Patient package insert in accordance with the pharmacists' regulations (preparations) - 1986

This medicine is dispensed only by a physician's prescription

Thalidomide BMS® 50mg Hard Capsules

Composition:
Name and Quantity of active ingredient:
Each capsule contains: Thalidomide 50mg

Inactive ingredients - See section "Additional information".

Read this package insert carefully in its entirety before using this medicine and every time this medicine is prescribed to you, as it may contain newer information. It is recommended to read this insert with another family member.
This leaflet contains summary information about this medicine. If you have any further questions, refer to the physician or the pharmacist.

This medicine has been prescribed for treating your illness. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

Do not give this medicine to a child under the age of 12 years.

Safety and effectiveness in children younger than 12 years have not been established.

Thalidomide has caused severe birth defects when taken during pregnancy. Thalidomide should never be used by women who are pregnant or who could become pregnant whilst taking the medicine or could become pregnant within 4 weeks after stopping the medicine. Even a single dose can cause birth defects.

1. What is this medicine intended for?

This medicine is indicated for the treatment of multiple myeloma and certain symptoms of leprosy.

Therapeutic group: Immunosuppressive agent

2. Before using this medicine

Do not use this medicine if:

Women:

! Do not use this medicine **if you are pregnant, think you may be pregnant or are planning to become pregnant or are breastfeeding**. If you take it during pregnancy, Thalidomide BMS 50mg Hard Capsules causes birth defects (deformed babies) and death to an foetus and may affect your developing foetus.

Thalidomide BMS 50mg Hard Capsules should never be used by women who are pregnant, and women of childbearing potential who are not using, not willing or not able to use adequate contraceptive measures to prevent pregnancy or not willing to choose continuous abstinence from heterosexual sexual contact as a contraceptive method in order to prevent pregnancy (please see **warnings**).
You should wait 4 weeks after the end of the treatment before trying to get pregnant.

! Breastfeeding - do not use Thalidomide BMS 50mg Hard Capsules if you are breastfeeding. Do not begin breastfeeding within 4 weeks after stopping treatment.

Men:

! Do not use this medicine **if you are not able or willing to comply with adequate contraceptive measures** (please see **warnings**).

Male patients who are taking Thalidomide BMS 50mg Hard Capsules should use a condom with every sexual intercourse with a female partner of childbearing potential, during treatment, during dose interruptions and for 4 weeks after stopping treatment, even if you have undergone a successful vasectomy.

! Do not donate semen while taking the medicine, during any breaks (interruptions) in your treatment, and for 4 weeks after stopping the medication.

All patients:

! Do not donate blood during treatment and for 4 weeks after stopping treatment.

! Do not take Thalidomide BMS 50mg Hard Capsules if you are hypersensitive (allergic) to thalidomide, or any of the other ingredients of Thalidomide BMS 50mg Hard Capsules - see section “Additional information".

Special warnings regarding the use of the medicine
Do not use this medicine without consulting a physician before starting treatment:

For men:

If your female partner is pregnant or intends to become pregnant.

For all patients:
If you have or have had any of the following medical conditions:

- Heart attack, blood clots, high blood pressure or high cholesterol
- Diabetes
- Frequent infections
- Hepatitis B virus infection
- Numbness, tingling or pain in your hands and feet
- Severe skin rash
- Seizures
- Thyroid problems
- You have had surgery in the previous 7 days or have wounds which are healing

- Kidney or liver problems.

It is important to note that a small number of patients with multiple myeloma may develop additional types of cancer (regardless of their type of therapy). At this stage it cannot be excluded that this risk may be slightly increased with Thalidomide BMS 50mg Hard Capsules treatment. Therefore, your doctor will carefully evaluate the benefit and risk when you are prescribed this medicine.

If you feel light-headed, dizzy or faint when getting out of bed or standing up, get up slowly. Standing up slowly, especially when you get up from bed or chairs, will help your body get used to the change in position and blood pressure. If this problem continues or gets worse, talk to your physician.

Your physician will enroll you in the Risk Management Program/Pregnancy Prevention Program (RMP/PPP).
This program intends to help your physician advise you concerning the risks involved in thalidomide treatment and ensures that you are aware of the precautions that you should take before, during and after treatment.
Follow your physician's instructions carefully.

You will have been given specific instructions by your physician particularly on the effects of thalidomide on foetuses.

If you have not fully understood these instructions, please ask your physician again before taking thalidomide.

Children and adolescents
Do not give this medicine to a child under the age of 12 years.

Safety and effectiveness in children younger than 12 years have not been established.

Drug interactions
Tell the physician or the pharmacist if you are taking or have recently taken other medicines, including non-prescription medicines, food supplements or herbal medicines in order to prevent any risks or ineffectiveness resulting from drugs interactions.

It is especially important to inform your physician or pharmacist if you are taking:
- medicines that cause drowsiness, such as sleeping pills
- medicines used to treat depression or anxiety
- medicines used to treat heart problems and/or high blood pressure
- medicines that can induce bleeding, such as aspirin
- hormonal contraceptives
- medicines used to treat anaemia
- hormone replacement therapy
- medicines used in the treatment of cancer such as vincristine
- medicines used in the treatment of AIDS such as zalcitabine and didanosine.

These medicines may be affected by Thalidomide BMS 50mg Hard Capsules or may affect how it works. You may need to take different amounts of your medicines, or you may need to take different medicines.

Taking this medicine with food
This medicine should be taken with water, at least one hour after food.

Use of this medicine and alcohol consumption
Do not drink wine or other alcoholic beverages during treatment with this medicine, because of the increasing of the sleepiness effect of the medicine by alcohol.

Pregnancy and Breastfeeding

Pregnancy:
Thalidomide causes severe birth defects or death of the foetus when taken during pregnancy. As little as one capsule taken by a pregnant woman can cause a baby to have serious birth defects. If you are pregnant, you must not take Thalidomide BMS. In addition, you must not become pregnant while taking Thalidomide BMS.
If you have any delay in your period, or there is any fear that you have become pregnant, you must stop treatment immediately, a pregnancy test should be performed and you should immediately inform your physician.
If you become pregnant during the treatment, you must stop treatment immediately and inform your physician. If your partner becomes pregnant during the treatment, you must inform your physician.

Women of childbearing potential (including women that chose complete abstention from heterosexual sexual intercourse as a contraceptive measure) must undergo a pregnancy test to exclude pregnancy prior to starting treatment (just before prescribing, within 3 days prior to prescribing Thalidomide BMS) and then monthly during treatment including dose interruptions of Thalidomide BMS 50mg Hard Capsule, and for 4 weeks following discontinuation of thalidomide therapy.

Women of childbearing potential should have pregnancy tests (even in case of complete abstention from heterosexual sexual intercourse) except in the following cases*:
If you have undergone a hysterectomy.
If you have undergone a bilateral oophorectomy.
If you have been postmenopausal naturally for at least 24 consecutive months.
if you are a child/adolescent who has not received her first period or in any other case indicated by your physician.

* the physician may take different measures to exclude pregnancy and to verify that women are not of childbearing potential status.

Please pay attention: Cecession of menses due to anti-cancer therapy does not exclude the potential to become pregnant.

Women of childbearing potential should use two methods of birth control at the same time every time (at least one highly effective method, e.g. hormonal contraception (e.g. contraceptive pills) and one additional barrier contraceptive method – (e.g. condom)), at least 4 weeks before starting Thalidomide BMS treatment, during this treatment, during dose interruptions and for 4 weeks following termination of this treatment unless continuous abstinence from heterosexual sexual contact is the chosen method.

Reliable contraception methods are indicated even where there has been a history of infertility, unless due to hysterectomy, a bilateral oophorectomy, because the patient has been postmenopausal naturally for at least 24 consecutive months or in any other case indicated by the physician.

Your physician will advise you regarding the choice of adequate contraceptive methods.

Do not donate blood during treatment and for 4 weeks after stopping its use.

Breastfeeding:
Do not take Thalidomide BMS if you are breastfeeding. It is not known if thalidomide is passed into breast milk. However, as thalidomide is known to cause birth defects, do not breastfeed while you are receiving this medicine and for 4 weeks after the end of treatment.

Driving and using machines
Do not drive or operate machinery until you know how Thalidomide BMS 50mg Hard Capsules affects you.

This medicine may cause drowsiness or dizziness in some people.

Warnings:

Male Patients:
Male patients who are taking Thalidomide BMS should always use a condom during sexual intercourse with a female partner of childbearing potential, during treatment and for 4 weeks after stopping treatment, even if they have undergone a successful vasectomy.
In the case of a male patient with an allergy to latex or polyurethane, at least one highly efficacious method should be used by any female sexual partner.
Contraception should be started in this partner at least 4 weeks prior to the start of a sexual relationship with the patient, and continued throughout Thalidomide treatment and for an additional 4 weeks following cessation of treatment.
Male patients taking Thalidomide should not donate semen during treatment including dose interruptions and for 4 weeks after stopping treatment.

Male patients taking Thalidomide should not donate blood during treatment and for 4 weeks after stopping treatment**.**

3. How to use this medicine?

Always use according to the physician's prescription. Your physician will choose the dose for you, monitor your progress and may adjust your dose. Your physician will tell you how much Thalidomide BMS Hard Capsule to take and for how long you will need to take it.

If you are not sure, ask your physician or a pharmacist. **Do not exceed the recommended dose.**
Do not break, open or chew the hard capsule. Swallow the capsules whole with a full glass of water.

If you have to take multiple capsules, take them as a single dose before going to bed.

This will make you feel less sleepy at other times.

The dosage and treatment will be determined by the physician only. The usual dose for the treatment of newly diagnosed multiple myeloma, is 200mg a day, taken in treatment cycles lasting 4 to 6 weeks, in combination with the following medicines:

- melphalan and prednisolone which are taken on days 1 to 4 of each 6-week cycle.

- dexamethasone which is taken on days 1 to 4, 9 to 12 and 17 to 20 of each 4-week cycle.

For newly diagnosed multiple myeloma patients above 75 years of age taking Thalidomide BMS 50mg Hard Capsules in combination with melphalan and prednisone, the thalidomide recommended starting dose is 100 mg per day.

For the treatment of multiple myeloma after failure of other treatments, doses of Thalidomide BMS 50mg Hard Capsules from 200mg a day up to 400mg a day may be given.

For the treatment of erythema nodosum leprosum, Thalidomide BMS 50mg Hard Capsules may be given in doses of 100 to 400mg a day.

Tests and Follow-up:
Women of childbearing potential – before starting treatment your physician will perform pregnancy testing and will repeat the test each month during the treatment. Your physician may perform some tests (blood tests, nerve function tests, etc.) from time to time to make sure the medicine is working and to prevent unwanted side effects.

If you forgot to take this medicine at the specified time, and less than 12 hours have passed, take your capsule immediately. Take your next capsule at the usual time.

If more than 12 hours have passed, do not take your capsule. Take your next capsule at the usual time the next day.
If you are not sure what to do, ask your physician or pharmacist.

If you have trouble remembering when to take your medicine, ask your pharmacist for some tips.

Persist with the treatment as recommended by the physician.
If you have taken an overdose, or if a child accidentally swallowed the medicine, proceed immediately to a hospital emergency room and bring the package of the medicine with you. Do it even if you don't feel uncomfortable or symptoms of poisoning.

Complete the full course of treatment as instructed by the physician.
Even if there is an improvement in your health, do not discontinue use of this medicine without consulting your physician.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take your medicine. Wear glasses if you need them.

If you have any additional questions regarding the use of the medicine, consult the physician or the pharmacist.

4. <u>Side effects</u>

Like all medicines, Thalidomide BMS 50 mg Hard Capsules can cause side effects in some of the patients. Do not be alarmed by the list of side effects. You may not experience any of them.

Tell your physician or pharmacist as soon as possible if you do not feel well while you are taking Thalidomide BMS 50 mg Hard Capsules.

Stop taking Thalidomide BMS and see a physician immediately or go to a Hospital Emergency Room if you notice the following serious side:

- Sudden signs of allergy such as rash, itching or hives on the skin; swelling of the face, lips or tongue or other parts of the body; and/or shortness of breath, wheezing or trouble breathing.
- Severe skin reactions including painful red patches on the skin; blisters; bleeding in the lips, eyes, mouth and nose; and peeling of the skin. You may have a high temperature (fever), chills and muscle ache at the same time. This could be due to rare but severe skin reactions such as Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis and Drug Reaction with Eosinophilia and Systemic Symptoms.
- Blurred vision; severe headache; weakness or numbness in the face, arm or leg; trouble speaking or understanding; loss of balance.

  This may be due to a stroke which could be a result of blood clots in the blood vessels of your brain.
- Sudden pain in your chest or difficulty in breathing.

  This may be due to a heart attack or blood clots in the artery leading to your lungs. 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. These can happen during treatment, or after treatment has stopped.
- Feeling short of breath or getting tired easily after light physical activity, and swollen ankles and feet.

  This could be due to high blood pressure in the lungs or heart failure, a condition where the heart muscle cannot pump blood strongly enough to supply blood throughout the body.
- Vomiting blood or material that looks like coffee grounds, bleeding from the back passage, black sticky bowel motions (stools) or bloody diarrhoea.

  These could be signs of bleeding in your gut.
- Abdominal pain, dark urine, fever, joint pain, loss of appetite, nausea and vomiting, yellowing of the skin and/or eyes.

  These are symptoms of liver failure which, in some cases, may be due to Hepatitis B virus infection. Some cases of Hepatitis B virus infection may not result in symptoms initially.

The above list includes very serious side effects. You may need urgent medical attention. Most of these side effects are uncommon (affects 1 to 10 users in 1,000).

Contact your physician immediately if you notice any of the following:

- Numbness, tingling, abnormal co-ordination or pain in your palms hands and feet. This may be due to nerve damage. It may become very severe, painful and disabling. If you experience such symptoms, refer to your physician immediately, 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 some time after treatment has stopped. It may not go away, or may go away slowly.

- Signs of frequent infections such as fever, severe chills, sore throat or mouth ulcers; bleeding or bruising more easily than normal; and tiredness, headaches, shortness of breath, dizziness and looking pale.

  This may be due to low numbers of blood cells in your body. Your doctor may monitor your blood cell numbers during treatment with Thalidomide.
- Chest pain and dry cough.

  This may be due to a chest infection e.g. pneumonia, or other lung problems.
- Seizures, fits or convulsions.
- Blurred, loss of or double vision, difficulty speaking, weakness in an arm or a leg, a change in the way you walk or problems with your balance, persistent numbness, decreased sensation or loss of sensation, memory loss or confusion. These may be symptoms of a serious and potentially fatal brain condition known as progressive multifocal leukoencephalopathy (**PML**).

The above list includes serious side effects that may require medical attention.

Other side effects:
Tell your physician or pharmacist if you notice any of the following and they worry you:

- Constipation, indigestion, feeling sick (nausea), being sick (vomiting), stomach pain, dry mouth
- Rash, dryness of the skin
- Fainting, dizziness, sleepiness, feeling tired, shaking (tremor), headache, blurred vision, difficulty in co-ordinating movement, loss of balance
- Swelling of hands and feet, feeling generally unwell, feeling weak, feeling cold
- Depression, confusion, mood changes, anxiety
- Low blood pressure; a spinning feeling in your head, making it difficult to stand up and move normally
- Slow heart rate
- Muscle cramps
- Decreased sexual drive, abnormal periods

The above list mainly includes the more common side effects of your medicine.

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

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" that appears on the homepage of the Ministry of Health's website (www.health.gov.il) which links to an online form for reporting side effects, or by the following link:
https://sideeffects.health.gov.il
in addition, you can report by emailing the Registration Holder's Patient Safety Unit at: drugsafety@neopharmgroup.com

5. How to store this medicine?

Avoid poisoning! This medicine, and all other medicines, must be stored in a closed place out of the reach and sight of children and/or infants, to avoid poisoning.

Do not induce vomiting unless explicitly instructed to do so by a physician!
Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.

Keep out of the reach and sight of children and any other person not directly involved in the treatment.
Store the blister in the original carton pack, at a temperature below 25°C, protect from light.
Even if kept in their original container and stored as recommended, medicines may be kept for a limited period only. Please note the expiry date of the medicine! In case of doubt, consult the pharmacist who dispensed the medicine to you.
Do not store different medications in the same package.

6. Additional information

In addition to the active ingredient this medicine contains:
Pregelatinized maize starch, Magnesium stearate, Titanium Dioxide, Gelatin, Printing ink.

How does the medicine look like and what is the content of the package - Thalidomide BMS are white hard capsules marked “Thalidomide BMS 50 mg”. The capsules are supplied in a wallet card containing 28 capsules (2 blisters of 14 capsules each).

Registration Holder: Neopharm Ltd., 8 Hashiloach St., P.O.B. 7063, Petach Tiqva 49170.
Manufacturer:
Celgene International Sarl, Boudry, Switzerland
Or
Celgene Distribution BV, Utrecht, The Netherlands

Revised in April 2022 according to MOH guidelines

Registration number of the medicine in the Ministry of Health’s National Drug Registry: 131 42 31004