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Zynteglo (*autologous CD34^{+} cells encoding $\beta^{A\text{-}T87Q}$-globin gene*)

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

What is Zynteglo and what is it used for?

Zynteglo is a medicine used to treat a blood disorder known as beta thalassaemia in patients 12 years and older who require regular blood transfusions.

People with this genetic condition cannot make enough beta-globin, a component of haemoglobin, the protein in red blood cells that carries oxygen around the body. As a result, these patients have low red blood cell levels and need frequent blood transfusions.

Zynteglo is used in patients who do not completely lack beta-globin and who are eligible for stem cell transplantation but do not have a matching related donor.

Beta thalassaemia is rare, and Zynteglo was designated an 'orphan medicine' (a medicine used in rare diseases) on 24 January 2013. Further information on the orphan designation can be found here: ema.europa.eu/en/medicines/human/orphan-designations/eu3121091.

Zynteglo contains as its active substance stem cells taken from the patients that have been genetically modified to contain a working gene for beta-globin.

How is Zynteglo used?

Zynteglo is made individually for each patient out of stem cells collected from their blood, and must only be given to the patient for whom it is made. It is given as an infusion (drip) into a vein and the dose depends on the bodyweight of the patient.

Before Zynteglo is given, the patient will receive conditioning chemotherapy treatment to clear their bone marrow of cells.

Zynteglo can only be obtained with a prescription and must be given in an approved centre by a doctor experienced in stem cell transplantation and in the treatment of beta thalassaemia. For more information about using Zynteglo, see the package leaflet or contact your doctor or pharmacist.

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How does Zynteglo work?

To make Zynteglo, the stem cells taken from the patient's blood are modified by a virus that carries working copies of the beta-globin gene into the cells. When these modified cells are given back to the patient, they are transported in the bloodstream to the bone marrow where they start to make healthy red blood cells that produce beta-globin. The effects of Zynteglo are expected to last for the patient's lifetime.

What benefits of Zynteglo have been shown in studies?

Zynteglo has been shown to be effective at reducing the need for blood transfusion in 2 main studies in patients with beta thalassaemia who required regular blood transfusions. In these studies, out of the 14 patients who did not completely lack beta-globin and were given Zynteglo, 11 of them had sufficiently high levels of red blood cells so that they did not need blood transfusions for at least 1 year after treatment.

What are the risks associated with Zynteglo?

A small number of patients have been treated with Zynteglo to date, and the most serious side effect observed is thrombocytopenia (low blood levels of platelets, components that help the blood to clot).

Zynteglo must not be used in pregnant or breastfeeding women, and in patients who have previously had gene therapy treatment (medicine that delivers genes). Doctors should consider whether patients can be given the required pre-treatments needed before Zynteglo.

For the full list of restrictions, see the package leaflet.

Why is Zynteglo authorised in the EU?

Transfusion-dependent beta thalassaemia is a severe condition for which treatment options are limited. Studies show that with a one-time treatment with Zynteglo most patients no longer need blood transfusions to increase their levels of working red blood cells. This means that the patients can avoid the excessive build-up of iron that occurs with regular transfusions and which itself requires treatment.

Regarding safety, because Zynteglo is produced using a virus, there could be a theoretical risk of cancer caused by unintended changes in the genetic material, although no such cases have been seen so far. There is also a potential risk of bleeding since the medicine may cause a drop in platelets. However, measures are in place to monitor such events through a registry of patients and a long-term study to assess patients' long-term outcomes.

Although information on the safety of the medicine is limited because of the small number of patients treated to date and the lack of long-term data, the European Medicines Agency decided that Zynteglo's benefits are greater than its risks and it can be authorised for use in the EU.

Zynteglo has been given 'conditional authorisation'. This means that there is more evidence to come about the medicine, which the company is required to provide. Every year, the European Medicines Agency will review any new information that becomes available and this overview will be updated as necessary.

What information is still awaited for Zynteglo?

Since Zynteglo has been given conditional authorisation, the company that markets Zynteglo will provide results of ongoing studies to further assess the effectiveness and safety of the medicine.

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

The company that markets Zynteglo will provide educational materials for healthcare professionals expected to use the medicine with information on its safety, including the potential risks of cancer and bleeding, and how it should be given. Patients will also receive a guide and a card that they should carry with them. In addition, the company will ensure that the medicine is only provided from approved centres.

The company will also provide data from a registry of patients treated with Zynteglo to study its long-term safety and effectiveness, as well as further data on the tests used in the manufacturing of the medicine to ensure its quality.

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

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

Other information about Zynteglo

Zynteglo received a conditional marketing authorisation valid throughout the EU on 29 May 2019.

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

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