abstaining from sexual intercourse

DO NOT START TREATMENT

Refer patient to a physician specialised or experienced in teratology for evaluation and advice

DO NOT START TREATMENT

Patient must use an effective pregnancy prevention method for at least 4 weeks prior to starting treatment

Warning:

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 who could become pregnant. The conditions of the Thalidomide Celgene® Pregnancy Prevention Programme must be fulfilled for all male and female patients.

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UK-THA130005
## Combined checklist for commencing Thalidomide Celgene® treatment

### Counselling

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Women CBP</th>
<th>Women NCBP</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inform of expected teratogenic risk to the unborn child</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inform of the need for effective contraception at least 4 weeks before starting treatment, during treatment interruption, throughout the entire duration of treatment and for at least 4 weeks after the end of treatment or absolute and continued abstinence</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Inform that even if patient has amenorrhoea they must comply with advice on contraception</td>
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<tr>
<td>Inform of the requirement to discuss with the physicians prescribing Thalidomide Celgene and the pregnancy prevention method if the patient needs to change or stop their method of pregnancy prevention</td>
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<tr>
<td>Confirm patient is capable of complying with contraceptive measures</td>
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<tr>
<td>Inform of the potential consequences of pregnancy and the need to stop treatment and consult rapidly if there is a risk of pregnancy</td>
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<tr>
<td>Confirm patient agrees to undergo pregnancy testing at 4 weekly intervals</td>
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<tr>
<td>Inform of hazards and necessary precautions associated with use of Thalidomide Celgene</td>
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<tr>
<td>Inform patient not to share medication</td>
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<tr>
<td>Inform to return unused capsules to pharmacist</td>
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<tr>
<td>Inform not to donate blood whilst taking Thalidomide Celgene or for 1 week after stopping</td>
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<tr>
<td>Inform not to donate semen whilst taking Thalidomide Celgene or for 1 week after stopping</td>
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<tr>
<td>Inform of need to use condoms throughout treatment duration, during dose interruption, and for one week after cessation of treatment if partner is of childbearing potential</td>
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</tr>
<tr>
<td>Inform of requirement to provide a copy of the Treatment Initiation Form (TIF) to the pharmacy prior to the dispensing of the first prescription</td>
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</tr>
</tbody>
</table>

### Contraceptive referral

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Women CBP</th>
<th>Women NCBP</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contraceptive referral required</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contraceptive referral made</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contraceptive consultation completed</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

### Contraception

**Patient is currently established on one of the following for at least 4 weeks**

<table>
<thead>
<tr>
<th>Method</th>
<th>Women CBP</th>
<th>Women NCBP</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levonorgestrel-releasing intrauterine system (IUS)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Medroxyprogesterone acetate depot</td>
<td></td>
<td></td>
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<tr>
<td>Sterilisation</td>
<td></td>
<td></td>
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<tr>
<td>Sexual intercourse with a vasectomised male partner only: vasectomy must be confirmed by negative semen analysis</td>
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<tr>
<td>Ovulation inhibitory progesterone-only pill (desogestrel)</td>
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<td></td>
</tr>
<tr>
<td>Patient commits to complete and absolute abstinence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative pregnancy test before starting treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Not of childbearing potential

**One of the following criteria have been met to determine patient is women NCBP**

| Criterion                                                      | Women CBP | Women NCBP | Male |
|                                                               |           |            |      |
| Age ≥50 years and naturally amenorrhoeic for ≥1 year not induced by chemotherapy |           |            |      |
| Premature ovarian failure confirmed by specialist gynaecologist |           |            |      |
| Bilateral salpingo-oophorectomy                              |           |            |      |
| XY genotype, Turner’s syndrome, uterine agenesis              |           |            |      |
Pharmacy registration and dispensing of Thalidomide Celgene®

Patient presents at pharmacy, pharmacist:
- Cross-checks Prescription Authorisation Form
- Signs Prescription Authorisation Form
- Dispenses Thalidomide Celgene® to patient
- Retains Prescription Authorisation Form in pharmacy for at least 2 years

Counsel patient:
- Pregnancy prevention
- Complete Treatment Initiation Form
- Complete Prescription Authorisation Form
- Provide patient educational materials

Pharmacist

1. Identify patient for Thalidomide Celgene®, obtain Healthcare Professional’s Information Pack from Celgene

2. Read Pack, fax Pharmacy Registration Form to Celgene

Distributor

Celgene update registered list with distributors

Physician

3. Read Pack

4. Order Thalidomide Celgene®
Frequently asked questions
Where can I get further copies of the Thalidomide Celgene® Healthcare Professional’s Information Pack or the patient materials?

The CD provided with the Thalidomide Celgene® Healthcare Professional’s Information Pack contains electronic versions of all the materials and may be used to print out further copies. The materials can also be downloaded from the Celgene website (www.celgene.co.uk).

If you would like further copies of the Thalidomide Celgene® Healthcare Professional’s Information Pack or any other materials for healthcare professionals or patients, please telephone or e-mail Celgene using the contact details below, or by speaking to any Celgene representative.

Tel: 0808 156 3059  
Fax: 0808 156 3058  
Email: rmp.uk.ire@celgene.com  
Web: www.celgene.co.uk

What must I do prior to ordering or dispensing Thalidomide Celgene®?

All pharmacies must register with Celgene prior to ordering or dispensing Thalidomide Celgene®. You will need to register the dispensing pharmacy using the Pharmacy Registration Form. This form is contained within this pack. Completed Pharmacy Registration Forms should be faxed to Celgene (Fax: 0808 156 3058). Once you have returned a completed Pharmacy Registration Form, we will inform the distributors who will place you on the registered list.

Do I need a registration number to order Thalidomide Celgene®?

No, you just need to register with Celgene by returning the Pharmacy Registration Form. We will register you and inform the distributor that you are registered and can receive Thalidomide Celgene®.

Where do I order Thalidomide Celgene®?

Once registered, to order Thalidomide Celgene® please contact Celgene in the UK and Northern Ireland. You must have returned the Pharmacy Registration Form to Celgene before you can place an order. You will need to fax or email your order to the distributors (all orders must be received in writing).

Distributor: Celgene Order Contact Centre (UK and Northern Ireland)  
Tel: 0208 831 8483  
Fax: 0208 831 8792  
Email: orders-uk@celgene.com

Orders placed Mondays – Fridays before 13.30 will generally be delivered the following working day.
How should I report an adverse event?

Adverse events should be reported to Celgene Drug Safety. Adverse event reporting forms are included in this Healthcare Professional’s Information Pack. Completed forms should be forwarded to the Celgene Drug Safety using the contact details below:

Tel: 0808 238 9908
Fax: 0844 801 0468
Email: drugsafetyuk@celgene.com

You may also report any adverse events to the MHRA using a ‘Yellow Card’. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.

What are the contact details for Celgene Medical Information?

To contact Celgene in the UK for medical information, please telephone or Email the Medical Information department using the contact details below:

Tel: 0844 801 0045
Fax: 0844 801 0046
Email: medinfo.uk.ire@celgene.com

How will Celgene audit pharmacies registered for the Thalidomide Celgene® Pregnancy Prevention Programme?

The terms of the Thalidomide Celgene® Marketing Authorisation include a mandatory requirement for annual feedback to be collected on the effectiveness of the Pregnancy Prevention Programme, at a national level. An agreement to assist with this process was a pre-condition for Celgene approving the registration of pharmacies and thereby granting authorisation to procure Thalidomide Celgene®.

Celgene have agreed with the Medicines and Healthcare Products Regulatory Agency (MHRA) that pharmacies can fulfill their obligations in this respect, by conducting a manual self-audit and reporting the results to Celgene. This information will be provided, in an anonymised and aggregated format, to the MHRA and the European Medicines Agency (EMEA). Celgene will supply pharmacies with an audit pack, such that annual self-auditing of pharmacies and feedback of the audit results to Celgene can occur.

It is therefore critical for pharmacies to ensure that all documentation associated with the Pregnancy Prevention Programme is completed accurately and that audit results are provided faithfully and diligently, in the interests of patient safety.
Contact details

Risk Management:
For information and questions on the risk management of Celgene’s products,
the Pregnancy Prevention Programme and pharmacy registrations.
Tel: 0808 156 3059
Fax: 0808 156 3058
Email: rmp.uk.ire@celgene.com

Drug Safety:
To report any adverse events to Celgene.
Tel: 0808 238 9908
Fax: 0844 801 0468
Email: drugsafetyuk@celgene.com
Adverse events can also be reported to the MHRA using a ‘Yellow Card’ –
reporting forms and information can be found at www.mhra.gov.uk/yellowcard.

Medical Information:
To obtain Medical Information on Celgene’s products.
Tel: 0844 801 0045
Fax: 0844 801 0046
Email: medinfo.uk.ire@celgene.com

Website:
Reference safety information (including the summary of product characteristics)
and educational materials for all of Celgene’s products are available from our
website - www.celgene.co.uk

Distributor:
For product delivery enquiries.

In Great Britain and Northern Ireland
Tel: 0208 831 8483
Fax: 0208 831 8792
Email: orders-uk@celgene.com