EMA/13846/2020
EMEA/H/C/000717

Revlimid (*lenalidomide*)

An overview of Revlimid and why it is authorised in the EU

What is Revlimid and what is it used for?

Revlimid is a medicine used for the treatment of certain cancers and serious conditions affecting blood cells and bone marrow, namely multiple myeloma, myelodysplastic syndromes and mantle cell and follicular lymphoma.

In **multiple myeloma**, a cancer of a type of white blood cells called plasma cells, Revlimid is used:

- in adults who have had a stem cell transplant (a procedure where the patient's bone marrow is cleared of cells and replaced by stem cells from a donor);
- in adults with previously untreated (newly diagnosed) multiple myeloma, who cannot have stem cell transplantation. It is used in combination with dexamethasone, or bortezomib and dexamethasone, or melphalan and prednisone;
- in adults whose disease has been treated at least once. It is used in combination with dexamethasone.

In **myelodysplastic syndromes**, a group of bone marrow disorders that cause anaemia (low red blood cell counts), Revlimid is used in patients who need blood transfusions to manage their anaemia. It is used in patients with a genetic abnormality (called deletion 5q) when other treatments are not adequate.

In **mantle cell lymphoma** and **follicular lymphoma**, blood cancers that affect a type of white blood cell called B lymphocytes, Revlimid is used in adults whose disease has come back after treatment or does not improve with treatment. In follicular lymphoma it is used with the medicine rituximab.

Revlimid contains the active substance lenalidomide.

How is Revlimid used?

Revlimid can only be obtained with a prescription and treatment should be supervised by doctors who have experience in the use of cancer medicines. It is available as capsules (2.5, 5, 7.5, 10, 15, 20 and 25 mg) to be taken by mouth.

Treatment is given in cycles, with Revlimid being used once a day on certain days of the cycles. Treatment cycles are continued until the disease is no longer being controlled or side effects become

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unacceptable. The dose of Revlimid depends on the disease it is being used for, the patient's overall health and blood test results. The dose may need to be reduced or treatment interrupted in case of certain side effects.

For more information about using Revlimid, see the package leaflet or contact your doctor or pharmacist.

How does Revlimid work?

The active substance in Revlimid, lenalidomide, is an immunomodulator. This means that it affects the activity of the immune system (the body's natural defences). Lenalidomide works in several ways: it blocks the development of abnormal cells, prevents the growth of blood vessels within tumours and also stimulates specialised cells of the immune system to attack the abnormal cells.

What benefits of Revlimid have been shown in studies?

Multiple myeloma

Revlimid was more effective than placebo (a dummy treatment) in two main studies in 1,074 patients with newly diagnosed multiple myeloma and who had had stem cell transplantation. In the first study, patients taking Revlimid lived longer on average without their disease getting worse (57 months) than patients in the placebo group (29 months). In the second study, patients taking Revlimid also lived longer without their disease getting worse (44 months) than patients in the placebo group (24 months).

In newly diagnosed multiple myeloma, Revlimid has been studied in two main studies involving 2,082 patients. The first study compared Revlimid with placebo, both taken with melphalan and prednisone. In this study, patients taking Revlimid (plus melphalan and prednisone) lived longer without their disease getting worse (27 months) than patients receiving placebo (13 months). In the second study, Revlimid taken with low-dose dexamethasone was compared with standard treatment of melphalan, prednisone and thalidomide. It took 26 months for the disease to get worse in patients taking Revlimid plus dexamethasone, compared with 22 months for those on standard treatment.

Another main study involved 523 patients with multiple myeloma who had not been treated previously and for whom stem cell transplantation had not been planned. Patients treated with Revlimid and dexamethasone lived for around 30 months on average without their disease getting worse compared with around 43 months for those who also received bortezomib.

Revlimid was also studied in two main studies involving 704 patients with previously treated multiple myeloma. In both studies, Revlimid was compared with placebo, both taken with dexamethasone. The results of the two studies taken together showed that, on average, patients taking Revlimid lived longer without their disease getting worse (48 weeks) than patients receiving placebo (20 weeks).

Myelodysplastic syndromes

Two main studies have also been carried out involving a total of 353 patients with lower risk myelodysplastic syndromes. The first study did not compare Revlimid with any other treatment, while the second study compared it with placebo. In the first study, 97 out of 148 patients (66%) taking 10 mg Revlimid did not need a blood transfusion for at least 8 weeks. In the second study, 38 out of 69 patients (55%) taking 10 mg Revlimid did not need a blood transfusion for at least 26 weeks, compared with 4 out of 67 patients (6%) taking placebo.

Mantle cell lymphoma

One main study involved 254 patients with mantle cell lymphoma that had come back after previous treatment or had not improved on previous treatment. Revlimid was compared with a medicine chosen by the patients' doctors. The average time before the disease got worse was 38 weeks in those treated with Revlimid, compared with 23 weeks in those given other treatments.

Follicular lymphoma

The main study involved 358 patients with slow-growing blood cancers (marginal zone lymphoma or follicular lymphoma) that had come back or not improved after previous treatment: 295 of them had follicular lymphoma. The study compared Revlimid with placebo when added to another cancer medicine, rituximab. The average length of time that patients lived without follicular lymphoma getting worse was around 39 months with Revlimid plus rituximab, compared with 14 months with the placebo plus rituximab.

What are the risks associated with Revlimid?

The most common side effects with Revlimid when used for the treatment of **multiple myeloma** are: bronchitis (inflammation of the airways in the lungs), nasopharyngitis (inflammation of the nose and throat), cough, gastroenteritis (inflammation of the stomach and intestines with diarrhoea and vomiting), upper respiratory tract infection (nose and throat infections), tiredness, neutropenia (low levels of neutrophils, a type of white blood cell), constipation, diarrhoea, muscle cramps, anaemia, thrombocytopenia (low platelet counts), rash, back pain, insomnia (difficulty sleeping), decreased appetite, fever, peripheral oedema (swelling of the limbs due to fluid retention), leucopenia (low white blood cell counts), weakness, peripheral neuropathy (nerve damage in the hands and feet) and hypocalcaemia (low levels of calcium in the blood).

The most common side effects with Revlimid when used for the treatment of **myelodysplastic syndromes** are neutropenia, thrombocytopenia, diarrhoea, constipation, nausea (feeling sick), itching, rash, tiredness and muscle spasms.

The most common side effects with Revlimid when used for the treatment of **mantle cell lymphoma** are neutropenia, anaemia, diarrhoea, tiredness, constipation, fever and rash.

The most common side effects with Revlimid when used to treat **follicular lymphoma** are neutropenia, leucopenia, diarrhoea, constipation, tiredness and cough.

The most serious side effects with Revlimid are: neutropenia, venous thromboembolism (blood clots in the veins) including pulmonary embolism (blood clots in the lungs), lung infections including pneumonia, hypotension (low blood pressure), dehydration, kidney failure, febrile neutropenia (neutropenia with fever), diarrhoea and anaemia.

Lenalidomide can be harmful to the unborn child. Therefore, Revlimid must not be used in women who are pregnant. It must also not be used in women who could become pregnant, unless they take all the necessary steps to ensure that they are not pregnant before treatment and that they do not become pregnant during or soon after treatment.

For the full list of side effects and restrictions of Revlimid, see the package leaflet.

Why is Revlimid authorised in the EU?

Revlimid prolongs the time patients live without their cancer getting worse and reduces the need for blood transfusions in myelodysplastic syndromes. Side effects are considered manageable. Therefore,

the European Medicines Agency decided that Revlimid's benefits are greater than its risks and it can be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of Revlimid?

The company that makes Revlimid will provide a letter and educational kits for healthcare professionals, and brochures for patients, explaining that the medicine can be harmful to the unborn child and detailing the steps that need to be taken for the medicine to be used safely. It will also supply cards to patients about the safety measures patients should take.

The company has also set up a pregnancy prevention programme in each member state and will collect information on the medicine's use outside its approved uses. The boxes containing Revlimid capsules also include a warning stating that lenalidomide can be harmful to the unborn child.

In addition, the company will carry out a study in patients with myelodysplastic syndromes to gather further safety data, as well as a safety study in patients with newly diagnosed multiple myeloma not eligible for transplantation.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Revlimid have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Revlimid are continuously monitored. Side effects reported with Revlimid are carefully evaluated and any necessary action taken to protect patients.

Other information about Revlimid

Revlimid received a marketing authorisation valid throughout the EU on 14 June 2007.

Further information on Revlimid can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/revlimid.

This overview was last updated in 12-2019.