

Package leaflet: Information for the patient

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 because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Thalidomide Celgene is and what it is used for
2. What you need to know before you take Thalidomide Celgene
3. How to take Thalidomide Celgene
4. Possible side effects
5. How to store Thalidomide Celgene
6. Contents of the pack and other information

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 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 who are aged 65 years and over, or aged less than 65 years 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. What you need to know 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 Thalidomide Celgene Pregnancy Prevention Programme).

You will have been given an educational brochure for patient 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 “Warnings and precautions” 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, unless you are able to follow or comply with the required contraceptive measures to prevent you from becoming pregnant (see section 2 “Warnings and precautions” and “Pregnancy and breast-feeding”).
- if you are able to become pregnant, your doctor will record with each prescription that the necessary measures have been taken and will provide you with this confirmation.
- if you are allergic to thalidomide or any of the other ingredients of this medicine listed in section 6 “Contents of the pack and other information”.

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.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking this medicine in the following situations:

For women 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. Even if you do not have a menstrual bleeding following cancer therapy, you may become pregnant.

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 one effective method of contraception:
 - for at least 4 weeks before starting treatment
 - during treatment
 - until at least 4 weeks after stopping treatment

Your doctor will tell you what method of contraception to use.

If you are able to become pregnant, your doctor will record with each prescription that the necessary measures, as outlined above, have been taken

For men taking Thalidomide Celgene

Thalidomide passes into semen. Therefore, do not have unprotected intercourse, even if you had a vasectomy.

- Pregnancy and any exposure during pregnancy must be avoided. Always use a condom:
 - during treatment
 - for at least 7 days after stopping treatment
- You must not donate semen:
 - during treatment
 - for at least 7 days after stopping treatment

For all patients

Talk to your doctor before taking Thalidomide Celgene if

- 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 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 (see also section 4 “Possible side effects”).
- you have experienced or have existing neuropathy i.e. nerve damage causing tingling, abnormal co-ordination or pain in your hands or feet (see also section 4 “Possible side effects”).
- you experienced or have existing slow heart rate (this may be a symptom of bradycardia).
- you have high blood pressure in the arteries of the lungs (see also section 4 “Possible side effects”).
- you have a fall in the number of white blood cells (neutropenia) accompanied by fever and infection.
- you have a fall in the number of platelets. You will be more prone to bleeding and bruising.
- you have or have had injury to the liver (hepatic disorders) including abnormal liver test results.
- you experience or have experienced in the past severe skin reactions called Stevens-Johnson syndrome, toxic epidermal necrolysis or drug reaction with eosinophilia and systemic symptoms (which is also known as DRESS or drug hypersensitivity syndrome). (For description of symptoms see section 4 “Possible side effects”).
- you have had an allergic reaction whilst taking Thalidomide Celgene such as rash, itching, swelling, dizziness or trouble breathing.
- you have experienced sleepiness.
- 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 or have ever had previous viral infection, particularly varicella zoster, hepatitis B infection, or HIV. If you are in doubt, talk to your doctor. Treatment with Thalidomide Celgene may cause a 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.
- you have kidney or liver problems (see also section 4 “Possible side effects”).

Your doctor may check if you have a high total amount of tumour throughout the body, including your bone marrow. This could lead to a condition where the tumours break down and cause unusual levels of chemicals in the body which can lead to kidneys failure (this condition is called Tumour Lysis Syndrome) (see also section 4 “Possible side effects”).

Your doctor should evaluate if you develop additional types of haematological malignancies (called acute myeloid leukaemia and myelodysplastic syndromes) during your treatment with Thalidomide Celgene (see also section 4 “Possible side effects”).

You must not donate blood during Thalidomide Celgene treatment and for at least 7 days 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.

Other medicines and Thalidomide Celgene

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines. 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 antihistamines, opiate derivatives and barbiturates).
- slow the heart rate (induce bradycardia, such as anticholinesterases and beta blockers).
- are used for heart problems and complications (such as digoxin), or for thinning the blood (such as warfarin).
- are associated with neuropathy such as other treatments for cancer.
- are used for contraception.

Thalidomide Celgene with food, drink and alcohol

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 one effective method of contraception if you are a woman who is able to become pregnant (see section 2, “What you need to know before you take 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 “What you need to know before you take Thalidomide Celgene”. If your partner becomes pregnant whilst you are taking thalidomide, you should inform your doctor immediately.

Breast-feeding

Do not breastfeed when taking Thalidomide Celgene 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 or pharmacist has told you to. Check with your doctor or pharmacist 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

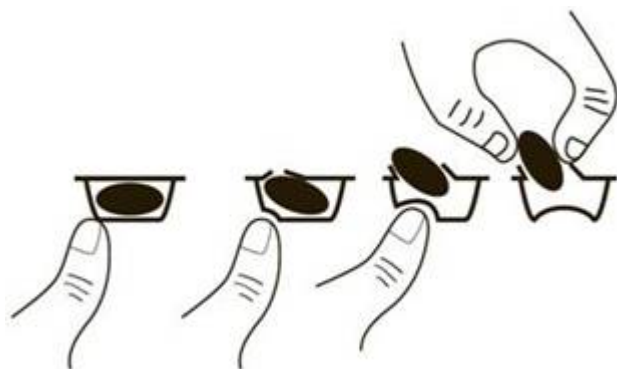
dose for you, monitor your progress and may adjust your dose. Your doctor will tell you how to take Thalidomide Celgene and for how long you will need to take it (see section 2, “What you need to know before you take Thalidomide Celgene”).

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.
- Healthcare professionals, caregivers and family members should wear disposable gloves when handling the blister or capsule. Gloves should then be removed carefully to prevent skin exposure, placed in a sealable plastic polyethylene bag and disposed of in accordance with local requirements. Hands should then be washed thoroughly with soap and water. Women who are pregnant or suspect they may be pregnant should not handle the blister or capsule.
- 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 medicine, 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:

- Extremely intense and serious skin reactions. The adverse reaction of the skin may appear as rashes with or without blisters. Skin irritation, sores or swelling in the mouth, throat, eyes, nose and around the genitals, oedema and fever and flulike symptoms may occur. These symptoms may be signs of the rare and serious skin reactions Stevens-Johnson syndrome, toxic epidermal necrolysis or DRESS syndrome.
- Allergic reactions such as a localised or generalised pruritic rash, angioedema and anaphylactic reaction (serious types of allergic reaction that may be manifested as hives, rashes, swelling of eyes, mouth or face, difficulty of breathing, or itching).

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

- **Numbness, tingling, abnormal coordination 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).
- Decreased or abnormal sensation (dysaesthesia).
- 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.
- A fall in the number of white blood cells (neutropenia) accompanied by fever and infection.

- A fall in the number of red and white blood cells and platelets at the same time (pancytopenia).
- Feeling weak, faint or unsteady, lack of energy or strength, low blood pressure.
- Fever, feeling generally unwell.
- Convulsions.
- 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.
- Hearing decreased or deafness.
- Kidney disease (renal failure).

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.
- Bowel obstruction.
- Fall of blood pressure on standing which may lead to fainting.
- Irregularities of the heartbeat (heart block or atrial fibrillation), feeling faint or fainting.

Not known (frequency cannot be estimated from the available data) :

- Underactive thyroid (hypothyroidism).
- Sexual dysfunction, for example impotence.
- Severe blood infection (sepsis) accompanied by fever, chills and severe shaking, and possibly complicated by low blood pressure and confusion (septic shock).
- 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.
- Injury to the liver (hepatic disorder) including abnormal liver test results.
- Bleeding from the stomach or bowels (gastrointestinal haemorrhage).
- 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 heartbeat, 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).
- A brain condition with symptoms including vision changes, headache, seizures, and confusion, with or without high blood pressure (Posterior Reversible Encephalopathy Syndrome or PRES).
- A condition affecting the skin caused by inflammation of small blood vessels, along with pain in the joints and fever (leukocytoclastic vasculitis).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Thalidomide Celgene

Keep this medicine out of the sight and reach of children.

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

Do not use if you notice any damage or signs of tampering.

This medicine does not require any special storage conditions.

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

6. Contents of the pack and other information

What Thalidomide Celgene contains

- The active substance is thalidomide. Each capsule contains 50 mg of thalidomide.
- The other excipients are:
 - The capsule content contains pregelatinised 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).

Marketing Authorisation Holder

Celgene Europe B.V.
Winthontlaan 6 N
3526 KV Utrecht
Netherlands

Manufacturer

Celgene Distribution B.V.
Winthontlaan 6 N
3526 KV Utrecht
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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: <http://www.ema.europa.eu>. There are also links to other websites about rare diseases and treatments.