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Public summary of opinion on orphan designation

Mitapivat sulfate for the treatment of pyruvate kinase deficiency

On 22 April 2020, orphan designation EU/3/20/2270 was granted by the European Commission to Agios Netherlands B.V., the Netherlands, for mitapivat sulfate (also known as AG-348) 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 the body's tissues and organs. It is caused by mutations (changes) in the gene for making an enzyme called pyruvate kinase, which is essential for the normal function of red blood cells. This results in a lack of functioning 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 less than 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 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).

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

*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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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?

In patients with pyruvate kinase deficiency, gene mutations cause the enzyme to be less stable and to work less effectively. This medicine is thought to work by stabilising the defective enzyme and helping it to work better, thus reducing the symptoms of the disease.

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, clinical trials with the medicine in patients with pyruvate kinase deficiency were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of pyruvate kinase deficiency. Orphan designation of the medicine had been granted in the United States for the treatment of this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 19 March 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

Sponsor's contact details:

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.

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

Language	Active ingredient	Indication
English	Mitapivat sulfate	Treatment of pyruvate kinase deficiency
Bulgarian	Митапиват сулфат	Лечение на пируват киназна недостатъчност
Croatian	Mitapivat-sulfat	Liječenje nedostatka piruvat kinaze
Czech	Mitapivat sulfát	Léčba deficitu pyruvát-kinázy
Danish	Mitapivatsulfat	Behandling af pyruvat kinase-mangel
Dutch	Mitapivatsulfaat	Behandeling van pyruvaatkinasedeficiëntie
Estonian	Mitapivaatsulfaat	Püruvaatkinaasi puudulikkuse ravi
Finnish	Mitapivaattisulfaatti	Pyruvaattikinaasin puutostilan hoito
French	Sulfate de mitapivat	Traitement du déficit en pyruvate kinase
German	Mitapivat-sulfat	Behandlung eines Pyruvatkinasemangels
Greek	Θειική μιταπιβάτη	Αντιμετώπιση της Ανεπάρκειας Πυροσταφυλικής Κινάσης
Hungarian	Mitapivát-szulfát	A piruvát-kináz-hiány kezelése
Italian	Mitapivat solfato	Trattamento del deficit da piruvato chinasi
Latvian	Mitapivāta sulfāts	Piruvāta kināzes nepietiekamības ārstēšana
Lithuanian	Mitapivato sulfatas	Piruvato kinazės stokos gydymas
Maltese	Sulfat tal-mitapivat	Kura ta’ nuqqas ta' pyruvate kinase
Polish	Siarczan mitapiwatu	Leczenie niedoboru kinazy pirogronianowej
Portuguese	Sulfato de mitapivato	Tratamento da deficiência de piruvato quinase
Romanian	Sulfat de mitapivat	Tratamentul deficitului de piruvat kinază
Slovak	Mitapivat sulfát	Liečba deficitu pyruvátkinázy
Slovenian	Mitapivatov sulfat	Zdravljenje pomanjkanja piruvat kinaze
Spanish	Sulfato de mitapivat	Tratamiento de la deficiencia de la quinasa del piruvato
Swedish	Mitapivatsulfat	Behandling av pyruvatkinasbrist
Norwegian	Mitapivatsulfat	Behandling av mangel på pyruvatkinase mangel
Icelandic	Mítapívat súlfat	Meðferð við skorti á pýruvat kínasa

[1] At the time of designation