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Public summary of opinion on orphan designation

Humanised IgG1 monoclonal antibody against the extracellular domain of receptor tyrosine kinase-like orphan receptor 1 coupled via a proteolytically cleavable maleimidocaproyl-valine-citrulline-para-aminobenzoate linker to monomethyl auristatin E for the treatment of mantle cell lymphoma

On 9 December 2020, orphan designation EU/3/20/2373 was granted by the European Commission to TMC Pharma (EU) Limited, Ireland, for humanised IgG1 monoclonal antibody against the extracellular domain of receptor tyrosine kinase-like orphan receptor 1 coupled via a proteolytically cleavable maleimidocaproyl-valine-citrulline-para-aminobenzoate linker to monomethyl auristatin E (also known as VLS-101 or MK-2140) for the treatment of mantle cell lymphoma.

The sponsorship was transferred to Merck Sharp & Dohme B.V. in April 2021.

What is mantle cell lymphoma?

Mantle cell lymphoma (MCL) is an aggressive cancer of a type of white blood cells called B lymphocytes, or B cells. In MCL, the B cells multiply quickly and live for too long, so they build up in the lymph nodes. The first sign of the disease is usually a lump in the neck, under the arm or in the groin, which is caused by an enlarged lymph node. Patients may also have fever, weight loss, tiredness and night sweats. MCL is usually diagnosed in people over 50 years of age. It is more common in men than in women.

MCL is a long-term debilitating and life-threatening disease associated with poor survival.

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

At the time of designation, MCL affected approximately 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 31,000 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 main treatments for MCL included chemotherapy (medicines to treat cancer), immunotherapy (medicines that act on the body's immune system) and radiotherapy (treatment with radiation). Bortezomib, ibrutinib, lenalidomide and temsirolimus were specifically authorised in the EU for the treatment of MCL that has returned after previous treatment or when other treatments have not worked. High-dose chemotherapy with haematopoietic (blood) stem-cell transplantation was also used. This is a procedure where cells in the patient's bone marrow are replaced by stem cells to form new bone marrow that produces healthy blood cells.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with MCL because early results from patients in whom previous treatments had not worked or whose disease had returned showed that their condition might respond to the medicine. 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 made up of a monoclonal antibody (a type of protein) combined with a substance called monomethyl auristatin E (MMAE). The monoclonal antibody is designed to attach to a receptor (target) protein called ROR1 that cancer cells such as those in MCL can carry on their surface. When the antibody part of the medicine attaches to ROR1, MMAE is released inside the cancer cells where it disrupts the internal skeleton of the cells. By targeting the cancer cells in this way, the medicine is expected to cause the death of cancer cells and thereby slow down the advance of the disease.

What is the stage of development of this medicine?

The effects of this 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 MCL were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for the treatment of MCL 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 5 November 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.