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.

In addition to this leaflet, there is a patient information booklet for Lenalidomide Teva. This booklet contains important safety information that you must know before starting treatment with Lenalidomide Teva and during the treatment, and act accordingly. The booklet focuses on the risk of fetal defects. Read the patient booklet and the consumer leaflet before you start using the preparation. You should keep the booklet in case you need to review it again.

1. What is the medicine intended for?

Lenalidomide Teva is used in adult patients for treatment of:
- Multiple myeloma.
- Myelodysplastic syndromes (MDS).
- Mantle Cell Lymphoma (MCL).

Lenalidomide Teva 7.5 mg is not indicated for treatment of MDS.

Therapeutic class:
Immunomodulating agents.

How does Lenalidomide Teva work?
Lenalidomide Teva works by affecting the body's immune system and directly attacking the cancer. It has a number of different modes of action:
- Stopping the development of cancer cells
- Stopping the growth of blood vessels in the cancer
- Stimulating part of the immune system to attack the cancer cells

Multiple myeloma
Multiple myeloma is a type of cancer that affects a certain kind of white blood cell called 'plasma cell'. The collection and division of these cells in the bone marrow gets out of control. This can damage the bones and the 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 'response'.

Newly diagnosed multiple myeloma – in patients who have had a bone marrow transplant:
Lenalidomide Teva is used as a maintenance therapy after patients have recovered enough following a bone marrow transplant.

Newly diagnosed multiple myeloma – in patients who cannot have a bone marrow transplant:
Lenalidomide Teva is taken with other medicines:
- An anti-inflammatory medicine called 'dexamethasone'
- A chemotherapy medicine called 'melphalan'
- An immunosuppressant medicine called 'prednisone'

You will take these other medicines at the beginning of the treatment and then continue the treatment with Lenalidomide Teva on its own.
If you are 75 years old or older or if you have a moderate to severe kidney problem, your treating doctor should examine your condition carefully before starting treatment.

Multiple myeloma – in patients who have had treatment before:
Lenalidomide Teva is taken together with an anti-inflammatory medicine called 'dexamethasone'.
Lenalidomide Teva can stop the signs and symptoms of multiple myeloma from getting worse. Lenalidomide has also been shown to delay relapse of multiple myeloma following the treatment.

Myelodysplastic syndromes (MDS)
MDS is a group of many different blood and bone marrow diseases. The blood cells become abnormal and do not function properly. Patients can experience a variety of signs and symptoms including a low red blood cell count (anemia), the need for a blood transfusion, and be at risk of infection.
Lenalidomide Teva is used to treat adult patients who have been diagnosed with MDS.
Lenalidomide 7.5 mg is not indicated for treatment of MDS.
Lenalidomide Teva can increase the number of normal red blood cells that the body produces by reducing the number of abnormal cells. The treatment can reduce the number of blood transfusions needed. It is possible that no blood transfusions will be needed.

Mantle Cell Lymphoma (MCL)
MCL is a cancer of part of the immune system (the lymph tissue). It affects a type of white blood cell called 'B-lymphocytes' or B-cells. MCL is a disease where B-cells grow in an uncontrolled way and build up in the lymph tissue, bone marrow or blood. Lenalidomide Teva is used to treat adult patients who have previously been treated with other medicines.

2. Before using the medicine

Do not use this medicine if:

All patients:
You are sensitive (allergic) to lenalidomide or to any of the other ingredients this medicine contains (see section 6 – "Additional information").
Women:
- Do not use this medicine if **you are pregnant, think you may be pregnant or are planning to become pregnant.** Lenalidomide Teva may be dangerous to the fetus (please see the section "Pregnancy, breastfeeding and fertility – information for men and women"); therefore, if you are a woman of childbearing age – do not use the medicine without using the required contraception (please see the section "Pregnancy, breastfeeding and fertility – information for men and women").

Special warnings regarding the use of the medicine:
Before treatment with Lenalidomide Teva, inform the doctor if:
- You have a history of blood clots or if you take medicines that can increase the risk for blood clots. The risk to develop blood clots increases during the treatment.
- You have any sign of an infection, such as cough or fever.
- You have or have had a viral infection, particularly viral hepatitis B infection, herpes zoster, 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 kidney problems – your doctor may need to adjust your dose of Lenalidomide Teva.
- You have had a heart attack, stroke, have had a blood clot, or if you smoke, have high blood pressure or high cholesterol levels.
- You have had an allergic reaction while taking thalidomide (another medicine used to treat multiple myeloma), such as rash, itching, swelling, dizziness or trouble breathing.
- You have experienced in the past one or more of the following symptoms: facial rash or widespread rash, red skin, high fever, flu-like symptoms, enlarged lymph nodes (these are signs of a severe skin reaction called Drug Reaction with Eosinophilia and Systemic Symptoms, also known as DRESS, see section 4 – "Side effects").
- If you have a myelodysplastic syndrome, you are at risk of getting an advanced syndrome called acute myeloid leukemia (AML). In addition, it is not known how Lenalidomide Teva affects your chances of getting AML. Your doctor should perform tests to check for signs which may better predict the likelihood of you getting AML syndrome during your treatment with Lenalidomide Teva.

Children and adolescents:
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 to 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.
Your doctor will ask you to have periodic blood tests:
- Before treatment.
- Every week for the first 8 weeks of treatment.
- Thereafter at least once a month.

For patients with MCL taking Lenalidomide Teva, your doctor will ask you to have blood tests:
- Before treatment.
- Every week for the first 8 weeks (2 cycles) of treatment.
- Thereafter every 2 weeks in cycles 3 and 4 (see section 3 "Duration of treatment" for more information).
- After this, tests should be performed at the beginning of each treatment cycle and at least once a month.

- 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. If you are newly diagnosed with multiple myeloma, your doctor may assess your treatment based on your age and other conditions you may already have.
- Your doctor may check you for changes to your skin, such as red spots or rashes.
- For information about tests and follow-up related to using the medicine at childbearing age (for both men and women), please see the information in the box at the top of the leaflet, as well as the information under the section "Pregnancy, breastfeeding and fertility".

Blood donation:
Do not donate blood during Lenalidomide Teva therapy, during dose interruptions and for 4 weeks after stopping therapy.

The elderly and patients with kidney problems:
If you are 75 years old or older or if you have a moderate to severe kidney problem, your treating doctor should examine your condition carefully before starting treatment.

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 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).
- Some medicines used to thin the blood – such as warfarin. It is recommended to closely monitor (follow-up) warfarin blood levels during combination therapy with dexamethasone.
- Some medicines used for heart problems – such as digoxin. Periodic monitoring (follow-up) of digoxin blood levels is advised during treatment with Lenalidomide Teva.

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

Pregnancy, breastfeeding and fertility – information for men and women:

Pregnancy:
Information for women taking Lenalidomide Teva:
- Do not use this medicine if you are pregnant or are planning to become pregnant. Lenalidomide Teva may be harmful to the fetus; therefore, if you are a woman of childbearing age, do not take this medicine without using effective forms of contraception (see the section "Contraceptives").
- If you do become pregnant during Lenalidomide Teva therapy, you must stop the therapy and inform your physician immediately.
- You should wait 4 additional weeks after the end of the treatment before trying to become pregnant.

Information for men taking Lenalidomide Teva:
- If your female partner becomes pregnant while you are taking Lenalidomide Teva, inform the doctor immediately. Your partner is advised to seek medical advice as soon as possible.
- You must use effective methods of contraception (see the section "Contraceptives").

Breastfeeding:
Do not breastfeed during treatment with Lenalidomide Teva and during dose interruptions.

Contraceptives:
Information for women taking Lenalidomide Teva:
Before starting to use the preparation, ask your doctor about your ability to become pregnant, even if you think this is unlikely.
If there is a chance that you may become pregnant:
- You should get tested for pregnancy under your physician's supervision (before starting the treatment, and then monthly during the treatment, during dose interruptions and 4 weeks after stopping the treatment), unless you underwent a procedure that prevents your eggs from moving through the fallopian tubes into the uterus.

In addition -
- 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 abstinence from heterosexual sexual contact is the chosen method.

Your physician will advise you on appropriate methods of contraception.
Information for men taking Lenalidomide Teva:
Lenalidomide passes into human semen. If your female partner is pregnant or may become pregnant, you must use a condom while using the preparation and for at least 4 weeks after the end of the treatment (even if you underwent a vasectomy).
If using a condom is not possible, make sure that your partner uses at least one effective method of contraception for 4 weeks before starting the treatment, during the treatment, during dose interruptions and for 4 weeks after stopping the treatment.
You should not donate sperm during treatment with Lenalidomide Teva, during any dose interruptions and for 4 weeks after the end of the treatment.

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.

Do not exceed the recommended dose. This medicine should be used at set intervals as determined by the treating doctor. It is important not to skip any dose.

Duration of treatment:
This medicine is given in 28-day treatment cycles. You will take this medicine alone or in combination with other medicines as the treatment cycle advances. After 28 days, you will start a new 28-day treatment cycle. You should continue these treatment cycles until your doctor says otherwise.

How to take the medicine:
Swallow the medicine whole (preferably with water) once daily.
You should take the medicine at about the same time every day.
The medicine can be taken either with or without food.
Crushing/halving/chewing:
Do not open, chew or break the hard capsule.
If powder from a broken capsule comes into contact with the skin, wash the skin immediately and thoroughly with soap and water.

If you accidentally took 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 forgot 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.
Follow the treatment as recommended by the doctor.

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 stop treatment with the medicine without consulting the doctor.

Do not take medicines in the dark! Check the label and the dose every time 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 – may affect more than 1 in 10 users:
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:
- Shortness of breath, chest pain, or swelling in the arm or leg.
- Fever, chills, sore throat, cough, mouth ulcers or any other symptom of infection, including an infection within the blood stream (sepsis).
- Bleeding or bruising in the absence of injury.

Other severe side effects:
Risk of new cancers (malignancies). A small number of patients may develop additional types of cancer, and this risk is higher when using Lenalidomide Teva.
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.

Very common side effects - side effects that occur in more than 1 out of 10 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 shortness of breath, 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 - side effects that occur 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.
- Rise or 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.
- Urticaria (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), 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).
- Excess of iron.
- Thirst.
- Confusion.
- Toothache.
- Weight loss.

Uncommon side effects - side effects that occur in 1-10 out of 1,000 users:
- Bleeding within the skull.
- Circulatory problems.
- Loss of vision.
- Loss of sex drive (libido).
- Passing a large amount of urine with bone pain and weakness, which may be symptoms of a kidney impairment (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 manifest as urticaria (hives), rash, swelling of the eyes, mouth or face, breathing difficulties or itching (hypersensitivity/allergic angioedema).

Rare side effects - side effects that occur in 1-10 out of 10,000 users:
- A 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 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 levels of potassium, phosphorus, uric acid and low levels of calcium, consequently leading to changes in kidney function, heart rate (pulse), seizures, and sometimes death.

Side effects with unknown frequency (effects whose frequency has not yet been determined):
- 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 indicate 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 impairment).
- Rare cases of muscle breakdown (muscle pain, weakness or swelling) which can lead to kidney problems (rhabdomyolysis) have been observed, some of them when lenalidomide is prescribed 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, nausea).
- Widespread rash, high body temperature, liver enzyme elevations, blood abnormalities (eosinophilia), enlarged lymph nodes and other body organs involvement (Drug Reaction with Eosinophilia and Systemic Symptoms, also known as DRESS or drug hypersensitivity syndrome). Stop using Lenalidomide Teva if you develop these symptoms. You must inform your physician immediately or seek medical help (see the section "Special warnings regarding the use of the medicine").
- Rejection of solid organ transplant (such as kidney/heart).

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects:
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: https://sideeffects.health.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.

Storage:
Store below 25°C.
You should return any unused capsules to the pharmacy.

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 2.5 mg, 7.5 mg, 10 mg and 20 mg), Indigotine (E132) (Lenalidomide Teva 2.5 mg, 10 mg, 15 mg and 20 mg).
Printing ink:
Shellac, propylene glycol, black iron oxide (E172), potassium hydroxide, concentrated ammonia solution.

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 mark '2.5' is printed in black on the capsule's body.
Lenalidomide Teva 5 mg: A hard, opaque, white capsule. The mark '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 mark '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 mark '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 mark '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 mark '20' is printed in black on the capsule's body.
Lenalidomide Teva 25 mg: A hard, opaque, white capsule. The mark '25' is printed in black on the capsule's body.
Each package of Lenalidomide Teva 2.5 mg, 5 mg, 7.5 mg, 15 mg, 20 mg and 25 mg contains 7 or 21 hard capsules.
Each package of Lenalidomide Teva 10 mg contains 7, 21 or 42 hard capsules.
Not all package sizes may be marketed.

License holder and address:
Abic Marketing Ltd. P.O. box 8077 Netanya.

Name and address of the manufacturer:
Teva Pharmaceutical Industries Ltd., P.O. box 3190, Petah Tikva.
The leaflet was revised in December 2020.

Registration numbers 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

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