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Reblozyl (*luspatercept*)

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

What is Reblozyl and what is it used for?

Reblozyl is a medicine used to treat anaemia (low levels of red blood cells) in adults with the following blood disorders:

- myelodysplastic syndromes, a group of conditions where too few blood cells are produced by the bone marrow. Reblozyl is used in patients who need regular blood transfusions and who have a very low to moderate risk of their condition developing into acute myeloid leukaemia (a blood cancer);
- beta thalassaemia, a genetic condition in which patients cannot make enough beta globin, a component of haemoglobin (the protein in red blood cells that carries oxygen around the body).

These diseases are rare, and Reblozyl was designated an 'orphan medicine' (a medicine used in rare diseases). Further information on the orphan designations can be found on the European Medicines Agency's website (myelodysplastic syndromes: 22 August 2014; beta thalassaemia: 29 July 2014).

The medicine contains the active substance luspatercept.

How is Reblozyl used?

Reblozyl can only be obtained with a prescription. Treatment should be started by a doctor experienced in the treatment of blood diseases.

The medicine is given as an injection under the skin of the upper arm, thigh or belly. The recommended dose depends on the patient's weight and is adjusted depending on the patient's response. Treatment is given once every 3 weeks. If the patient develops serious side effects, treatment should be delayed until side effects have improved.

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

How does Reblozyl work?

The active substance in Reblozyl, luspatercept, regulates the development of red blood cells. It does this by blocking a signalling pathway called Smad2/3 that slows down the maturation of red blood cells

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and is overactive in patients with beta thalassaemia and myelodysplastic syndromes. Blocking Smad2/3 increases the production of red blood cells and allows them to develop normally.

What benefits of Reblozyl have been shown in studies?

Myelodysplastic syndromes

A main study involved 229 adults with myelodysplastic syndromes requiring regular blood transfusions. Patients received either Reblozyl or placebo (a dummy treatment) in addition to normal standard of care; 58 out of 153 patients (38%) taking Reblozyl did not need a blood transfusion for at least 8 weeks compared with 10 out of 76 (13%) patients receiving placebo.

In another main study involving 363 adults with myelodysplastic syndromes requiring regular blood transfusions, patients were given Reblozyl or epoetin alfa (another medicine for anaemia): 60% (110 out of 182) of patients given Reblozyl did not need a blood transfusion for at least 12 weeks and had an increase in their haemoglobin levels of at least 1.5 g/dL, compared with 35% (63 out of 181) of patients given epoetin alfa.

Beta thalassaemia

One main study involved 336 patients with beta thalassaemia requiring regular blood transfusions. Patients received either Reblozyl or placebo in addition to standard treatment. Blood transfusions were reduced by at least one third (33%) in 47 out of 224 patients (21%) taking Reblozyl compared with 5 out of 112 (4.5%) patients receiving placebo.

A second main study involved patients with beta thalassaemia not requiring regular blood transfusions. Patients received either Reblozyl or placebo together with standard treatment for at least 48 weeks. After 12 weeks, 74 out of 96 patients receiving Reblozyl (77%) had a rise of at least 1 g/dL in their haemoglobin level without needing transfusions, compared with none of the 49 patients who received placebo.

What are the risks associated with Reblozyl?

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

The most common side effects with Reblozyl in patients with myelodysplastic syndromes (which may affect more than 15 in 100 people) include tiredness, diarrhoea, nausea (feeling sick), weakness, dizziness, peripheral oedema (swelling due to fluid retention, especially of the ankles and feet) and back pain. The most common serious side effects include urinary tract infection (infection of the structures that carry the urine), dyspnoea and back pain.

The most common side effects of Reblozyl in patients with beta thalassaemia requiring transfusion (which may affect more than 15 in 100 people) include headache, bone pain and joint pain. The most common serious side effect include effects due to blood clots in the veins such as deep vein thrombosis, portal vein thrombosis (clots in the veins supplying the liver), ischaemic stroke (a sudden interruption of blood flow in the brain caused by a blockage in blood supply) and pulmonary embolism (clots in the veins supplying the lungs).

The most common side effects of Reblozyl in patients with beta thalassaemia not requiring regular transfusion (which may affect more than 15 in 100 people) include bone, back and joint pain, headache, and prehypertension (high normal blood pressure) and hypertension (high blood pressure). The most common serious side effects are traumatic fracture (a fracture caused for example by a fall or an accident) and compression of the spinal cord due to extramedullary haemopoiesis (blood cell development outside the bone marrow).

Reblozyl must not be given during pregnancy. Women who can become pregnant must use effective contraception during treatment and for at least 3 months after the last dose of Reblozyl. Patients requiring treatment to control the growth of extramedullary haemopoiesis masses (the formation of blood cells outside the bone marrow) must not use Reblozyl.

Why is Reblozyl authorised in the EU?

Treatment with frequent blood transfusions can lead to accumulation of iron in the body, which can damage organs. Reblozyl can reduce the need for blood transfusions in patients with myelodysplastic syndromes or with beta thalassaemia while its side effects are considered manageable. In patients with beta thalassaemia not requiring regular transfusions, higher haemoglobin levels are expected to improve outcomes for patients. The European Medicines Agency therefore decided that Reblozyl'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 Reblozyl?

The company that markets Reblozyl will provide educational packs for doctors who prescribe Reblozyl 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 women who can become pregnant about the measures they should take to avoid pregnancy.

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

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

Other information about Reblozyl

Reblozyl received a marketing authorisation valid throughout the EU on 25 June 2020.

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

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