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EMA/COMP/436864/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Lentiviral vector containing the human liver and erythroid pyruvate kinase (*PKLR*) gene for the treatment of pyruvate kinase deficiency

On 22 August 2014, orphan designation (EU/3/14/1330) was granted by the European Commission to Centro de Investigación Biomédica en Red (CIBER), Spain, for lentiviral vector containing the human liver and erythroid pyruvate kinase (*PKLR*) gene for the treatment of pyruvate kinase deficiency.

What is pyruvate kinase deficiency?

Pyruvate kinase deficiency is an inherited disease that affects red blood cells, which carry oxygen to all tissues in the body. It is caused by mutations (defect) in the gene that makes an enzyme called pyruvate kinase, which is essential for the normal function of red blood cells. This results in a lack of the enzyme and reduced lifespan and early breakdown of these cells in the blood (haemolytic anaemia). Symptoms can include very pale skin, yellowing of the eyes and skin (jaundice), tiredness, shortness of breath (dyspnoea), enlarged spleen (splenomegaly) and heart problems. Anaemia and associated complications may be severe enough to require periodic blood transfusions.

Pyruvate kinase deficiency is a long-term debilitating disease because of its symptoms and the periodic blood transfusions. The condition can also be life threatening because the anaemia can worsen during pregnancy or during a viral infection.

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

At the time of designation, pyruvate kinase deficiency affected approximately 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 26,000 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).

[*]Disclaimer: 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 (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 511,100,000 (Eurostat 2014).

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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 pyruvate kinase deficiency. Patients were given treatments to help alleviate their symptoms such as periodic red blood cell transfusions. In some patients, allogeneic stem-cell transplantation was used. This is a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow.

How is this medicine expected to work?

This medicine is made up of a virus that contains a working copy of the *PKLR* gene which is responsible for making the pyruvate kinase enzyme that is missing in patients with pyruvate kinase deficiency. Immature bone marrow cells (called CD34+) with the ability to develop into red blood cells are taken from the patient and the virus is used to deliver the gene into these cells. When these modified cells are transplanted back into the patient, they are expected to produce red blood cells that can produce the missing enzyme and have a more normal lifespan, thus improving the symptoms of the disease.

The type of virus used in this medicine (lentivirus) is modified so that it 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 pyruvate kinase deficiency had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for pyruvate kinase deficiency or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 July 2014 recommending the granting of this designation.

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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

Sponsor's contact details:

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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.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Lentiviral vector containing the human liver and erythroid pyruvate kinase (*PKLR*) gene	Treatment of pyruvate kinase deficiency
Bulgarian	Лентивирусен вектор, съдържащ гена на човешка чернодробна и еритроидна пируват киназа *(PKLR)*	Лечение на пируват киназна недостатъчност
Croatian	Lentiviralni vektor koji sadrži ljudski gen za piruvatkinazu jetre i eritrocita *(PKLR)*	Liječenje nedostatka piruvat kinaze
Czech	Lentivirový vektor obsahující lidský gen pyruvát-kinázy jater a eritrocytů *(PKLR)*	Léčba deficitu pyruvát-kinázy
Danish	Lentiviral vektor indeholdende det humane lever og erythrocyt pyruvat kinase *(PKLR)* gen	Behandling af pyruvat kinase-mangel
Dutch	Lentivirusdrager die het menselijk pyruvaatkinasegen *(PKLR)* van de lever en de rode bloedcellen bevat	Behandeling van pyruvaatkinasedeficiëntie
Estonian	Lentiviraalne vektor, mis sisaldab inimese maksa ja erütroidset püruvaatkinaasi geeni *(PKLR)*	Püruvaatkinaasi puudulikkuse ravi
Finnish	Lentivirusvektori, joka sisältää ihmismaksan ja erytroidin pyruvaattikinaasin geenin *(PKLR)*	Pyruvaattikinaasin puutostilan hoito
French	Vecteur lentiviral contenant le gène humain de la pyruvate kinase hépatique érythroïde *(PKLR)*	Traitement du déficit en pyruvate kinase
German	Lentiviraler Vektor, der das humane Pyruvatkinase-L-R-Gen *(PKLR)* beinhaltet	Behandlung eines Pyruvatkinasemangels
Greek	Λεντιικός φορέας που περιέχει το ανθρώπινο γονίδιο πυροσταφυλικής κινάσης ήπατος και ερυθροειδών κυττάρων *(PKLR)*	Αντιμετώπιση της Ανεπάρκειας Πυροσταφυλικής Κινάσης
Hungarian	Az emberi májból és vörösvérsejtekből származó piruvát-kináz *(PKLR)* génjét tartalmazó lentivirális vector	A piruvát-kináz-hiány kezelése
Italian	Vettore lentivirale contenente il gene piruvato chinasi di fegato ed eritrociti *(PKLR)*	Trattamento del deficit da piruvato chinasi
Latvian	Lentivīrusa vektors, kas satur cilvēka aknu un eritroīdās piruvāta kināzes *(PKLR)* gēnu	Piruvāta kināzes nepietiekamības ārstēšana
Lithuanian	Lentivirusinis vektorius, turintis žmogaus kepenų ir eritroidinių ląstelių piruvato kinazės geną *(PKLR)*	Piruvato kinazės stokos gydymas
Maltese	Vettur lentivirali li fih il-ġene tal-fwied uman u eritrojdi 'Pyruvate Kinase' *(PKLR)*	Kura ta' nuqqas ta' pyruvate kinase

[1] At the time of designation

Language	Active ingredient	Indication
Polish	Wektor lentiwirusowy zawierający genludzkiej kinazy pirogronianowej typu L,R (wątroba i erytrocyty) *(PKLR)*	Leczenie niedoboru kinazy pirogronianowej
Portuguese	Vetor lentiviral que contém o gene piruvato quinase humano do fígado e dos eritrócitos *(PKLR)*	Tratamento da deficiência de piruvato quinase
Romanian	Vector lentiviral ce conține gena umană a piruvat kinazei hepatice şi eritrocitare*(PKLR)*	Tratamentul deficitului de piruvat kinază
Slovak	Lentivírusový vektor obsahujúci ľudský pečeňový a erytroidný gén pyruvátkinázy *(PKLR)*	Liečba deficitu pyruvátkinázy
Slovenian	Lentivirusni vektor, ki vsebuje človeški gen piruvat kinazo iz jeter in eritroida *(PKLR)*	Zdravljenje pomanjkanja piruvat kinaze
Spanish	Vector lentiviral que conteniene el gen piruvato quinasa humano de hígado y eritroide *(PKLR)*	Tratamiento de la deficiencia de la quinasa del piruvato
Swedish	Lentiviral vektor som innehåller den mänskliga genen for liver and erythroid pyruvate kinase (*PKLR*)	Behandling av pyruvatkinasbrist
Norwegian	Lentiviral vektor som inneholder det humane lever og erytrocytt pyruvat kinase genet *(PKLR)*	Behandling av mangel på pyruvatkinase
Icelandic	Lentiveiru genaferja sem inniheldur manna lifrar og rauðkorna pýruvat kínasa (PKLR) gen	Meðferð við skorti á pýruvat kínasa