

PACKAGE LEAFLET: INFORMATION FOR THE USER

Thalidomide Celgene® 50 mg hard capsules
Thalidomide

WARNING

Thalidomide causes birth defects and foetal death. Do not take thalidomide if you are pregnant or could become pregnant. You must follow the contraception advice given to you by your doctor.

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of your side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

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1. WHAT THALIDOMIDE CELGENE IS AND WHAT IT IS USED FOR

What Thalidomide Celgene is

Thalidomide Celgene contains an active substance called thalidomide. This belongs to a group of medicines which affect how your immune system works.

What Thalidomide Celgene is used for

Thalidomide Celgene is used with two other medicines called 'melphalan' and 'prednisone' to treat adults aged 65 years and over, with a type of cancer called multiple myeloma. It is used in people who have recently been diagnosed and who have not been prescribed another medicine for their multiple myeloma before, or who cannot be treated with high dose chemotherapy, which can be very difficult for the body to handle.

What is multiple myeloma

Multiple myeloma is a type of cancer which affects a certain type of white blood cell, called the plasma cell. These cells collect in the bone marrow and divide out of control. This can damage the bone and kidneys. Multiple myeloma generally cannot be cured. However, the signs and symptoms can be greatly reduced or disappear for a period of time. This is called a 'remission'.

How Thalidomide Celgene works

Thalidomide Celgene works by helping the body's immune system and directly attacking the cancer. It works in a number of different ways:

- by stopping the cancer cells developing
- by stopping blood vessels growing in the cancer
- by stimulating part of the immune system to attack the cancer cells.

2. BEFORE YOU TAKE THALIDOMIDE CELGENE

You will have been given specific instructions by your doctor, particularly on the effects of thalidomide on unborn babies (outlined in the *i-SECURE* program).

You will have been given a Thalidomide *i-SECURE* patient brochure by your doctor. Read it carefully and follow the related instructions.

If you do not fully understand these instructions, please ask your doctor to explain them again before you take thalidomide. See also further information in this section under "Take special care with Thalidomide Celgene" and "Pregnancy and breast-feeding".

Do not take Thalidomide Celgene

- If you are pregnant or think you may be pregnant or are planning to become pregnant, as **Thalidomide Celgene causes birth defects and foetal death.**
- If you are able to become pregnant but are unable to follow the necessary pregnancy prevention measures (outlined in the *i-SECURE* program).
- If you are allergic (hypersensitive) to thalidomide or any of the other ingredients of Thalidomide Celgene (listed in section 6. "What Thalidomide Celgene contains:").

Do not take Thalidomide Celgene if any of the above applies to you. If you are not sure, talk to your doctor or pharmacist before taking Thalidomide Celgene.

Take special care with Thalidomide Celgene:

For females taking Thalidomide Celgene Before starting the treatment, you should ask your doctor if you are able to become pregnant, even if you think this is unlikely.

If you are able to become pregnant:

- Your doctor will make sure that you have pregnancy tests
 - before treatment
 - every 4 weeks during treatment
 - 4 weeks after stopping treatment
- You must use two effective methods of contraception at the same time:
 - for 4 weeks before starting treatment
 - during treatment
 - during dose interruptions
 - until 4 weeks after stopping treatment

You should talk to your doctor about the following birth control methods.

Examples of Effective Methods of Contraception

Highly Effective Methods:

- Intra Uterine Device (IUD)
- Hormonal (hormonal implants, levonorgestrel-releasing intrauterine system (IUS), medroxyprogesterone acetate depot injections, ovulation inhibitory progesterone-only pills e.g. desogestrel)
- Tubal ligation
- Partner's vasectomy

Effective Methods:

- Male condom
- Diaphragm
- Cervical cap

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 the patient should switch to two of the effective methods listed above. The risk of venous thromboembolism continues for 4–6 weeks after discontinuing combined oral contraception.

If you are able to become pregnant, your doctor will record with each prescription that the necessary measures, as outlined above, have been taken and will state that on the relevant *i-SECURE* documents.

For men taking Thalidomide Celgene Thalidomide passes into semen. Therefore, do not have unprotected intercourse.

- Pregnancy and any exposure during pregnancy must be avoided. Always use a condom:
 - during treatment
 - during dose interruptions
 - for 4 weeks after stopping treatment
- You must not donate semen:
 - during treatment
 - during dose interruptions
 - for 4 weeks after stopping treatment

For all patients taking Thalidomide Celgene Check with your doctor before taking this medicine if

- you have had a heart attack, have ever had a blood clot in the past, or if you smoke, have high blood pressure or high cholesterol levels. During the treatment with Thalidomide Celgene you have an increased risk of developing blood clots in the veins and arteries.
- you experienced or have existing slow heart rate (this may be symptoms of bradycardia).

- you have experienced or have existing neuropathy i.e. tingling, abnormal co-ordination or pain in your hands or feet.
- you have experienced sleepiness.
- you have a high total amount of tumor throughout the body, including your bone marrow. This could lead to a condition where the tumors break down and cause unusual levels of chemicals in the body which can lead to kidneys failure (this condition is called Tumor Lysis Syndrome).
- you have experienced fever, chills and severe shaking, and possibly complicated by low blood pressure and confusion (these may be symptoms of severe infections).
- you have had an allergic reaction whilst taking thalidomide such as rash, itching, swelling, dizziness or trouble breathing.
- you do not understand the contraception advice given to you by your doctor or if you do not feel able to follow this advice.
- you have high blood pressure from the heart to the lungs.
- you have or have ever had previous viral infection, particularly varicella, zona, hepatitis B infection, or HIV. If you are in doubt, talk to your doctor. Treatment with thalidomide may cause virus to become active again in patients who carry it, resulting in a recurrence of the infection. Your doctor should check whether you have ever had hepatitis B infection.

Donating Blood:

You must not donate blood during Thalidomide Celgene treatment, during dose interruptions and for 4 weeks after stopping treatment.

If you are not sure if any of the above apply to you, talk to your doctor before taking Thalidomide Celgene.

Children and adolescents

Thalidomide Celgene is not recommended for use in children and young people under 18 years.

Taking other medicines:

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines since other medicines could interfere with the effect of thalidomide. This includes medicines obtained without a prescription, including herbal medicines.

Make sure you tell your doctor if you are taking any medicines which:

- cause sleepiness as thalidomide may increase their effects. This includes sedatives (such as anxiolytics, hypnotics, antipsychotics, H₁ anti-histamines, opiate derivatives and barbiturates).
- slow the heart rate (induce bradycardia, such as anti-cholinesterases and beta blockers).
- are used for heart problems and complications (such as digoxin), or for thinning the blood (such as warfarin).
- are other treatments for cancer.
- are used for contraception.

Taking Thalidomide Celgene with food and drink:

Thalidomide Celgene can be taken with or without food (see section 3, "How to take Thalidomide Celgene").

Do not drink alcohol while you are taking Thalidomide Celgene. This is because alcohol can make you sleepy and Thalidomide Celgene can make you even sleepier.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy

Thalidomide causes severe birth defects or death to an unborn baby.

- As little as one capsule taken by a pregnant woman can cause a baby to have serious birth defects.
- These defects can include shortened arms or legs, malformed hands or feet, eye or ear defects, and problems with internal organs.

If you are pregnant, you must not take Thalidomide Celgene. In addition, you must not become pregnant while taking Thalidomide Celgene.

You must use two effective methods of contraception at the same time every time you have sex with a male if you are a woman who is able to become pregnant (see section 2, "Take special care with Thalidomide Celgene").

You must stop treatment and inform your doctor straight away if:

- You miss or think you have missed a period, or you have unusual menstrual bleeding, or suspect you are pregnant.
- You have heterosexual intercourse without using an effective method of contraception.

If you do become pregnant during the treatment with thalidomide, you must stop the treatment and inform your doctor immediately.

For men taking Thalidomide Celgene who have a female partner who is able to become pregnant, please see section 2 "Take special care with Thalidomide Celgene". If your partner becomes pregnant whilst you are taking thalidomide, you should inform your doctor immediately.

Breast-feeding:

Do not breastfeed during Thalidomide Celgene treatment, during dose interruptions and for 4 weeks after stopping treatment as it is not known if thalidomide is passed into human breast milk.

Driving and using machines:

Do not drive or use any tools or machines if you experience side effects, such as dizziness, tiredness, sleepiness or blurred vision.

3. HOW TO TAKE THALIDOMIDE CELGENE

Always take Thalidomide Celgene exactly as your doctor has told you to. You should check with your doctor if you are not sure.

How much to take

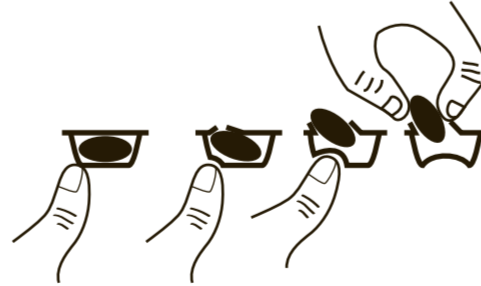
The recommended dose is 200 mg (4 x 50 mg capsules) a day for adults aged 75 years and under or 100 mg (2 x 50 mg capsules) a day for adults aged over 75 years. However your doctor will choose the dose for you, monitor your progress and may adjust your dose. Your doctor will tell you how to take Thalidomide Celgene and for how long you will need to take it (see section 2, "Before you take Thalidomide Celgene").

Thalidomide Celgene is taken daily in treatment cycles, each cycle lasting 6 weeks, in combination with melphalan and prednisone which are taken on days 1 to 4 of each 6 week cycle.

Taking this medicine

- Do not break, open or chew the capsules. If powder from a broken Thalidomide Celgene capsule makes contact with the skin, wash the skin immediately and thoroughly with soap and water.
- Take this medicine by mouth.
- Swallow the capsules whole with a full glass of water.
- Do not crush or chew.
- Take the capsules as a single dose before going to bed. This will make you less likely to feel sleepy at other times.

To remove the capsule from the blister, press only one end of the capsule out to push it through the foil. Do not apply pressure on the centre of the capsule as this can cause it to break.



If you take more Thalidomide Celgene than you should

If you take more Thalidomide Celgene than you should, talk to a doctor or go to a hospital straightaway. If possible, take the medicine pack and this leaflet with you.

If you forget to take Thalidomide Celgene

If you forget to take Thalidomide Celgene at your regular time and

- less than 12 hours have passed: take your capsules immediately.
- more than 12 hours have passed: do not take your capsules. Take your next capsules at the usual time the next day.

If you have any further questions on the use of this product, ask your doctor, pharmacist or nurse.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects although not everybody gets them.

The following side effects may happen with this medicine:

Stop taking Thalidomide Celgene and see a doctor straight away if you notice the following serious side effects – you may need urgent medical treatment:

- Severe skin reactions including rashes, which is a common side effect and blistering of the skin and mucosa (Stevens Johnson Syndrome and toxic epidermal necrolysis, which are rare side effects). 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, abnormal co-ordination or pain in your hands and feet.**

This may be due to nerve damage (called 'peripheral neuropathy'), which is a very common side effect. It may become very severe, painful and disabling. If you experience such symptoms, speak to your doctor straight away, who may reduce the dose or discontinue the treatment. This side effect usually happens after you have been taking this medicine for several months but can happen sooner than this. It can also happen sometime after treatment has stopped. It may not go away, or may go away slowly.

- **Sudden pain in your chest or difficulty in breathing.**

This may be due to blood clots in the arteries leading to your lungs (called 'pulmonary embolism'), which is a common side effect. These 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), which is a common side effect. These can happen during treatment, or after treatment has stopped.

- **Chest pain spreading to the arms, neck, jaw, back or stomach, feeling sweaty and breathless, feeling sick or vomiting.**

These may be symptoms of a heart attack/ myocardial infarction (which may be due to blood clots in the arteries of your heart).

- **Having difficulty in seeing or speaking, which is temporary.**

These may be symptoms of a stroke (which may be due to a clot in an artery in your brain).

- **Fever, chills, sore throat, cough, mouth ulcers or any other symptoms of infection.**
- **Bleeding or bruising in the absence of injury.**

Other side effects include:

It is important to note that a small number of patients with multiple myeloma may develop additional types of cancer, especially haematological malignancies, and it is possible that this risk may be increased with Thalidomide Celgene treatment; therefore your doctor should carefully evaluate the benefit and risk when you are prescribed Thalidomide Celgene.

Very common (may affect more than 1 in 10 people)

- Constipation.
- Feeling dizzy.
- Sleepiness, feeling tired.
- Shaking (tremor).
- Swelling of hands and feet.
- Low blood cell counts. This may mean that you are more likely to develop infections. Your doctor may monitor your blood cell counts during treatment with Thalidomide Celgene.

Common (may affect up to 1 in 10 people)

- Indigestion, feeling sick (nausea), being sick (vomiting), dry mouth.
- Rash, dryness of the skin.

- Feeling weak, faint or unsteady, lack of energy or strength, low blood pressure.
- Fever, feeling generally unwell.
- A spinning feeling in your head, making it difficult to stand up and move normally.
- Blurred vision.
- Chest infection (pneumonia), lung disease.
- A slow heart rate, heart failure.
- Depression, confusion, mood changes, anxiety.

Uncommon (may affect up to 1 in 100 people)

- Inflammation and swelling of the tubes in your lungs (bronchitis).
- Inflammation of the cells lining your stomach wall.
- A hole in part of your large bowel (colon) which can cause infection.

Additional side effects have been reported after this medicine was marketed. These include:

- Underactive thyroid (hypothyroidism).
- Bowel obstruction.
- Sexual dysfunction, for example impotence.
- A fall in the number of white blood cells (neutropenia) accompanied by fever and infection
- Severe blood infection (sepsis) accompanied by fever, chills and severe shaking, and possibly complicated by low blood pressure and confusion (septic shock).
- A fall in the number of red and white blood cells and platelets at the same time (pancytopenia).
- Tumour Lysis Syndrome - metabolic complications that can occur during the treatment of cancer and sometimes even without treatment. These complications are caused by the break-down products of dying cancer cells and may include the following: changes to blood chemistry; high potassium, phosphorus, uric acid, and low calcium consequently leading to changes in kidney function, heart beat, seizures, and sometimes death.
- Allergic reactions such as a localised or generalised pruritic rash and angioedema (types of allergic reaction that may be manifested as hives, rashes, swelling of eyes, mouth or face, difficulty of breathing, or itching).
- Hearing decreased or deafness.
- Convulsions.
- Kidney disease (renal failure).
- Injury to the liver (hepatic disorder) including abnormal liver test results.
- Bleeding from the stomach or bowels (gastrointestinal haemorrhage).
- Irregularities of the heartbeat (heart block or atrial fibrillation), feeling faint or fainting.
- Worsening of Parkinson's disease symptoms (such as tremor, depression or confusion).
- Pain in the upper abdomen and/or back, which may be severe and which remains for a few days, possibly accompanied by nausea, vomiting, fever and a rapid pulse – these symptoms may be due to the inflammation of the pancreas (pancreatitis).
- Increase in blood pressure within blood vessels that supply the lungs which can lead to shortness of breath, tiredness, dizziness, pain in the chest, a faster heart-beat, or swelling in the legs or ankles (pulmonary hypertension).
- Viral infections, including herpes zoster (also known as 'shingles', a viral disease that causes a painful skin rash with blisters) and recurrence of hepatitis B infection (which can cause yellowing of the skin and eyes, dark brown-coloured urine, right-sided stomach pain, fever and feeling nauseous or being sick).

If any of the **side effects** gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE THALIDOMIDE CELGENE

Keep out of the reach and sight of children and any other person not directly involved in the treatment.

Do not use after the expiry date stated on the wallet card and the blister after EXP. The expiry date refers to the last day of that month.

Store below 30°C in the original package.

At the end of your treatment you should return all unused capsules to the pharmacist or doctor. These measures will prevent misuse.

6. FURTHER INFORMATION

What Thalidomide Celgene contains:

- The active substance is thalidomide. Each capsule contains 50 mg of thalidomide.
- The other excipients are pregelatinized starch and magnesium stearate. The capsule shell contains gelatin and titanium dioxide (E171). The printing ink is composed of shellac, black iron oxide (E172) and propylene glycol.

What Thalidomide Celgene looks like and contents of the pack

Thalidomide Celgene are white hard capsules marked "Thalidomide Celgene 50 mg". The capsules are supplied in a wallet card containing 28 capsules (2 blisters of 14 capsules each).

This is a medicament

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament to you
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not, by yourself, interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Keep Medicament out of the reach and sight of children and any other person not directly involved in the treatment

Manufactured by Celgene International Sarl, Switzerland

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