10 February 2021
EMADOC-628903358-3459

Public summary of opinion on orphan designation

Autologous CD34+ cells transduced ex vivo with a lentiviral vector containing a modified gamma-globin gene for the treatment of sickle cell disease

On 13 November 2020, orphan designation EU/3/20/2356 was granted by the European Commission to Clinical Technology Centre (Ireland) Limited, Ireland, for autologous CD34+ cells transduced ex vivo with a lentiviral vector containing a modified gamma-globin gene (also known as ARU-1801) for the treatment of sickle cell disease.

What is sickle cell disease?

Sickle cell disease is a genetic disease in which the red blood cells become rigid and sticky and change from being disc-shaped to being crescent-shaped (like a sickle). The change in shape is caused by the presence of an abnormal form of haemoglobin, the protein in red blood cells that carries oxygen around the body.

In patients with sickle cell disease, the abnormal red blood cells stick to the walls of blood vessels and block them, restricting the flow of oxygen-rich blood to the internal organs such as the heart, lungs and spleen. The disease causes severe pain and damage to these organs as well as repeated infections and anaemia (low red-blood-cell counts).

Sickle cell disease is a severe disease that is long-lasting and may be life-threatening because of damage to the heart and the lungs, anaemia and infections.

What is the estimated number of patients affected by the condition?

At the time of designation, sickle cell disease affected less than 2 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 104,000 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

* For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

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What treatments are available?

At the time of designation, the only medicine authorised in the EU to treat sickle cell disease was hydroxycarbamide, also known as hydroxyurea. The main treatment for sickle cell disease was blood transfusion. Some patients received haematopoietic (blood) stem cell transplantation to help form new bone marrow that allows patients to produce red blood cells containing normal haemoglobin.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with sickle cell disease because early results showed that treatment with the medicine benefitted patients for whom hydroxycarbamide did not work well enough. The medicine would also have to be given once only, avoiding the need for ongoing treatment. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

The medicine is thought to work by encouraging the red cells forming in the bone marrow to produce a form of haemoglobin called fetal haemoglobin. Red cells that contain this type of haemoglobin become resistant to sickling and sticking together. For this one-time therapy, the patient's own stem cells are collected and are modified using a virus in a laboratory to contain a gene for fetal haemoglobin. These modified stem cells (medicine) are then given back to the patient, where they are expected to produce fetal haemoglobin, prevent crises involving blocked blood vessels and pain, and remove the need for medicines or transplants.

The virus used to carry the gene into the cells ('lentivirus') has been modified so that it does not cause disease in humans.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with sickle cell disease were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of sickle cell disease. Orphan designation of the medicine had been granted in the United States for the condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 8 October 2020, recommending the granting of this designation.

Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a

marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Contact details of the current sponsor for this orphan designation can be found on EMA website.

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.