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Public summary of opinion on orphan designation

Adeno-associated viral vector serotype 9 encoding human *ATP7B* for the treatment of Wilson's disease

On 9 December 2020, orphan designation EU/3/20/2378 was granted by the European Commission to Ultragenyx Germany GmbH, Germany, for adeno-associated viral vector serotype 9 encoding human *ATP7B* (also known as UX701) for the treatment of Wilson's disease.

What is Wilson's disease?

Wilson's disease is a genetic disorder that causes copper absorbed from food to build up in the body. In healthy people, liver cells remove excess copper. In people with Wilson's disease, due to a genetic mutation (change), the liver cannot remove copper, which builds up in the liver and in other organs such as the brain and damages them.

Wilson's disease is chronically debilitating and can be life threatening if not treated due to the toxicity of copper in the liver and brain.

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

At the time of designation, Wilson's disease 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).

What treatments are available?

At the time of designation, penicillamine, trientine and zinc acetate were authorised in the EU for the treatment of Wilson's disease. The only curative treatment for Wilson's disease was liver transplantation.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with Wilson's disease because laboratory studies suggest that a single treatment

*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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could lower levels of copper in the body and reduce liver damage. 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?

Because of a genetic mutation, in patients with Wilson's disease a protein in liver cells called ATP7B does not work properly. As a result, the liver cannot remove copper.

The medicine is made of a virus that has been modified to contain normal copies of the gene for producing the ATP7B protein. After being given to the patient as a single injection into a vein, the virus is expected to carry the *ATP7B* gene into the liver cells and enable them to produce a working ATP7B protein. This is expected to help relieve symptoms of the disease.

The type of virus used in this medicine ('adeno-associated virus') 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 medicine in patients with Wilson's disease had been started.

At the time of submission, adeno-associated viral vector serotype 9 encoding human ATP7B was not authorised anywhere in the EU for the treatment of Wilson's disease 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.