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Public summary of opinion on orphan designation

Erlotinib for the treatment of Olmsted syndrome

On 9 December 2020, orphan designation EU/3/20/2382 was granted by the European Commission to Institut Des Maladies Génétiques, France, for erlotinib for the treatment of Olmsted syndrome.

What is Olmsted syndrome?

Olmsted syndrome is an inherited disease of the skin with abnormal growth and thickening of the skin, with deep cracks (fissures) in the skin. It mostly affects the palms of the hands, the soles of the feet and the areas around the eyes and mouth. Patients experience pain and itching, which can be severe, and are more likely to get infections. The condition can also cause abnormal growth around the mouth and eyes, sparse hair and abnormal nails, and joint abnormalities.

Olmsted syndrome is caused by mutations in a gene called *TRPV3*, which is responsible for the production of a protein called transient receptor potential vanilloid 3 (TRPV3). This protein regulates several functions of the skin by controlling of the movement of calcium in and out of cells. The mutation causes overactivation of the TRPV3 protein, leading to excess levels of calcium in the cells, killing them and resulting in thickening of the skin.

Olmsted syndrome is a long-term debilitating disease due to the progressive worsening of symptoms, including severe pain and itching, which may lead to mobility problems and amputation.

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

At the time of designation, Olmsted syndrome affected less than 0.01 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 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).

*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, no satisfactory methods were authorised in the EU for the treatment of Olmsted syndrome. Patients received treatment to manage the abnormal skin growth and symptoms of pain and itching.

How is this medicine expected to work?

Erlotinib is a cancer medicine that blocks a protein called epidermal growth factor receptor (EGFR). EGFR is found in skin cells, especially keratinocytes, and is involved in the activation of TRPV3. By blocking the action of EGFR, the medicine is expected to reduce the activity of TRPV3, thereby reducing the abnormal skin growth, pain and itching.

What is the stage of development of this medicine?

The effects of erlotinib have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with Olmsted syndrome had been started.

At the time of submission, erlotinib was authorised in the EU as Tarceva for the treatment of advanced or metastatic non-small-cell lung cancer and pancreatic cancer.

At the time of submission, the medicine was not authorised anywhere in the EU for Olmsted syndrome 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.