Patient Information Leaflet

Revlimid®

hard capsules (5, 10, 15 and 25 mg)

Lenalidomide

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Health Care Professionals are asked to report any suspected adverse reactions.

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

In this leaflet:

1. What is Revlimid and when is it used?

On medical prescription.
Revlimid contains the active substance lenalidomide, which affects certain cells and substances of the immune system and thus leads to inhibition of the formation of malignant blood cells.

Revlimid is used in patients with multiple myeloma (a malignant disease with pronounced proliferation of certain cells in the bone marrow) as monotherapy, or in combination with other medicines.

Revlimid is used as monotherapy to treat adult patients with multiple myeloma who have undergone a bone marrow transplant.

Revlimid is used in combination with bortezomib (a proteasome inhibitor) and dexamethasone (an anti-inflammatory medicine) for the treatment of adult patients newly diagnosed with multiple myeloma.

For newly diagnosed multiple myeloma patients who cannot undergo a bone marrow transplant, there are two types of treatment:
- In the first treatment option Revlimid is used in combination with an anti-inflammatory medicine called 'dexamethasone'.
- In the second treatment option Revlimid is used in combination with a 'melphalan' (a chemotherapy medicine) and "prednisone' (an immunosuppressant medicine). You will take these other medicines at the start of treatment and then continue to take Revlimid on its own.

Multiple myeloma patients who have had at least one other type of treatment before, Revlimid is taken together with an anti-inflammatory medicine called 'dexamethasone'.

Revlimid is used on its own for the treatment of adult patients in whom certain types of myelodysplastic syndrome (MDS) have been diagnosed. In patients with MDS the bone marrow does not form enough healthy blood cells in the body. Revlimid is used in certain types of MDS in which the patients have fewer red blood cells than normal, are dependent on blood transfusions and also have a certain chromosome mutation.

Revlimid is used on its own in patients with recurring mantle cell lymphoma (MCL, a certain type of cancer in the lymph system), who have already previously received another therapy that included bortezomib and a chemotherapy together with Rituximab.

2. Before you take or use Revlimid

Do not take Revlimid:
If you are pregnant or think you may be pregnant or are planning to become pregnant.

In women of childbearing age, unless strict contraceptive measures are taken; see "When is caution indicated with the use of Revlimid?".

In cases of hypersensitivity to the active substance lenalidomide or to any of the inactive ingredients.

When is caution indicated with the use of Revlimid?
You will have been given specific instructions by your doctor, particularly on the effects of Revlimid on unborn babies (outlined in the *i-SECURE* program).

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

If you do not fully understand these instructions, please ask your doctor to explain them again before you take Revlimid.

Contraception
In special cases the doctor can prescribe Revlimid for women who are able to become pregnant. If this is so in your case, it is absolutely essential that you follow the doctor's instructions exactly. The following points are very important:
1. Before the start of the treatment your doctor will check that you are not pregnant and he/she will also carry out a pregnancy test every 4 weeks during the whole period of the treatment and again 4 weeks after the end of the treatment.
2. Your doctor, or another doctor, will advise you about appropriate methods of contraception suitable for you. You must begin to use two effective methods at the same time every time when having sexual contact with a male for 4 weeks before the start of the treatment and strictly keep to this not only during the period of the treatment, including periodic interruptions, but also for 4 weeks after the end of the treatment.

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

Effective Methods:
- Male condom
- Diaphragm
- Cervical cap

If you are able to become pregnant, your doctor will record with each prescription that the necessary measures, as outlined above, have been taken and will state that on the relevant *i-SECURE* documents.
3. If, despite keeping strictly to the methods of contraception, you become pregnant, or you think that you are pregnant, during the treatment with Revlimid or within one month after the end of the treatment, you must tell you doctor immediately. Your doctor will then take the necessary measures.

Male patients who have sexual relations with a woman of childbearing age must use condoms during the period of the treatment, including periodic interruptions, and for 4 weeks after the end of the treatment. They must also not donate sperm during, and for 4 weeks after the end of treatment with Revlimid.

To All Patients:
Because of the risk to the unborn child, you must never pass on Revlimid to other persons. You must not donate blood during the period of treatment, including periodic interruptions and for 4 weeks after the end of the treatment.

The marketing authorisation holder of Revlimid provides the following material:
- Information on the problems concerning pregnancy when taking Revlimid.
- A form for you to sign, in order to confirm that you have understood the need to prevent a pregnancy while on treatment with Revlimid.

Take special care with Revlimid
Other precautions
During the treatment with Revlimid your doctor will carry out regular blood tests, as a reduction in the white blood cell, red blood cell and platelet counts can occur. Such reductions can lead to an increase in infections and bleeding complications. If bleeding occurs and/or patches of bruising appear on your body (e.g. nosebleeds or bruising) or if fever, sore throat, ulcers in the mouth or other signs of an infection appear, you should contact your doctor immediately.

Your doctor will also check your thyroid function before and during the treatment with Revlimid, as your thyroid may become overactive or underactive.

Furthermore, your doctor will carefully perform checks for a tumour flare reaction, which is a temporary increase of the tumour-related symptoms. Due to a tumour flare reaction symptoms like swollen and tender lymph nodes, low fever, pain and rash can occur.

Especially in mantle-cell lymphoma patients suffering from a high tumour burden at the beginning of treatment with Revlimid a so called tumour lysis syndrome can appear, caused by the fast lysis of the cancer cells. Consult your doctor if you notice symptoms like nausea, dyspnoea, irregular heartbeat, cloudy urine, fatigue and or joint trouble.

He/she will possibly check your cardiac function by means of an ECG, especially if you are at the same time using a drug that affects the cardiac function or if you are suffering from a certain heart disorder (QT syndrome). Consult your doctor if you develop chest pain spreading to the arms, neck, jaw, back or stomach, break out in a sweat and become breathless, and feel sick or vomit: these could be symptoms of a heart attack.

If you are taking heart medication with the active ingredient digoxin during your treatment with Revlimid, your doctor will monitor the concentration of digoxin in your blood.

Under the treatment with Revlimid there is an increased risk of the formation of blood clots in the blood vessels, called arterial thrombosis (for example heart attack, stroke) and venous thromboembolic events (for example venous thrombosis, pulmonary embolism). If signs of blood clotting appear, such as pain and/or swelling in a leg or arm, chest pain, sudden respiratory symptoms or coughing, you should contact your doctor immediately.

It is important to note that a small number of patients with multiple myeloma or mantle-cell lymphoma may develop additional types of cancer, and it is possible that this risk may be increased with Revlimid treatment. Therefore, your doctor will carefully evaluate the benefit and risk when you are prescribed Revlimid.

Taking other medicines, herbal or dietary supplements
Because of the increased risk of formation of blood clots, hormone replacement therapy after the menopause and treatment with drugs that stimulate the formation of red blood cells (erythropoietin) should not be carried out.

During the treatment with Revlimid your liver function can be decreased or the liver can be impaired. Inform your doctor if you have suffered from a liver problem in the past or present, if your renal function is impaired or if you take medication especially antibiotics, because these circumstances can increase the risk for liver impairment.

In some cases, organ transplant patients developed a rejection reaction against the transplant after the start of treatment with Revlimid. If you have an organ transplant, your doctor will monitor you for rejection reactions.

Possible allergic reactions can occur in the form of hives, rash, swelling of the eyes, mouth or face, shortness of breath or itching. More severe cases of allergic reactions can cause rashes that are locally confined in the beginning but will spread over the whole body leading to large areas of detaching skin. In addition to skin reactions, allergic reactions may in very rare cases be accompanied by fever, tiredness, lymph node swelling, an increase in a specific type of white blood cell (eosinophilia) and effects on the liver, kidney or lung (called DRESS). These allergic reactions can be fatal. Tell your doctor immediately if you develop these symptoms.

Because of its inhibitory effect on the immune system, Revlimid can lead to vaccinations being ineffective or to vaccinations with live vaccines causing an infection. Therefore vaccinations should not be carried out during the treatment with Revlimid.

It is important to note that a small number of patients with multiple myeloma or mantle-cell lymphoma may develop additional types of cancer, and it is possible that this risk may be increased with Revlimid treatment. Therefore, your doctor will carefully evaluate the benefit and risk when you are prescribed Revlimid.

Revlimid should be used only with caution at the same time as other drugs which affect the immune system. Anticoagulant drugs should only be used after consulting the physician at the same time as Revlimid. You should therefore tell your doctor if you are using any other drugs.

If you have multiple myeloma you are susceptible to infections including pneumonia. Treatment with Revlimid in combination with dexamethasone can increase this susceptibility. Your doctor will monitor you for this and advise you to consult him/her immediately if you have signs of an infection, e.g. cough, fever.

Patients with poor general health are more likely to be intolerant of Revlimid combination therapies. For this reason your doctor will take your age and general health into consideration when carefully assessing whether you will be able to tolerate a combination therapy with Revlimid.

In a small number of patients who had previously been infected with the hepatits B virus, hepatitis B reactivation was observed during treatment with Revlimid. Your doctor will therefore carefully examine you for any signs or symptoms of an active infection with the hepatitis B virus while you are being treated with Revlimid. Inform your doctor if you have been infected with the hepatitis B virus in the past.

Pregnancy and Breast feeding
Revlimid must not be taken during pregnancy.
Women of child-bearing age should not become pregnant during treatment with Revlimid. In order to exclude the possibility of a pregnancy, pregnancy tests must be carried out before, during and at the end of the treatment with Revlimid, and effective methods of contraception must be used during and after the end of the treatment.

It is not known whether Revlimid passes into the mother's milk. Therefore Revlimid should not be administered during breast-feeding, or breast-feeding should be stopped and for 4 weeks after stopping treatment.

Lenalidomide has been shown to pass into human semen. Male patients with a partner of childbearing age must use condoms during and for 4 weeks after the end of the treatment with Revlimid.
Detailed information concerning contraception is to be found under the heading "When is caution indicated with the use of Revlimid?".

Driving and using machines
Because of possible side effects such as dizziness, fatigue or blurred vision, you should take special care when driving motor vehicles or operating machinery.

Important information about some of the ingredients of Revlimid:
Revlimid contains lactose. Therefore patients with certain rare hereditary disorders of the sugar metabolism (galactose intolerance, Lapp lactase deficiency, glucose-galactose malabsorption) should not take Revlimid.

Inform your doctor or your pharmacist if you are suffering from other diseases, have any allergies or are taking or applying externally other medicines (including medicines you have bought yourself!).

3. How to take or use Revlimid

How do you use Revlimid?
Always take Revlimid exactly as your doctor has told you. You should check with your doctor or your pharmacist if you are not sure.
Always take the Revlimid capsules at about the same time of day, with or without food, but with some water. The capsules must not be opened or chewed. Wash your hands immediately after they have come into contact with the capsules.

Take care not to inhale the powder contained in the capsules (e.g. if a capsule is damaged) and not to allow it to come into contact with the skin or the mucous membranes (eyes!). If it should nevertheless get onto the skin, wash with soap and water, and if it comes into contact with the eyes, rinse out thoroughly with water.

Dosage of Revlimid in combination with bortezomib and dexamethasone in patients with untreated multiple myeloma

The usual dose of Revlimid is 25 mg once daily. There are two different treatment schedules depending on your doctor's instructions:

a) Take Revlimid for 14 consecutive days. Then for the next 7 days, do not take Revlimid. A treatment cycle therefore lasts 21 days.
Or
b) Take Revlimid for 21 consecutive days. Then for the next 7 days, do not take Revlimid. A treatment cycle therefore lasts 28 days.

Your doctor will determine the dose of bortezomib, one of the medicines that you take in combination with Revlimid, based on your weight and height.

Depending on what your doctor has instructed, the dose of dexamethasone, the other medicine that you have to take in combination with Revlimid, is 20 mg once daily on days 1, 2, 4, 5, 8, 9, 11 and 12 of a treatment cycle or 40 mg once daily on days 1 to 4 and 9 to 12 of a treatment cycle.
This dosage can be individually adjusted at your doctor's discretion.

The usual administration schedule is described in the Tables below:

	Day (of 21-day cycle)													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15-21
Revlimid (25 mg)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	
Dexamethasone (20 mg)	•	•		•	•			•	•		•	•			

or

	Day (of 28-day cycle)																										
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22-28
Revlimid (25 mg)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	
Dexamethasone (40 mg)	•	•	•	•					•	•	•	•										

Dosage of Revlimid in multiple myeloma patients after bone marrow transplant
The usual dose of Revlimid is 10 mg once a day. This dose can be increased to 15 mg once a day after assessment by a doctor.

Dosage of Revlimid in combination with dexamethasone in patients with newly diagnosed multiple myeloma
The usual dose of Revlimid is 25 mg once a day. Take Revlimid for 21 consecutive days and then stop the treatment for the next 7 days. One treatment cycle thus lasts for 28 days.
The dosage of dexamethasone, the drug that you have to take in combination with Revlimid, is 40 mg once a day in patients under 75 years and 20 mg once a day in patients over 75 years. Take dexamethasone on days 1,8,15 and 22 of a 28-day treatment cycle. Your doctor may decide to adjust this dosage to your individual needs.

Dosage of Revlimid in combination with melphalan and prednisone in patients with newly diagnosed multiple myeloma
The usual dose of Revlimid is 10 mg once a day. Take Revlimid for 21 consecutive days and then stop the treatment for the next 7 days. One treatment cycle thus lasts for 28 days.
The dosage of melphalan, the drug that you have to take in combination with Revlimid, is 0.18 mg/kg once a day on days 1-4 of 28-day treatment cycle. The dosage of prednisone the drug that you have to take in combination with Revlimid, is 2 mg/kg once a day on days 1-4 of 28-day treatment cycle.

Dosage of Revlimid in combination with dexamethasone in patients with multiple myeloma who have received at least one other type of treatment before
The usual dose of Revlimid is 25 mg once a day. Take Revlimid for 21 consecutive days and then stop the treatment for the next 7 days. One treatment cycle thus lasts for 28 days.
The dosage of dexamethasone, the drug that you have to take in combination with Revlimid, is 40 mg once a day. The usual dosage regimen is as follows: during the first four 28-day treatment cycles you take dexamethasone on days 1-4, 9-12 and 17-20, and then during the subsequent treatment cycles only on days 1-4. Your doctor may decide to adjust this dosage to your individual needs.

Further data on dexamethasone are to be found in the package leaflet for the product concerned.

Your doctor will regularly test your blood during treatment with Revlimid since this treatment may lead to lower levels of white and red blood cells and blood platelets. If a significant decrease in the blood count occurs, your doctor will stop the treatment with Revlimid and will then resume it again at a reduced dosage.

Dosage in myelodysplastic syndrome
The recommended initial dose is 10 mg Revlimid once daily on days 1-21 of the repeating 28-day treatment cycles.

Dosage in mantle cell lymphoma
The recommended initial dose is 25 mg Revlimid once daily on days 1-21 of the repeating 28-day treatment cycles.

Revlimid is not used in children and adolescents, as no studies have been carried out in these age-groups.

In elderly patients the doctor will carry out the treatment with special care.

In patients with renal function disorders the doctor will carry out the treatment with particular care and will determine the kidney values more frequently.

If you take more Revlimid than was prescribed, tell your doctor immediately.

If you have forgotten to take Revlimid and less than 12 hours have elapsed, take the capsule that you have forgotten immediately.
If you have forgotten to take Revlimid and more than 12 hours have elapsed, do not take the capsule you missed. Wait until the next day and take the next capsule at the usual time.

Do not change the dosage prescribed for you on your own initiative. If you think that the effect of the medicine is too weak or too strong, talk to your doctor or your pharmacist.

4. Possible side effects

What side effects can Revlimid have?
Very common: Inflammations of the nose and throat region, bronchitis, urinary tract infections, infection of the upper respiratory tract, inflammation of the gastrointestinal tract, pneumonia, inflammation of the nasal mucosa, infection of the paranasal sinuses, influenza, fall in the white and red blood cell and platelet counts, loss of appetite, dehydration, weight loss, changes in laboratory values (potassium, calcium, sodium, blood sugar, liver values, enzymes) insomnia, taste disturbances, headache, chills, numbness in the extremities, dizziness, blurred vision, fall in blood pressure, cough, shortness of breath, diarrhoea, constipation, nausea, abdominal pain, vomiting, sore or dry mouth, itching, skin eruptions, dry skin, muscle cramps or muscle weakness, back pain, muscle pain, skeletal muscle pain, bone pain, exhaustion, fever, accumulation of fluid in the arms and legs, weakness, depression, cataract, venous thrombosis, digestive problems, joint pain, pains in the limbs, chest pain.

Common: Local or systemic infections (caused by bacteria, viruses or fungi, e.g. pneumonia, fungal infection in the mouth), lower respiratory tract infections, respiratory tract infections, sepsis, inflammation of the intestine, disorders of the haematopoietic system (acute myeloid leukaemia), disorders of the bone marrow (myelodysplastic syndrome), tumor lysis syndrome (metabolic complications that may occur during anticancer treatment or even sometimes in the absence of treatment), temporary worsening in the symptoms related to the tumor (Tumour-flare), tumors of the skin, weight gain, iron overload, accumulation of fluid in the tissues, hormonal (cortisone-like) changes (with swelling of the face, accumulation of fat on the trunk), mental confusion, changes of mood, hearing or seeing things that do not exist, mood swings, fear/anxiety, irritability, fatigue, drowsiness, disorders of cerebral blood flow, fainting fits, abnormal sensations in, or weakness of, the limbs, trembling, disturbed memory, nerve pain, visual disorders, watering of the eyes, conjunctivitis, rapid or irregular heartbeat, rise in blood pressure, bruising, hot flushes, pulmonary embolism, dyspnoea, runny nose, pain in the mouth and throat, nosebleeds, voice disturbance, hoarseness, hiccups, upper abdominal pain, flatulence, reddened skin, swelling of the face, discoloration of the skin, sweating, night sweats, loss of hair, impaired liver function, liver damage, reduced renal function, erection difficulties, enlargement of the breasts in men, abnormal periods, falls, chills, neck pain, (acute) renal failure, non-cardiac chest pain, contusion.

Uncommon: Inflammation of the cardiac wall, herpes infection in the eye, shingles, ear infections, disorders of the haematopoietic system (acute T-cell leukaemia), tumours of the nerve tissue, prolonged blood clotting, swelling of lymph nodes, reduced function of the adrenal cortex, thyroid underfunction, thyroid overfunction, increased body hair in women, diabetes, emaciation, gout, increased appetite, reduced sexual drive, psychiatric disorders, nervousness, aggression, nightmares, stroke, speech disorders, motor disorders or disorders of balance, impaired concentration, loss of the sense of smell, loss of vision, inflammation of the cornea, irritation or dryness of the eyes, tinnitus, earache, loss of hearing, cardiac insufficiency, slow heartbeat, circulatory collapse, circulatory disorders, asthma, blood in the vomit or in the stools (black stools), enteritis, difficulty in swallowing, bleeding of the gums, haemorrhoids, eczema, acne, photosensitivity of the skin, scaling or cracking of the skin, bone disorders, muscle stiffness, swelling of the joints, frequent urination, urinary incontinence, urine retention, thirst, a feeling of cold, rapid swelling of the skin, especially on back of hands or feet, or of eyelids, lips, face, tongue or genitals, , viral reactivation (hepatitis B virus, shingles).

Rare: serious allergic reaction that may begin as a skin rash in one area of the body but spreads with extensive loss of skin over the whole body. Inflammations of the tissue in the lungs, inflammation of the pancreas, acute graft-versus-host disease.

Very rare: serious allergic reaction (skin rash including eosinophilia and systemic symptoms, called DRESS), brain disorder caused by a virus (called progressive multifocal leukoencephalopathy

Not known (cannot be estimated from the available data):
Organ transplant rejection.

If you notice any side effects that are not described here you should inform your doctor or your pharmacist.

5. How to store Revlimid

What else has to be considered?
Store Revlimid below 30°C, in the original package and out of the reach and sight of children.
The medicine must not be used after the date indicated with "EXP" on the container.
Return any unused or damaged capsules to your doctor or your pharmacist for proper disposal.
Further information may be obtained from your doctor or your pharmacist, who are in possession of the complete data sheet.

6. Further information

What is contained in Revlimid?
One hard capsule of Revlimid contains 5 mg, 10 mg, 15 mg or 25 mg of lenalidomide as active substance, the colorant E132 (indigo carmine), which is only contained in the 10 mg and 15 mg capsules, and other excipients (lactose, anhydrous; microcrystalline cellulose; croscarmellose sodium; magnesium stearate).

Where do you obtain Revlimid? What packs are available?
In pharmacies on medical prescription, which may be used only once.

Revlimid 5 mg, 10 mg, 15 mg and 25 mg: each pack contains 21 hard capsules

To Report Any Side Effect(s):

Saudi Arabia:

– The National Pharmacovigilance and Drug Safety Centre (NPC)
- Fax: +966-11-205-7662
- Call NPC at +966-11-2038222, Exts: 2317-2356-2340.
- SFDA Call Center: 19999
- E-mail: npc.drug@sfda.gov.sa
- Website: https://ade.sfda.gov.sa

United Arab Emirates:

Pharmacovigilance and Medical Device Section
P.O. Box: 1853 Dubai UAE
Tel: 80011111
Email: pv@moh.gov.ae
Drug Department and Prevention
Ministry of Health & Prevention
Dubai

Oman:

Department of Pharmacovigilance & Drug Information
Directorate General of Pharmaceutical Affairs & Drug Control
Ministry of Health, Sultanate of Oman
Phone Nos. 0096822357687 / 0096822357686
Fax: 0096822358489
Email: dg-padc@moh.gov.om
Website : www.moh.gov.om

Other Countries:

– Please contact the relevant competent authority.

This is a medicament

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

Keep Medicament out of the reach and sight of children

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Celgene