

Patient Guide to **THALOMID REMS[®]** Risk Evaluation and Mitigation Strategy (REMS) Program

This guide provides you important information about:

- The risks of THALOMID[®] (thalidomide)
 - Birth defects (deformed babies) or death of an unborn baby
 - Blood clots in your veins (deep vein thrombosis) and lungs (pulmonary embolism)
- The THALOMID REMS program
 - What females who can get pregnant need to know
 - Birth control options
 - What females who can not get pregnant need to know
 - What males need to know

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Risks of THALOMID

THALOMID® (thalidomide) can cause harm to an unborn baby when given to a pregnant female. THALOMID causes a high frequency of severe and life-threatening birth defects (deformed babies) or death of an unborn baby, even after a single dose (1 capsule [regardless of strength]). THALOMID must not be used by pregnant females or by females who are able to get pregnant who are not using acceptable birth control or avoiding sex with a male. Females who are able to get pregnant must avoid pregnancy while taking THALOMID.

THALOMID causes a higher chance for blood clots in your veins (deep vein thrombosis) and lungs (pulmonary embolism).

This is not a comprehensive description of risks associated with the use of THALOMID. Please read the Medication Guide for THALOMID for additional information regarding risks associated with its use and see the Prescribing Information, including Boxed Warnings, enclosed.



THALOMID can cause severe birth defects, including missing or severely deformed legs and arms. These babies often have hands attached directly to their shoulders and feet attached directly to their hips. Photo reprinted by permission.

What is the THALOMID REMS program?

To avoid serious risks to unborn babies, THALOMID is only available under a restricted distribution program called the “THALOMID Risk Evaluation and Mitigation Strategy (REMS).” Only certified prescribers can prescribe THALOMID and only certified pharmacies can dispense THALOMID. In order to receive THALOMID, patients must be enrolled in the THALOMID REMS® program and agree to follow the requirements.

For more information about THALOMID and the THALOMID REMS program, please visit **www.ThalomidREMS.com**, or call the REMS Call Center toll-free at **1-888-423-5436**.

How to receive your first prescription for THALOMID

For Females:



Counseling

Your healthcare provider will counsel you on why and how you and your partner should prevent pregnancy. Your healthcare provider will also inform you not to share the drug, not to donate blood, and about using 2 effective birth control methods (at least 1 highly effective method and 1 effective method) at the same time. You should be instructed not to extensively handle or open THALOMID® (thalidomide) capsules



Pregnancy Test #1

If you can get pregnant, you must take an initial pregnancy test within 10-14 days before getting a THALOMID prescription



Pregnancy Test #2

If you can get pregnant, you must take a second pregnancy test within 24 hours before getting a THALOMID prescription



Enrollment

You and your healthcare provider will then complete and submit the THALOMID Patient-Physician Agreement Form



Complete Mandatory Confidential Survey

You and your healthcare provider will each complete a survey. Visit www.BMSREMSPatientSafety.com, access the REMS Companion App, or call **1-888-423-5436** and press 1 to take your survey



Prescription

Your healthcare provider will send your prescription to a certified pharmacy



Pharmacy Call

The certified pharmacy will contact you to provide counseling on the serious risks and safe-use conditions of THALOMID before you receive your prescription. They will also coordinate delivery of THALOMID to you



Receive THALOMID

THALOMID will be shipped with a Medication Guide to the address you provide. A signature will be required to receive this shipment

For each of your following prescriptions, pregnancy tests will be required depending on your ability to get pregnant. For specific pregnancy test requirements, please refer to page 9 of this guide. For full detailed information about the THALOMID REMS® program requirements, please visit www.ThalomidREMS.com or review the Patient Guide to THALOMID REMS Program.

For Males:



Counseling

Your healthcare provider will counsel you on why and how you and your partner should prevent pregnancy. Your healthcare provider will also inform you not to share the drug, not to donate blood or sperm, and about appropriate contraceptive use. You should be instructed not to extensively handle or open THALOMID® (thalidomide) capsules



Enrollment

You and your healthcare provider will then complete and submit the THALOMID Patient-Physician Agreement Form



Complete Mandatory Confidential Survey

You will not have to take a survey for your first prescription, but will have to for the following ones. Visit **www.BMSREMSPatientSafety.com**, access the REMS Companion App, or call **1-888-423-5436** and press 1 to take your survey



Prescription

Your healthcare provider will send your prescription to a certified pharmacy



Pharmacy Call

The certified pharmacy will contact you to provide counseling on the serious risks and safe-use conditions of THALOMID before you receive your prescription. They will also coordinate delivery of THALOMID to you



Receive THALOMID

THALOMID will be shipped with a Medication Guide to the address you provide. A signature will be required to receive this shipment

For each of your following prescriptions, you will need to follow a similar process. For full detailed information about the THALOMID REMS® program requirements, please visit www.ThalomidREMS.com or review the Patient Guide to THALOMID REMS Program.



What do all patients need to know about the THALOMID REMS program?

General guidelines

- This medicine is **only** for you. **Do not share it with anyone** even if they have symptoms like yours. Just **1 capsule** taken by a pregnant female can cause severe birth defects
- THALOMID® (thalidomide) does not induce abortion of the fetus and should never be used for contraception
- THALOMID must be kept out of the reach of children
- Do not open or unnecessarily handle THALOMID capsules. If a broken capsule (or the powder in the capsule) comes in contact with your skin, wash the area with soap and water
- Keep THALOMID in a cool, dry place
- Do **not** donate blood while you are taking THALOMID, during breaks (dose interruptions), and for 4 weeks after stopping THALOMID
- Unused THALOMID capsules should be returned for disposal to THALOMID REMS® by calling **1-888-423-5436**, or to your THALOMID prescriber, or to the pharmacy that dispensed the THALOMID to you

Warning

- **Blood clots** have been reported in patients taking THALOMID, especially when used with other cancer drugs. Your healthcare provider may recommend treatment that could help prevent blood clots. Talk to your healthcare provider if you have shortness of breath, chest pains, or arm or leg swelling
- THALOMID can cause other health problems called “side effects.” For a complete listing of possible side effects, please refer to the Medication Guide
- **Be sure to report all side effects to your healthcare provider immediately.** Ask your healthcare provider about other side effects associated with THALOMID



What do females who can get pregnant need to know about the THALOMID REMS program?

A. Before taking THALOMID® (thalidomide)

- You must sign the THALOMID Patient-Physician Agreement Form that says you understand that THALOMID should not be used during pregnancy, and that you agree not to become pregnant while taking THALOMID
- If there is **any** chance that you can get pregnant, you must agree to use **at the same time** at least 1 highly effective method and at least 1 additional effective method of birth control **every time** you have sex with a male starting at least 4 weeks **before** taking THALOMID
- Your healthcare provider must give you a pregnancy test 10 to 14 days before you receive your first prescription for THALOMID, and again within 24 hours before you receive your first prescription for THALOMID. If you are pregnant, you cannot take THALOMID
- You will have pregnancy tests before starting THALOMID and while taking THALOMID, even if you agree not to have sex with a male
- Before your healthcare provider can write your prescription for THALOMID, you must take part in a mandatory confidential survey. The survey will make sure that you understand and can follow information designed to prevent serious risks to unborn babies
- Before dispensing THALOMID, your THALOMID REMS® certified pharmacy will contact you to discuss treatment
- Your healthcare provider will talk with you about your birth control options

1. Choose at least 1 highly effective method and at least 1 additional effective method of birth control

Talk to your healthcare provider about the following acceptable birth control methods. See below.

Effective Methods of Birth Control Used at the Same Time

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

2. Use the 2 methods of birth control at the same time

- **Remember:** You must use **at the same time** at least 1 highly effective method and at least 1 additional effective method of birth control **every time** you have sex with a male. However, your healthcare provider may recommend that you use 2 different methods instead for medical reasons
- Talk to your healthcare provider to make sure that other medicines or dietary supplements you are taking do not interfere with your hormonal birth control methods
- **Remember, not having sex is the only method of birth control that is 100% effective**

3. Unacceptable methods of birth control

- Progesterone-only “mini-pills”
- IUD Progesterone T
- Female condoms
- Natural family planning (rhythm method) or breastfeeding
- Fertility awareness
- Withdrawal
- Cervical shield*

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

4. Take pregnancy tests

- You must have a pregnancy test performed by your healthcare provider 10 to 14 days before receiving your first prescription for THALOMID® (thalidomide) and again within 24 hours before receiving your first prescription for THALOMID. Both pregnancy tests must have a negative result

B. While taking THALOMID

- If you are able to get pregnant, you must continue (including during breaks [dose interruptions]) to use **at the same time** at least 1 highly effective method and at least 1 additional effective method of birth control **every time** you have sex with a male
- **Remember, not having sex is the only method of birth control that is 100% effective**
- You must talk to your healthcare provider before changing any birth control methods you have already agreed to use
- You will have a pregnancy test performed by your healthcare provider:
 - Every week during the first 4 weeks of treatment, then
 - Every 4 weeks if your menstrual cycles are regular, or
 - Every 2 weeks if your cycles are irregular
 - If you miss your period or have unusual menstrual bleeding, or
 - If your medication is not dispensed within 7 days of taking the pregnancy test

- If you had sex with a male without using birth control or if you think your birth control has failed, stop taking THALOMID® (thalidomide) immediately and call your healthcare provider right away. Your healthcare provider will discuss your options, which may include emergency birth control. Do not wait until your next appointment to tell your healthcare provider if you miss your menstrual period or if you think you may be pregnant
- If you get pregnant, or think you may be pregnant, you must immediately stop taking THALOMID. Contact your healthcare provider immediately to discuss your pregnancy. If you do not have an obstetrician, your healthcare provider will refer you to one for care and counseling. If your healthcare provider is not available, call the REMS Call Center at **1-888-423-5436**
- You must not breastfeed a baby while you are taking THALOMID
- In order to continue receiving THALOMID, you must take part in a mandatory confidential survey every month. You must also continue to discuss your treatment with your THALOMID REMS® healthcare provider. To take the survey, please visit **www.BMSREMSPatientSafety.com**, access the REMS Companion App, or call the REMS Call Center at **1-888-423-5436**

C. After you have stopped taking THALOMID® (thalidomide)

- You must continue to use **at the same time** at least 1 highly effective method and at least 1 additional effective method of birth control **every time** you have sex with a male:
 - For at least 4 weeks after stopping THALOMID, or
 - Do not have any sex with a male for 4 weeks after stopping THALOMID

See also “General guidelines” on page 6 for requirements for all patients.

Attention Females Who Can Get Pregnant:

Tear out this letter to take with you to your next medical appointment that discusses your birth control options.

This letter will help you and your healthcare provider understand what types of birth control options are the best for you.

THALOMID REMS®

Dear Healthcare Provider,

Your patient is being treated with THALOMID® (thalidomide). Thalidomide is a known teratogen and is only available under a restricted distribution program approved by the Food and Drug Administration. This program is called the THALOMID REMS (Risk Evaluation and Mitigation Strategy) program.

The goals of the THALOMID REMS program are:

1. To prevent the risk of embryo-fetal exposure to THALOMID.
2. To inform prescribers, patients, and pharmacists on the serious risks and safe-use conditions for THALOMID.

To enroll in the THALOMID REMS program, your patient, with the knowledge of the healthcare provider who prescribed THALOMID, agreed to follow the program's contraception requirements while on THALOMID therapy. Unless she completely abstains from sexual intercourse with a male partner, she is required to use **at the same time at least 1 highly effective birth control method and at least 1 additional effective method.**

The 2 effective contraceptive methods must be started at least 4 weeks before THALOMID therapy, during therapy (including dose interruptions), and for at least 4 weeks following discontinuation of therapy. Please refer to the table below of the acceptable forms of contraception to help facilitate the discussion on contraception.

Effective Methods of Birth Control Used at the Same Time

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

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

(continued on next page)

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

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.

Instruct patient to immediately stop taking THALOMID® (thalidomide) and contact her doctor if she becomes pregnant while taking this drug, if she misses her menstrual period or experiences unusual menstrual bleeding, if she stops taking birth control, or if she thinks FOR ANY REASON that she may be pregnant. Advise patient that if her doctor is not available, then she can call the REMS Call Center at **1-888-423-5436**.

There are other risks associated with THALOMID treatment as described in the Prescribing Information.

For Prescribing Information, including Boxed Warnings, or details about the THALOMID REMS® program, please visit www.ThalomidREMS.com.

You may contact the REMS Call Center at **1-888-423-5436** if you have any questions about the information contained in this letter or the safe and effective use of THALOMID.

Sincerely,

The THALOMID REMS Program



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What do females who can not get pregnant need to know about the THALOMID REMS program?

A. Before taking THALOMID® (thalidomide)

- You must sign the THALOMID Patient-Physician Agreement Form that says you are currently not pregnant and are not able to get pregnant. This means that:
 - You have been in natural menopause for at least 2 years, or
 - You have had both ovaries and/or uterus removed
- For females who have not started their period (menstruation) and are under the age of 18, a parent or legal guardian must sign the THALOMID Patient-Physician Agreement Form that says the patient is not pregnant, is not able to get pregnant, and/or will not be having sex with a male for at least 4 weeks before starting THALOMID
- Before your healthcare provider can write your prescription for THALOMID, you must take part in a mandatory confidential survey. The survey will make sure that you understand and can follow information designed to prevent serious risks to unborn babies
- Before dispensing THALOMID, your THALOMID REMS® certified pharmacy will contact you to discuss treatment

B. While taking THALOMID

- In order to continue receiving THALOMID, you must take part in a mandatory confidential survey every 6 months. You must also continue to discuss your treatment with your THALOMID REMS healthcare provider. To take the survey, please visit **www.BMSREMSPatientSafety.com**, access the REMS Companion App, or call the REMS Call Center at **1-888-423-5436**

See also “General guidelines” on page 6 for requirements for all patients.

What do males need to know about the THALOMID REMS program?

- You must use a latex or synthetic condom **every time** you have sex with a female who is able to get pregnant, even if you have had a successful vasectomy (tying of the tubes to prevent the passing of sperm)

A. Before taking THALOMID® (thalidomide)

- You must sign the THALOMID Patient-Physician Agreement Form. You must agree that while taking THALOMID you will use a latex or synthetic condom **every time** you have sex with a female who is pregnant or who is able to get pregnant, even if you have had a successful vasectomy (tying of the tubes to prevent the passing of sperm)
- Before dispensing THALOMID, your THALOMID REMS® certified pharmacy will contact you to discuss treatment

B. While taking THALOMID

- You must use a latex or synthetic condom **every time** (including during breaks [dose interruptions]) you have sex with a female who is pregnant or who is able to get pregnant, even if you have had a successful vasectomy (tying of the tubes to prevent the passing of sperm)
- **Remember, not having sex is the only method of birth control that is 100% effective**
- You must tell your healthcare provider right away if you had sex with a female without using a latex or synthetic condom, if you think for any reason that your partner may be pregnant, or if your partner is pregnant. If your healthcare provider is not available, call the REMS Call Center at **1-888-423-5436**
- You must **not** donate sperm while taking THALOMID (including during breaks [dose interruptions])
- In order to continue receiving THALOMID, you must take part in a mandatory confidential survey every month. You must also continue to discuss your treatment with your THALOMID REMS healthcare provider. To take the survey, please visit **www.BMSREMSPatientSafety.com**, access the REMS Companion App, or call the REMS Call Center at **1-888-423-5436**

C. After you have stopped taking THALOMID® (thalidomide)

- For 4 weeks after receiving your last dose of THALOMID, you must use a latex or synthetic condom **every time** you have sex with a female who is pregnant or who is able to get pregnant, even if you have had a successful vasectomy (tying of the tubes to prevent the passing of sperm)
- You must **not** donate sperm for 4 weeks after stopping THALOMID

See also “General guidelines” on page 6 for requirements for all patients.

Mandatory confidential patient surveys

As a patient who is enrolled in the THALOMID REMS® program for THALOMID® (thalidomide), you will need to complete a brief mandatory confidential survey as outlined below.

Adult females who can get pregnant

- Initial survey before first prescription
- Monthly

Adult females who can not get pregnant

- Initial survey before first prescription
- Every 6 months

Female children

- Initial survey before first prescription
- Monthly

Males

- No initial survey
- Monthly

Mandatory confidential survey process

- When your healthcare provider tells you to take the survey, go to the patient Mandatory Confidential Survey section of **www.BMSREMSPatientSafety.com**, the REMS Companion App, or call the REMS Call Center at **1-888-423-5436**
- Be prepared with your patient identification number
- After completing your survey, your healthcare provider will also complete a survey. Your healthcare provider will then receive authorization to write your prescription
- The prescription will be sent to a THALOMID REMS[®] certified pharmacy. The THALOMID REMS certified pharmacy will contact you to discuss your THALOMID[®] (thalidomide) therapy. You will not receive your medication until you speak with the THALOMID REMS certified pharmacy

For more information, contact the REMS Call Center at **1-888-423-5436**.



A letter from the Thalidomide Victims Association of Canada (TVAC)

The following letter from the Thalidomide Victims Association of Canada (TVAC) was written in 1998 upon U.S. approval of THALOMID® (thalidomide), and is included in this brochure to be transparent about public concerns for thalidomide victims regarding the marketing of THALOMID.

Dear Doctor/Patient:

Have you ever met someone who was born disabled after exposure to thalidomide?

We have. In fact, we are thalidomiders—the name we have adopted to describe the surviving children of mothers who were prescribed thalidomide during their pregnancy as a sedative or for nausea and other symptoms of “morning sickness.”

You’ve undoubtedly seen the **dramatic photographs of babies with severe birth defects** caused when thalidomide is taken EVEN ONCE by a pregnant woman. You know the risks!

The **Thalidomide Victims Association of Canada (TVAC)** was formed to meet the needs of the approximately 125 thalidomiders alive in Canada today, and to aid the surviving 10 thalidomiders living in the United States. Of the 10,000 to 12,000 children born with thalidomide deformities around the world in the early sixties, 5,000 survive today. No one will ever know how many children were miscarried or were stillborn because of thalidomide.

TVAC exists as a survivors group to determine and find solutions to the ongoing problems we face. TVAC has also undertaken a mandate of monitoring the responsible use of thalidomide and ensuring the tragedy of the past *never happens again*.

Because of our own personal traumas, and those of our families, we have always stated that we can never accept a world with thalidomide in it.

However, as we know first-hand how people may suffer, we also concede that no one should suffer needlessly. If thalidomide can extend a life, or offer a better quality of life to people with debilitating or chronic illnesses, then we are forced to accept the fact that thalidomide use may be their choice.

As well, we are forced to prefer the regulated use of thalidomide over the alternative:

One thalidomide baby born out of ignorance is far worse than one born out of a legitimate attempt to regulate and control the distribution process of this drug.

Since you may soon be involved in prescribing or taking thalidomide, we need for you to be **fully aware of the power you have...**

- the responsibility to see that you **fully understand the risks thalidomide poses...**
- the **commitment** to do whatever it takes to make sure that NOT EVEN ONE woman loses a child due to thalidomide

We were as surprised as anyone when the people at Celgene Corporation, makers of THALOMID® (thalidomide), sought the opinions and input of those of us at TVAC concerning the use of thalidomide in the United States. We felt it was a respectful step in the right direction that our feelings, opinions, and knowledge were being considered.

We are also consoled to know that Celgene Corporation has instituted a comprehensive program to help physicians and pharmacists inform patients about side effects and risks and ensure that they are aware of precautions they must take before, during, and after therapy.

The **THALOMID Risk Evaluation and Mitigation Strategy (REMS)** is a multifaceted program developed to help ensure that fetal exposure to THALOMID does not occur. All of the materials you need to comply with this system are enclosed.

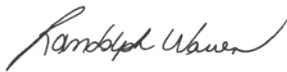
Meanwhile, we make you one promise:

The Thalidomide Victims Association of Canada will continue to watch the progression of events where thalidomide use is concerned.

We have to!

For further information regarding the history of thalidomide or the status of survivors today, please feel free to contact us.

Sincerely,



Randolph Warren
Chief Executive Office
Thalidomide Victims
Association of Canada



Giselle Cole
Past President
Thalidomide Victims
Association of Canada

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Warning to patients taking THALOMID

Attention females:

Do **not** take THALOMID® (thalidomide) if you are pregnant, if you are breastfeeding, or if you are able to get pregnant and are not using **at the same time** at least 1 highly effective method and at least 1 additional effective method of birth control **every time** you have sex with a male.

Attention males:

You must use a latex or synthetic condom **every time** you have sex with a female who is pregnant or who is able to get pregnant, even if you have had a successful vasectomy (tying of the tubes to prevent the passing of sperm).

You must **not** donate sperm while taking THALOMID, during breaks (dose interruptions), and for 4 weeks after stopping THALOMID.

Attention all patients:

You must **not** donate blood while taking THALOMID, during breaks (dose interruptions), and for 4 weeks after stopping THALOMID.

This medicine is **only** for you. **Do not share it with anyone** even if they have symptoms like yours. Just **1 capsule** taken by a pregnant female can cause severe birth defects.

THALOMID must be kept out of the reach of children. Return any unused THALOMID capsules for disposal to THALOMID REMS® by calling **1-888-423-5436**, or to your THALOMID prescriber, or to the pharmacy that dispensed the THALOMID to you.

For more information about THALOMID® (thalidomide) and the THALOMID REMS® program, please visit **www.ThalomidREMS.com**, or call the REMS Call Center at **1-888-423-5436**.

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

Please read the Medication Guide for THALOMID for additional information regarding risks associated with its use and see the Prescribing Information, including Boxed Warnings, enclosed.



THALOMID REMS®

 **THALOMID®**
(thalidomide) Capsules

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