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Public summary of opinion on orphan designation

Decitabine, tetrahydrouridine for the treatment of sickle cell disease

On 19 October 2020, orphan designation EU/3/20/2338 was granted by the European Commission to Novo Nordisk A/S, Denmark, for decitabine, tetrahydrouridine (also known as EPI01) 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 attach 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. Obstruction of blood vessels can cause episodes of severe pain (veno-occlusive crises) and long-term damage to organs. Patients with the disease suffer 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).

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

*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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transfusion. In some cases, haematopoietic (blood) stem cell transplantation (a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow) was used to allow the patient 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 studies found that it had a potentially beneficial effect on patients when hydroxyurea did not work. 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?

In sickle cell disease, the damaging effects of the abnormal haemoglobin (HbS) can be reduced by fetal haemoglobin, a type of haemoglobin which is normally produced only in the developing baby. The gene for making fetal haemoglobin is switched off after birth by an enzyme called DNMT1. The decitabine in this medicine lowers the amount of DNMT1 in body cells, so switching back on the production of fetal haemoglobin. The other active ingredient, tetrahydrouridine, prevents the breakdown of decitabine in the body and ensures that the medicine has a consistent effect. By increasing fetal haemoglobin, the medicine is expected to reduce the damaging effects of HbS and so relieve symptoms of the condition.

What is the stage of development of this medicine?

The effects of decitabine, tetrahydrouridine have been evaluated in experimental models.

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

At the time of submission, decitabine, tetrahydrouridine was not authorised anywhere in the EU for the treatment of sickle cell disease. Orphan designation of decitabine, tetrahydrouridine had been granted in the EU for sickle cell disease (EU/3/17/1881). Orphan designation had also been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 10 September 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.