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Public summary of opinion on orphan designation

Autologous bone marrow derived CD34+ cells transduced ex vivo with a self-inactivating lentiviral vector containing a normal version of the coding region of the *IL2RG* gene for the treatment of X-linked severe combined immunodeficiency

On 13 November 2020, orphan designation EU/3/20/2362 was granted by the European Commission to Real Regulatory Limited, Ireland, for autologous bone marrow derived CD34+ cells transduced ex vivo with a self-inactivating lentiviral vector containing a normal version of the coding region of the *IL2RG* gene (also known as MB-107) for the treatment of X-linked severe combined immunodeficiency.

What is X-linked severe combined immunodeficiency?

X-linked severe combined immunodeficiency is an inherited disease caused by a mutation (change) in a gene needed to make a protein of the immune system (the body's natural defences) called *IL2RG*. As a result, the immune system does not work well. The disease almost exclusively affects males who can catch serious infections soon after birth.

X-linked severe combined immunodeficiency is chronically debilitating and without effective treatment patients rarely live longer than 2 years.

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

At the time of designation, X-linked severe combined immunodeficiency affected approximately 0.01 in 10,000 people in the European Union (EU). This was equivalent to a total of around 500 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, intravenous immunoglobulin (IVIG) was authorised in the EU for use in X-linked severe combined immunodeficiency. In some patients, haematopoietic (blood) stem-cell

*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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transplantation was used. This is a procedure where the patient receives stem cells from a donor to form new bone marrow that produces healthy immune cells.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with X-linked severe combined immunodeficiency because early data found improvement in the immune function and some patients no longer needed IVIG after 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?

Patients with X-linked severe combined immunodeficiency have mutations in the *IL2RG* gene which is crucial for the normal development of the immune system. This medicine is made up of cells taken from the patient's bone marrow. To make this medicine, the cells are modified in the laboratory using a virus to insert a working copy of the *IL2RG* gene. When the modified cells (medicine) are transplanted back into the patient, they are expected to produce healthy cells that restore normal immune function.

The type of virus used in this medicine 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, no clinical trials with the current version of the medicine in patients with X-linked severe combined immunodeficiency had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of X-linked severe combined immunodeficiency or designated as an orphan medicinal product elsewhere for this 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.