PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Lenalidomide Teva 2.5 mg
Lenalidomide Teva 5 mg
Lenalidomide Teva 7.5 mg
Lenalidomide Teva 10 mg
Lenalidomide Teva 15 mg
Lenalidomide Teva 20 mg
Lenalidomide Teva 25 mg
Hard capsules
Composition:
Each hard capsule of Lenalidomide Teva 2.5 mg contains:
Lenalidomide 2.5 mg (as hydrochloride hydrate)
Each hard capsule of Lenalidomide Teva 5 mg contains:
Lenalidomide 5 mg (as hydrochloride hydrate)
Each hard capsule of Lenalidomide Teva 7.5 mg contains:
Lenalidomide 7.5 mg (as hydrochloride hydrate)
Each hard capsule of Lenalidomide Teva 10 mg contains:
Lenalidomide 10 mg (as hydrochloride hydrate)
Each hard capsule of Lenalidomide Teva 15 mg contains:
Lenalidomide 15 mg (as hydrochloride hydrate)
Each hard capsule of Lenalidomide Teva 20 mg contains:
Lenalidomide 20 mg (as hydrochloride hydrate)
Each hard capsule of Lenalidomide Teva 25 mg contains:
Lenalidomide 25 mg (as hydrochloride hydrate)
For a list of inactive ingredients and allergens in the preparation, see section 6 - "Additional information".
Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have additional questions, refer to the doctor or the pharmacist.
This medicine has been prescribed for treatment of 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.

Your doctor will register you to a risk management program/ pregnancy prevention program (RMP/PPP).
The aim of the program is to help the doctor keep you updated about the risks involved in treatment with Lenalidomide Teva and to make sure you are aware of the precautions you must take before, during and after treatment.

1. What is the medicine intended for?

Lenalidomide Teva is used:
- For treatment of adult patients who have low red blood cell counts, a condition called myelodysplastic syndrome (MDS). Lenalidomide Teva 7.5 mg is not indicated for treatment of MDS.
- For treatment of newly diagnosed patients with multiple myeloma who are unable to undergo a bone marrow transplant. In combination with dexamethasone, for treatment of adult patients who have been diagnosed with multiple myeloma who have received at least one prior therapy.
- For treatment of adults with refractory and/or relapsed mantle cell lymphoma (MCL).

Lenalidomide Teva can increase the number of red blood cells that the body produces by reducing the number of abnormal cells. The treatment can reduce the number of blood transfusions needed.
Therapeutic class:
Immunomodulating agents.

2. Before using the medicine

Do not use this medicine if:

- You are hypersensitive (allergic) to lenalidomide or any of the other ingredients the medicine contains (listed in section 6).
- Do not donate blood during Lenalidomide Teva therapy, during any breaks (discontinuations) in your therapy, and for 4 weeks after stopping therapy.

Women:
- Do not use this medicine if you are pregnant or are planning to become pregnant. Lenalidomide Teva may be dangerous to the fetus; therefore, if you are a woman of childbearing potential, do not use the medicine without using two reliable forms of contraception (please see section 2 "Special warnings regarding the use of the medicine").
- You should wait 4 weeks after the end of the treatment before trying to become pregnant.
- Do not breastfeed while using Lenalidomide Teva, during any breaks (discontinuations) in your therapy and for 4 weeks after stopping Lenalidomide Teva therapy.

Men:
- Do not use this medicine **If you are not able or willing to use a condom in every sexual intercourse with a woman of childbearing potential** (please see section 2 "Special warnings regarding the use of the medicine").
- Do not donate semen or sperm while taking Lenalidomide Teva, during breaks (discontinuations) in your therapy and for 4 weeks after stopping Lenalidomide Teva therapy.

Special warnings regarding the use of the medicine

Before treatment with Lenalidomide Teva, inform the doctor if:
- You have kidney problems or receive kidney dialysis treatment.
- You have liver problems.
- You have had a heart attack, stroke, have ever had a blood clot, or if you smoke, have high blood pressure or high cholesterol levels.
- You have a history of blood clots or if you are taking medicines that can increase the risk for blood clots. Blood clots in the arteries, veins, and lungs occur more often in people who take lenalidomide. This risk is even higher for people with multiple myeloma who take the medicine dexamethasone together with Lenalidomide Teva. Heart attacks and strokes also occur more often in people who take lenalidomide together with dexamethasone. To reduce this increased risk, most people who take Lenalidomide Teva will also take blood-thinning medicines.
- You have a high total amount of tumors throughout your body, including in your bone marrow. This could lead to a condition where the tumors break down and cause unusual levels of chemicals in the blood, which may lead to kidney failure (this condition is called Tumor Lysis Syndrome).
- You have any sign of inflammation, such as a cough or fever.
- You have or have ever had a viral infection, particularly viral hepatitis B infection, herpes zoster, or HIV. If you are in doubt, talk to your doctor. Treatment with Lenalidomide Teva may cause the virus to become active again in patients who carry the virus, resulting in a recurrence of the infection. Your doctor will check whether you have ever had viral hepatitis B infection.
- You have had an allergic reaction while taking thalidomide, such as rash, itching, swelling, dizziness or breathing difficulties.
- If you have a myelodysplastic syndrome, you may be more likely to get a more advanced condition called acute myeloid leukemia (AML). In addition, it is not known how Lenalidomide Teva affects your chances of getting AML. Your physician must perform tests to check for signs which may better predict the likelihood of getting AML syndrome during your treatment with Lenalidomide Teva.

Safety and efficacy of this medicine have not been studied in children and adolescents under the age of 18.

Tests and follow-up:
Before and during treatment with Lenalidomide Teva you will have regular blood tests, as the medicine may cause a fall in the blood cells that help to fight infections and help the blood to clot.
If you have 5q del myelodysplastic syndromes (MDS), you will be required to have your blood counts checked weekly during the first 8 weeks of treatment with Lenalidomide Teva, and at least monthly until the end of the treatment.
If you have multiple myeloma (MM), you will be required to have your blood counts checked every 2 weeks for the first 12 weeks and then at least monthly until the end of the treatment.
If you have mantle cell lymphoma (MCL), you will be required to have a complete blood count every week for the first treatment cycle (28 days), every 2 weeks during cycles 3-4, and then monthly until the end of treatment.
Your physician may adjust your dose of Lenalidomide Teva or stop your treatment depending on the results of your blood tests and your general condition.

Women of childbearing potential:
You should get tested for pregnancy under your physician's supervision (before starting therapy and then monthly during therapy, during dose interruptions and 4 weeks after stopping therapy), apart from the following cases: if you have undergone a hysterectomy, if you have undergone a bilateral oophorectomy, have been postmenopausal naturally for at least 24 consecutive months or in any other case indicated by your physician.
***Cessation of menses due to anti-cancer therapy does not exclude the potential to become pregnant.**
You must use 2 methods of birth control at the same time every time for 4 weeks before starting therapy, during therapy, during dose interruptions and for 4 weeks after stopping therapy, unless continuous abstinence from heterosexual sexual contact is the chosen method. Your physician will advise you on appropriate methods of contraception.

Men:
If your female partner is able to become pregnant or is pregnant, you must use a condom during Lenalidomide Teva therapy and for 4 weeks after the end of therapy, even if you have undergone a successful vasectomy.
In the case of a male patient with an allergy to latex or polyurethane, at least one effective form of contraception 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 Lenalidomide Teva therapy, and for additional 4 weeks following discontinuation of therapy.
You should not donate semen or sperm during therapy, during any breaks (discontinuations) in your therapy, and for 4 weeks after the end of therapy.

Drug-drug interactions:
If you are taking or have recently taken other medicines, including non-prescription medicines and food supplements, tell the doctor or the pharmacist.
Especially inform the doctor or pharmacist if you are taking:
- Erythropoietic agents (treating anemia), or other agents that may increase the risk of thrombosis in blood vessels, such as hormone replacement therapy and oral contraceptives (birth control pills).
- Warfarin – close monitoring of warfarin blood concentration is advised during combined treatment with dexamethasone.
- Digoxin – periodic monitoring of digoxin blood concentration is advised during treatment with Lenalidomide Teva.

Use of the medicine and food:
The medicine can be taken either with or without food.

Pregnancy and breastfeeding:
Do not use this medicine if you are pregnant or are planning to become pregnant. Lenalidomide may be dangerous to the fetus; therefore if you are a woman of childbearing potential do not take this medicine without using effective forms of contraception. (See section 2 "Special warnings regarding the use of the medicine").
If you do become pregnant during Lenalidomide Teva therapy, you must stop the therapy and inform your physician immediately. You should wait 4 extra weeks after the end of the treatment before trying to become pregnant.
Do not breastfeed during Lenalidomide Teva therapy, during any breaks (discontinuations) in your therapy, and for 4 weeks after stopping Lenalidomide Teva therapy.

Driving and operating machinery:
The use of this medicine may cause dizziness, tiredness, sleepiness or blurred vision and therefore caution should be exercised when driving a vehicle, operating dangerous machinery or performing any other activity that requires alertness.

3. How should you use the medicine?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the preparation.
The dosage and treatment regimen will be determined only by the doctor.
This medicine should be used at set intervals as determined by the treating doctor. It is important not to skip any dose.
Do not exceed the recommended dose.
Method of administration:
Do not open, chew or break the hard capsule!
The medicine should be swallowed whole with water.
You should take the medicine at about the same time every day.
The medicine can be taken either with or without food.
If powder from a broken capsule makes contact with the skin, wash the skin immediately and thoroughly with soap and water.
If you take a higher dosage:
If you took an overdose or a child accidentally swallowed this medicine, go to the doctor or the emergency room of the hospital immediately and take the package of the medicine with you.
If you forgot to take the medicine:
If you forget to take the medicine at your regular time and less than 12 hours have passed: take your hard capsule immediately.
If more than 12 hours have passed: do not take your hard capsule. Take your next hard capsule at the usual time the next day.
If you stop taking the medicine:
Do not discontinue use of this medicine without consulting your physician.
How can you contribute to the success of the treatment?
Complete the full course of treatment as recommended by the physician.
Even if there is an improvement in your health, do not discontinue this medicine without consulting your physician or a pharmacist.
Do not take medicines in the dark! Check the label and the dose <u>every time</u> you take the medicine. Wear glasses if you need them.
If you have any other questions regarding use of the medicine, consult the doctor or the pharmacist.

4. Side effects

As with any medicine, using Lenalidomide Teva may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Very common severe side effects (appear in more than 1 in 10 patients):
Lenalidomide Teva may reduce the number of white blood cells that fight infections and also the blood cells which help the blood to clot (platelets); this may lead to bleeding disorders e.g. nosebleeds and bruising. Lenalidomide Teva may also cause blood clots in the veins (thrombosis), arteries or lungs that can lead to pulmonary embolism, heart attack or stroke. Therefore, you **must tell your physician immediately** or get medical help if you experience:
- Signs or symptoms of a blood clot in the lung, arm, or leg may include: shortness of breath, chest pain, or arm or leg swelling.
- Signs or symptoms of a heart attack may include: chest pain that may spread to the arms, neck, jaw, back or abdominal area, feeling sweaty, shortness of breath, nausea or vomiting.
- Signs or symptoms of stroke may include: sudden numbness or weakness, especially on one side of the body, severe headache or confusion, or problems with vision, speech, or balance.
- Fever, chills, sore throat, cough, mouth ulcers or any other symptom of infection, including within the blood stream (sepsis).
- Bleeding or bruising in the absence of injury.

Other severe side effects:
Risk of new cancers (malignancies). People with multiple myeloma who receive melphalan (a type of chemotherapy) and have had stem cells transplant with the addition of lenalidomide have a higher risk of developing new cancers, including certain blood cancers (acute myeloid leukemia or AML) and a type of lymphoma called Hodgkin lymphoma.
Talk with your doctor about your risk of developing new cancers if you take Lenalidomide Teva. Your doctor will monitor you for new cancers during your treatment with Lenalidomide Teva.
Severe liver problems, including liver failure and death. Tell your doctor right away if you develop one or more of the following symptoms of liver problems:
- Yellowing of your skin or the white part of your eyes (jaundice).
- Dark or brown (tea-colored) urine.
- Pain in the upper-right side of your stomach area (abdomen).
- Bleeding or bruising more easily than usual.
- Feeling very tired.

Your doctor will order blood tests to check your liver function during your treatment with Lenalidomide Teva.
Severe skin reactions.
Severe skin reactions may occur with Lenalidomide Teva and may even lead to death. Call your doctor right away if you have any skin reaction while taking Lenalidomide Teva.
Tumor lysis syndrome (TLS).
TLS is caused by the fast breakdown of cancer cells. TLS can cause kidney failure and the need for dialysis treatment, abnormal heart rhythm, seizures and sometimes death. Your doctor may order blood tests to check you for TLS.
Worsening of your tumor (tumor flare reaction).
Tell your doctor if you get any of these symptoms while taking Lenalidomide Teva: light swelling of the lymph nodes, low-grade fever, pain or rash.

Other side effects are cited below
It is important to note that a small number of patients with multiple myeloma may develop additional types of cancer, and it is possible that this risk may be increased with Lenalidomide Teva treatment. Therefore, your physician should carefully evaluate the benefit versus the risk when you are prescribed Lenalidomide Teva.

Very common side effects (occurring in more than one out of ten users):
- A fall in the number of white blood cells (the cells that fight infections), platelets (the cells that help the blood to clot, which may lead to bleeding disorders) and red blood cells (anemia leads to tiredness and weakness).
- Constipation, diarrhea, nausea, redness of the skin, rashes, vomiting, muscle cramps, muscle aches, back, bone, limb or joint pain, tiredness, generalized swelling including swelling of the limbs.
- Fever and flu-like symptoms including fever, muscle aches, headache, earache and chills.
- Numbness, tingling or burning sensation in the skin, pain in hands or feet, dizziness, tremor, taste disturbance.
- Chest pain spreading to the arms, neck, jaw, back or stomach, feeling sweaty and breathless, nausea or vomiting, which may be symptoms of a heart attack (myocardial infarction).
- Decreased appetite, low levels of potassium in the blood.
- Leg pain (which could be a symptom of thrombosis), chest pain or shortness of breath (which may be symptoms of blood clots in the lungs, a condition called pulmonary embolism).
- Infections of all types.
- Infection of the lungs and the upper respiratory tract, shortness of breath, nosebleed.
- Blurry vision.
- Clouding of your eye (cataract).
- Kidney problems.
- Changes to protein values in the blood that can cause swelling of the arteries (vasculitis).
- Increase in your blood sugar level (diabetes).
- Dry skin.
- Abdominal pain.
- Mood swings, difficulty sleeping.
- Headaches.

Common side effects (occurring in 1-10 out of 100 users):
- Infection of the sinuses around the nose.
- Increase in pain sensation, tumor size and the redness around the tumor.
- Breathing difficulties.
- Bleeding from the gums, stomach or bowels, bruising.
- Increased blood pressure or a fall in blood pressure. Slow, fast or irregular heartbeat.
- Increased pigmentation of skin, increased hair growth.
- Skin eruptions, skin cracking, peeling skin, decreased tactile sensitivity.
- Hives, itching, dry skin, increased sweating, night sweats, dehydration.
- Sore and inflamed nasal membranes, mouth or stomach, dry mouth, difficulty swallowing, cough, hoarseness.
- Heartburn.
- Production of much more or much less urine than usual (which may be a symptom of kidney failure), passing blood in the urine, painful urination.
- Shortness of breath, especially when lying down (which may be a symptom of heart failure).
- Difficulty in obtaining an erection.
- Stroke, fainting.
- Muscle weakness.
- Joint swelling.
- Changes in blood levels of thyroid hormone, low levels of calcium, phosphate or magnesium in the blood.
- Depression, hallucinations, mood swings.
- Cataract (an eye disease that manifests as cloudy eye).
- Deafness.
- Abnormal liver test results.
- Impaired balance, movement difficulty.
- Ringing in the ears (tinnitus).
- Iron overload.
- Thirst.
- Confusion.
- Toothache.
- Weight loss.

Uncommon side effects (occurring in 1-10 out of 1,000 users):
- Bleeding within the skull.
- Circulatory problems.
- Loss of vision.
- Loss of sex drive (libido).
- Passing large amount of urine with bone pain and weakness, which may be symptoms of a kidney disorder (Fanconi syndrome).
- Inflammations of the large intestine (colitis and cecitis), both of which may be manifested as abdominal pain, bloating or diarrhea.
- Irritable bowel syndrome.
- Renal tubular necrosis (a type of kidney impairment) which may manifest in production of much more or much less urine than usual.
- Skin discoloration, sensitivity to sunlight.
- Certain types of skin tumors.
- Types of allergic reaction that may be manifested as hives, rash, swelling of the eyes, mouth or face, breathing difficulties or itching (hypersensitivity/angioedema).
- Fractures of bones, arthritis, low blood sugar.

Rare side effects (occurring in 1-10 out of 10,000 users):
- Serious allergic reaction that may begin as a rash in one area but spread with extensive loss of skin all over the body (Stevens-Johnson syndrome and/or toxic epidermal necrolysis).
- Tumor lysis syndrome - metabolic complications that can occur during treatment of cancer and sometimes even without treatment. These complications are caused by the breakdown products of dead 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, heartbeat, seizures, and sometimes death.

Side effects with unknown frequency:
- Sudden or mild but worsening pain in the upper abdomen and/ or back, which remains for a few days, possibly accompanied by nausea, vomiting, fever and a rapid pulse − these symptoms may be due to inflammation of the pancreas.
- Wheezing, shortness of breath or a dry cough, which may be symptoms caused by inflammation of lung tissue.
- Yellow pigmentation of the skin, mucus membranes or eyes (jaundice), pale-colored stools, dark-colored urine, skin tingling, rash, pain or swelling of the abdomen – these may be symptoms of injury to the liver (hepatic disorder).
- Rare cases of muscle breakdown (muscle pain, weakness or swelling) which may lead to kidney problems (rhabdomyolysis) have been observed, some of them when lenalidomide was prescribed together with a statin (a type of cholesterol-lowering medicine).
- A condition affecting the skin caused by inflammation of small blood vessels, accompanied by joint pain and fever (leukocytoclastic vasculitis).
- Breakdown of the wall of the stomach or intestine. This may lead to serious infections. Tell your doctor if you have severe stomach pain, fever, nausea, vomiting, blood in your stool, or changes in bowel habits (bowel movements).
- 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-colored urine, right-sided abdominal pain, fever and nausea).

If one of the side effects worsens, or when you suffer from a side effect not mentioned in the leaflet, consult a doctor.
Side effects may be reported to the Ministry of Health by clicking on the link "report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link:
http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/ or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor!
- 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.
- **The medicine should be stored below 25˚C.**

6. Additional information

In addition to the active ingredient the medicine also contains:
Capsule contents:
Microcrystalline cellulose, Croscarmellose Sodium, Talc, Silica Colloidal Anhydrous.
Capsule shell:
Gelatin, Titanium dioxide (E 171), Yellow iron oxide (E172) (Lenalidomide Teva 2.5mg, 7.5mg, 10mg and 20mg), Indigotine (E132) (Lenalidomide Teva 2.5mg, 10mg, 15mg and 20mg).
What does the medicine look like and what are the contents of the package:
Lenalidomide Teva 2.5 mg:
A hard, opaque capsule with a white body and a green cap. The number '2.5' is printed in black on the capsule's body.
Lenalidomide Teva 5 mg:
A hard, opaque, white capsule. The number '5' is printed in black on the capsule's body.
Lenalidomide Teva 7.5 mg:
A hard, opaque capsule with a white body and an ivory-colored cap. The number '7.5' is printed in black on the capsule's body.
Lenalidomide Teva 10 mg:
A hard, opaque capsule with an ivory-colored body and a green cap. The number '10' is printed in black on the capsule's body.
Lenalidomide Teva 15 mg:
A hard, opaque capsule with a white body and a blue cap. The number '15' is printed in black on the capsule's body.
Lenalidomide Teva 20 mg:
A hard, opaque capsule with a blue body and a green cap. The number '20' is printed in black on the capsule's body.
Lenalidomide Teva 25 mg:
A hard, opaque, white capsule. The number '25' is printed in black on the capsule's body.
Each package contains 7 or 21 hard capsules.
Not all package sizes may be marketed.
License holder and the address:
Abic Marketing Ltd. P.O.B 8077 Netanya.
Name and address of the manufacturer:
Teva Pharmaceutical Industries Ltd., Petah Tikva.
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Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Lenalidomide Teva 2.5 mg:	161.79.35877
Lenalidomide Teva 5 mg:	161.80.35500
Lenalidomide Teva 7.5 mg:	161.81.35501
Lenalidomide Teva 10 mg:	161.82.35502
Lenalidomide Teva 15 mg:	161.83.35503
Lenalidomide Teva 20 mg:	161.84.35504
Lenalidomide Teva 25 mg:	161.85.35505