

Prescriber Guide to

((THALOMID REMS[®] logo))

Risk Evaluation and Mitigation Strategy (REMS) Program

A known teratogen, THALOMID[®] (thalidomide) is approved for marketing only under a restricted distribution program approved by the Food and Drug Administration. This program is called the THALOMID Risk Evaluation and Mitigation Strategy (REMS) program (formerly known as the *S.T.E.P.S.*[®] program).

This guide contains important information for prescribers about:

- The risks of THALOMID, including a boxed warning for
 - Embryo-fetal toxicity
 - Venous thromboembolism (deep venous thrombosis [DVT] and pulmonary embolism [PE])
- The THALOMID REMS[®] program
 - Prescriber Certification
 - Patient Enrollment
 - Contraceptive Requirements and Counseling for Patients
 - Initial and Subsequent Prescription Requirements

THALOMID REMS[®] Resources for Prescribers Include:

- Prescriber Guide to THALOMID REMS[®] Program
- CD-ROM, including Patient-Physician Agreement Form and Patient Prescription Form Software and Installation Instructions
- Full Prescribing Information for THALOMID

((THALOMID logo))

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About THALOMID® (thalidomide)

THALOMID in combination with dexamethasone is indicated for the treatment of patients with newly diagnosed multiple myeloma (MM).

THALOMID is indicated for the acute treatment of the cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL).

THALOMID is not indicated as monotherapy for such ENL treatment in the presence of moderate to severe neuritis.

THALOMID is also indicated as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence.

Risks of THALOMID

THALOMID has a Boxed Warning for embryo-fetal toxicity and venous thromboembolism (deep venous thrombosis [DVT] and pulmonary embolism [PE]).

A known teratogen, THALOMID is contraindicated in pregnant females or females capable of becoming pregnant. Females of reproductive potential may be treated with THALOMID if they take adequate precautions to avoid pregnancy.

The use of THALOMID in MM results in an increased risk of venous thromboembolism, such as deep venous thrombosis and pulmonary embolism. This risk increases significantly when THALOMID is used in combination with standard chemotherapeutic agents including dexamethasone. Patients and physicians should be observant for the signs and symptoms of thromboembolism. Instruct patients to seek medical care if they develop symptoms such as shortness of breath, chest pain, or arm or leg swelling. Consider thromboprophylaxis based on an assessment of individual patients' underlying risk factors.

The THALOMID REMS[®] program

To avoid embryo-fetal exposure, THALOMID[®] (thalidomide) is only available under a restricted distribution program called “THALOMID Risk Evaluation and Mitigation Strategy (REMS).” Only certified prescribers can prescribe THALOMID and only certified pharmacies can dispense THALOMID in the THALOMID REMS[®] program.

In order to receive THALOMID, all patients must be enrolled in THALOMID REMS[®] and agree to comply with the requirements of the THALOMID REMS[®] program. Information about THALOMID and the THALOMID REMS[®] program can be obtained by visiting www.CelgeneRiskManagement.com, accessing the Celgene REMS mobile app, or calling the Celgene Customer Care Center toll-free at **1-888-423-5436**.

Key points of the THALOMID REMS[®] program

Prescriber

- The prescriber enrolls and becomes certified with Celgene for the THALOMID REMS[®] program
- The prescriber counsels patient on benefits and risks of THALOMID
- The prescriber provides contraception and emergency contraception counseling
- The prescriber verifies negative pregnancy test for all female patients of reproductive potential
- The prescriber completes a THALOMID[®] (thalidomide) Patient-Physician Agreement Form with each patient and sends to Celgene
- The prescriber/patient completes applicable mandatory confidential survey
- The prescriber obtains an authorization number from Celgene and writes it on every prescription, along with the patient risk category
- The prescriber writes no more than a 4-week (28-day) supply, with no automatic refills or telephone prescriptions
- The prescriber sends THALOMID prescription to certified pharmacy

Pharmacy

- The pharmacy certifies with Celgene for THALOMID REMS[®]
- The certified pharmacy must obtain a confirmation number from Celgene before dispensing
- The certified pharmacy dispenses THALOMID to patient along with a Medication Guide

Prescribing THALOMID® (thalidomide) under the THALOMID REMS® program

FEMALES	MALES
<p><u>Patient Counseling</u> Instruct your patients on why and how they and their partners should prevent pregnancy. Also inform them not to share the drug, not to donate blood, and about appropriate contraceptive use. Patient should be instructed not to extensively handle or open THALOMID capsules</p> <p><u>Pregnancy Tests Only in Females of Reproductive Potential</u> Conduct initial pregnancy test within 10-14 days. Confirm the patient is not pregnant with a second pregnancy test within 24 hours prior to writing an initial prescription. During treatment, pregnancy testing should be repeated every 4 weeks if the patient has regular menses or is amenorrheic, or every 2 weeks if the patient has irregular menses</p> <p><u>Enrollment</u> Both you and your patients must understand and agree to comply with the THALOMID REMS® program, including the pregnancy prevention steps. The THALOMID® (thalidomide) Patient-Physician Agreement Form must be signed by both patient and physician and faxed to the Celgene Customer Care Center at 1-888-432-9325 or generated, signed, and submitted electronically at www.CelgeneRiskManagement.com. If enrolling a patient online, the system generates an online prescription that you should complete and print, sign (include the authorization number and risk category), and fax to the certified pharmacy</p> <p><u>Complete Mandatory Confidential Survey</u> Your female patients need to complete a brief survey by phone or online. You will also need to complete a mandatory survey by phone or online, after which you will receive an authorization number. You must complete this survey to obtain a new authorization number every time a THALOMID prescription is written. Female patients of reproductive potential and all female children must complete surveys monthly in order to obtain subsequent prescriptions. Adult female patients not of reproductive potential must complete surveys every 6 months</p>	<p><u>Patient Counseling</u> Instruct your patients on why and how they and their partners should prevent pregnancy. Also inform them not to share the drug, not to donate blood or sperm, and about appropriate contraceptive use. Patients should be instructed not to extensively handle or open THALOMID capsules.</p> <p><u>Enrollment</u> Both you and your patients must understand and agree to comply with the THALOMID REMS® program, including the pregnancy prevention steps. The THALOMID® (thalidomide) Patient-Physician Agreement Form must be signed by both patient and physician and faxed to the Celgene Customer Care Center at 1-888-432-9325 or generated, signed, and submitted electronically at www.CelgeneRiskManagement.com. If enrolling a patient online, the system generates an online prescription that you should complete and print, sign (include the authorization number and risk category), and fax to the certified pharmacy</p> <p><u>Complete Mandatory Confidential Survey</u> Your male patients will need to complete a brief survey by phone or online. You will also need to complete a mandatory survey by phone or online, after which you will receive an authorization number. You must complete this survey to obtain a new authorization number every time a THALOMID prescription is written. The <i>initial survey</i> is <i>not required</i> for male patients, but they must complete surveys monthly for subsequent prescriptions</p>

ALL PATIENTS

Fax Prescription Obtain an authorization number from Celgene and write it on the prescription, along with the patient risk category, and then fax it to a certified pharmacy. The certified pharmacy will contact patients for mandatory counseling and coordinate delivery of THALOMID to them.

THALOMID REMS[®] patient enrollment

- Obtain, review, and complete the THALOMID[®] (thalidomide) Patient-Physician Agreement Form online by visiting www.CelgeneRiskManagement.com, accessing the Celgene REMS mobile app, using the CD-ROM software, or by calling the Celgene Customer Care Center for assistance at **1-888-423-5436**
- Prescribers who do not have access to a computer, or whose computer systems are not compatible with the software, will be provided with THALOMID REMS[®] program materials. For additional assistance, please contact the Celgene Customer Care Center or your Celgene Hematology Oncology Consultant
- Patient, parent/legal guardian, and/or authorized representative must read the THALOMID[®] (thalidomide) Patient-Physician Agreement Form in the language of their choice

Help Ensure Timely Processing of Each Prescription

Fill Out Form as Directed

- Write only in the designated areas on the THALOMID[®] (thalidomide) Patient-Physician Agreement Form
- The box next to each statement must be marked (with an “X”) to indicate understanding
- The form must be completed and signed by both prescriber and patient

Instructions for Female Patients

- For female patients, the prescriber will need to provide information on whether the patient has been in surgical menopause, chemical menopause, or natural menopause for at least 24 months

Instructions for Minors

- If the patient is under 18 years of age, his or her legal guardian must read this material, mark the statement in each block of the form (with an “X”) and agree to ensure compliance by signing and dating the form

Instructions for Incompetent Adult Patients

- For an incompetent adult patient, an authorized representative must sign the THALOMID[®] (thalidomide) Patient-Physician Agreement Form
- An authorized representative is a caretaker authorized under applicable state law to consent to treatment on the incompetent patient’s behalf

THALOMID REMS[®] patient enrollment (continued)

- The authorized representative must read the material, mark the statements, and agree to ensure compliance by signing and dating the form
- If the authorized representative does not have the power of attorney, **a signed and dated letter from the prescriber, on the prescriber's letterhead, must be submitted to the Celgene Customer Care Center, along with the THALOMID[®] (thalidomide) Patient-Physician Agreement Form.** This letter must contain the following: a statement that the incompetent patient lacks the capacity to complete the THALOMID[®] (thalidomide) Patient-Physician Agreement Form, including identification of the medical condition causing the incapacity; the name and address of the authorized representative; the authorized representative's relationship to the patient; and an opinion that the authorized representative accepts responsibility for the patient's compliance with the THALOMID REMS[®] program and is authorized to consent to treatment with THALOMID on behalf of the patient

Send in Completed Forms

- Send the completed THALOMID[®] (thalidomide) Patient-Physician Agreement Form online through **www.CelgeneRiskManagement.com**, the Celgene REMS mobile app, or to the Celgene Customer Care Center by faxing to **1-888-432-9325**
- You will receive confirmation electronically or via fax to your office once the patient is enrolled
- Once the THALOMID[®] (thalidomide) Patient-Physician Agreement Form is received, both female patients and prescriber can take their surveys as required. Male patients do not take initial surveys
- In the event that you do not receive this confirmation within 15 minutes, call the Celgene Customer Care Center

Note: If therapy with THALOMID is discontinued for 12 consecutive months, the patient must enroll again in the THALOMID REMS[®] program. Follow the above procedures to re-enroll the patient.

Prescription requirements

All Patients

- Provide comprehensive counseling on the benefits and risks of therapy with THALOMID® (thalidomide)
- Patients must be counseled on the risks of birth defects, venous thromboembolism, other side effects, and important precautions associated with THALOMID
- Provide counseling not to share THALOMID capsules, and not to donate blood during treatment (including dose interruptions) and for 4 weeks after receiving their last dose of THALOMID, as well as counseling on appropriate contraceptive use, including emergency contraception
- Provide patients with educational materials provided in the THALOMID REMS® Patient Resource Pack
- Patients should be instructed to not extensively handle or open THALOMID capsules and to maintain storage of capsules in blister packs until ingestion
- Instruct patients to return unused THALOMID capsules for disposal to Celgene or to their THALOMID prescriber, or to the pharmacy that dispensed the THALOMID to them

Female Patients

Determine if female patient is of reproductive potential

Two categories:
<ol style="list-style-type: none">Females of Reproductive Potential<ul style="list-style-type: none">• All females who are menstruating, amenorrheic from previous medical treatments, under 50 years of age, and/or perimenopausal, and do not qualify for the females not of reproductive potential categoryFemales Not of Reproductive Potential<ul style="list-style-type: none">• Females who have been in natural menopause for at least 24 consecutive months, or who have had a hysterectomy and/or bilateral oophorectomy, or female children who have not started menstruating

- Females of Reproductive Potential**

- All females who are menstruating, amenorrheic from previous medical treatments, under 50 years of age, and/or perimenopausal, and do not qualify for the females not of reproductive potential category

- Females Not of Reproductive Potential**

- Females who have been in natural menopause for at least 24 consecutive months, or who have had a hysterectomy and/or bilateral oophorectomy, or female children who have not started menstruating

1. Females of Reproductive Potential

Pregnancy test requirements

- Obtain a **negative** pregnancy test 10 to 14 days prior to writing an initial prescription for THALOMID® (thalidomide) and again within 24 hours prior to writing an initial prescription for THALOMID even if continuous abstinence is the chosen method of birth control
 - The pregnancy test must be sensitive to at least 50 mIU/mL
 - Pregnancy testing should occur weekly during the first 4 weeks of use

Prescription requirements (continued)

- Pregnancy testing should be repeated every 4 weeks if patient has regular menses or is amenorrheic, or every 2 weeks if irregular menses
- If a patient misses her period or if there is any abnormality in menstrual bleeding, THALOMID should be discontinued immediately. Obtain a pregnancy test and counsel the patient
- **If pregnancy does occur during treatment, THALOMID must be immediately discontinued.** Any suspected embryo-fetal exposure to THALOMID must be reported immediately to the FDA via the MedWatch number at **1-800-FDA-1088** and also to the Celgene Customer Care Center at **1-888-423-5436**. The patient should be referred to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling
- The patient must not breastfeed a baby while being treated with THALOMID

Patient Counseling on Contraception Requirements

Contraception requirements

- Female patients of reproductive potential must either completely abstain from heterosexual sexual contact or must use 2 methods of reliable contraception
- Reliable contraceptive methods include using at the same time at least 1 highly effective method and at least 1 additional method of birth control every time they have sex with a male
- Reliable contraceptive methods must be started at least 4 weeks before THALOMID® (thalidomide) therapy, during therapy (including dose interruptions), and for at least 4 weeks following discontinuation of therapy

Effective Methods of Birth Control to Use Together

Highly effective birth control methods	Additional effective birth control methods
Intrauterine device (IUD)	Male latex or synthetic condom Diaphragm Cervical cap
Hormonal methods (birth control pills, hormonal patches, injections, vaginal rings, or implants)	
Tubal ligation (having your tubes tied) +	
Partner's vasectomy (tying of the tubes to prevent the passing of sperm)	

Prescription requirements (continued)

Remind all patients that not having any sexual intercourse is the only birth control method that is 100% effective.

- **Unacceptable forms of contraception:**
 - Progesterone-only “mini-pills”
 - IUD Progesterone T
 - Female condoms
 - Natural family planning (rhythm method) or breastfeeding
 - Fertility awareness
 - Withdrawal
 - Cervical shield*
- Patients should be counseled that concomitant use of certain prescription drugs and/or dietary supplements can decrease the effects of hormonal contraception. If hormonal or IUD contraception is medically contraindicated, 2 other contraceptive methods may be used simultaneously during periods of concomitant use and for 4 weeks after stopping therapy

*A cervical shield should not be confused with a cervical cap, which is an effective secondary form of contraception.

2. Females Not of Reproductive Potential

- The patient must confirm that she is currently not pregnant, nor of reproductive potential as she has been in natural menopause for at least 24 months, or had a hysterectomy and/or bilateral oophorectomy
- The parent or guardian must confirm that a prepubertal female child is not now pregnant, nor is of reproductive potential as **menstruation has not yet begun**, and/or the child will not be engaging in heterosexual sexual contact for at least 4 weeks before THALOMID[®] (thalidomide) therapy, during therapy, and for at least 4 weeks after stopping therapy

Male Patients

- Male patients must be instructed to use a latex or synthetic condom every time they have sexual intercourse with a female of reproductive potential, even if they have undergone a successful vasectomy. The risk to the developing baby from the semen of male patients taking THALOMID is unknown
- Male patients must be instructed not to donate sperm during treatment (including dose interruptions) and for 4 weeks after their last dose of THALOMID

Initial mandatory confidential survey

Females

- Instruct the female patient to complete a brief initial mandatory confidential survey by visiting **www.CelgeneRiskManagement.com**, accessing the Celgene REMS mobile app, or by calling **1-888-423-5436**. See page 12 for subsequent prescription requirements

Males

- Males do not need to take the initial survey

Prescribers

- Prescriber will complete a brief mandatory confidential survey by visiting **www.CelgeneRiskManagement.com**, accessing the Celgene REMs mobile app, or by calling the Celgene Customer Care Center at **1-888-423-5436**, for **every patient** before each prescription is written. Be prepared to enter some of the following information:
 - Prescriber's identification number
 - Patient's identification number
 - Date and result of patient's pregnancy test(s) (if applicable); valid only for 7 days from date of last pregnancy test
 - Average daily dose
 - Total number of days supply (cannot exceed 28 days)
- An authorization number will be issued upon completion of the survey and must be written along with the patient risk category on the prescription. Authorization numbers are valid for 7 days from date of last pregnancy test for females of reproductive potential and 30 days from the date it is issued for all other patients. No automatic refills or telephone prescriptions are permitted

Additional Information for the Prescriber

- Healthcare provider must send the prescription to a THALOMID REMS[®] certified pharmacy. To locate a certified pharmacy, please visit **www.Celgene.com/PharmacyNetwork**
- Prescribe no more than 4 weeks (28 days) of therapy, with no automatic refills

Subsequent prescription requirements

The prescriber must complete a brief mandatory confidential survey to obtain a new authorization number **every time** a prescription for THALOMID® (thalidomide) is written.

No automatic refills or telephone prescriptions are permitted. The patient risk category must be written on the prescription.

Female Patients

- Provide counseling as outlined in the “Female patients” section on pages 8-10
- Follow pregnancy test requirements as outlined in “Pregnancy test requirements” section on page 8
- Female patients must complete a brief mandatory confidential survey according to the following schedule:
 - Before prescription is obtained
 - Monthly
 - Adult females of reproductive potential
 - All female children
 - Every 6 months
 - Adult females not of reproductive potential

Male Patients

- Provide patient counseling as outlined in the “Male patients” section on page 10
- Male patients must complete a brief mandatory confidential survey once a month
 - Males do not complete an initial survey

After the last dose of THALOMID[®] (thalidomide)

After patients have stopped taking THALOMID, they must do the following:

All Patients

- Must not share THALOMID capsules—especially with females of reproductive potential
- Must return any unused THALOMID capsules for disposal to Celgene or their THALOMID prescriber, or to the pharmacy that dispensed the THALOMID to them
- Must not donate blood for 4 weeks after stopping THALOMID

Female Patients

- Must not get pregnant for at least 4 weeks after stopping THALOMID by using the appropriate contraceptives each time engaging in sexual activity with a male

Male Patients

- Must use a latex or synthetic condom each time when engaging in sexual activity for 4 weeks after stopping THALOMID, even if they have undergone a successful vasectomy
- Must not donate sperm for 4 weeks after stopping THALOMID

Ordering English and non-English materials

Call Celgene Customer Care Center AT 1-888-423-5436

- Materials are available in 16 languages and include:
 - THALOMID[®] (thalidomide) Patient-Physician Agreement Forms
 - Patient Guide to THALOMID REMS[®] Program
 - Mandatory confidential survey forms

Available languages:

Arabic	French	Japanese	Portuguese
Cambodian	German	Korean	Russian
Chinese	Greek	Laotian	Spanish
English	Italian	Polish	Vietnamese

- THALOMID[®] (thalidomide) Patient-Physician Agreement Forms, Patient Guide to THALOMID REMS[®] Program, and mandatory confidential survey forms requested will be faxed directly to the number you indicate. Please be prepared to provide:

Prescriber's:

Name

Identification Number

Full Address

Fax Number

Patient's:

Name

Full Address

Phone Number

Date of Birth

Identification Number

Diagnosis (most recent version of ICD code)

Adverse drug experience reporting procedure for healthcare professionals

Celgene is committed to ensuring patient safety through the monitoring of adverse drug experiences associated with the use of THALOMID[®] (thalidomide).

Please report adverse drug experiences that are suspected to be associated with the use of THALOMID and any suspected pregnancy occurring during the treatment with THALOMID to Celgene using any of the following methods.

Reporting to Celgene

- Email: **drugsafety@celgene.com**
- Telephone: **1-908-673-9667**
- Toll-free: **1-800-640-7854** (Global Drug Safety & Risk Management) or **1-888-423-5436** (Celgene Customer Care Center)
- Fax: **1-908-673-9115**
- Mail to: Global Drug Safety & Risk Management, Celgene Corporation, 300 Connell Dr., Suite 6000, Berkeley Heights, NJ 07922

Reporting to the FDA

Adverse drug experiences that are suspected to be associated with the use of THALOMID and any suspected pregnancy occurring during the treatment with THALOMID may also be reported to the FDA MedWatch Reporting System using any of the following methods:

- Online: **<https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>**
- Telephone: **1-800-FDA-1088**
- Fax: **1-800-FDA-0178**
- Mail to: MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787

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For more information about THALOMID[®] (thalidomide) and the THALOMID REMS[®] program, please visit www.CelgeneRiskManagement.com, or call the Celgene Customer Care Center at **1-888-423-5436**.

Celgene Corporation

86 Morris Ave

Summit, NJ 07901

THALOMID is only available under a restricted distribution program, THALOMID REMS[®].

Please see full Prescribing Information, including Boxed WARNINGS, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE REACTIONS, enclosed.

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