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EMA/COMP/493776/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant protein derived from the saliva of the *Ornithodoros moubata* tick for the treatment of paroxysmal nocturnal haemoglobinuria

On 29 August 2016, orphan designation (EU/3/16/1725) was granted by the European Commission to Akari Therapeutics Plc, United Kingdom, for recombinant protein derived from the saliva of the *Ornithodoros moubata* tick (also known as coversin or rEV576) for the treatment of paroxysmal nocturnal haemoglobinuria.

What is paroxysmal nocturnal haemoglobinuria?

Paroxysmal nocturnal haemoglobinuria (PNH) is a condition in which there is excessive breakdown of red blood cells, leading to the release into the urine of a large amount of haemoglobin (the pigment contained in the cells). Because of the red colour of haemoglobin, the passing of red urine, particularly in the mornings, is usually the most obvious sign of the disease. Patients may also experience problems related to blood clotting.

The condition is due to the lack of certain proteins on the surface of the red blood cells which normally protect them from being destroyed by the immune system (the body's natural defences).

PNH is a long-term debilitating and life-threatening condition due to its complications including abdominal pain, infection and kidney problems, and problems due to bleeding and blood clots.

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

At the time of designation, PNH affected approximately 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 10,000 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 513,700,000 (Eurostat 2016).

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What treatments are available?

At the time of designation, the medicine Soliris (eculizumab) was authorised in the EU for the treatment of PNH. Bone marrow transplantation to replace the defective cells was another therapy available to patients, however this treatment is available to only a small proportion of patients since a suitable donor is required. Other methods such as blood transfusions and treatment to prevent clotting with blood-thinning compounds were used in some patients to improve symptoms.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with PNH because initial studies suggest that it can be used in patients for whom Soliris does not work. 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?

This medicine consists of a protein obtained from a blood-feeding tick, *Ornithodoros moubata*, which the tick uses to suppress the immune response of its host so as to go undetected. The protein works by blocking part of the immune system known as the complement system, which consists of a series of proteins that can enhance the actions of antibodies and immune cells. In patients with PNH, the complement proteins are overactive and cause damage to the patients' own blood cells. By blocking the complement system, the medicine is expected to prevent complement proteins from damaging the blood cells, thereby helping to relieve 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, a clinical trial with the medicine in patients with PNH was planned.

At the time of submission, the medicine was not authorised anywhere in the EU for PNH 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 13 July 2016 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	Recombinant protein derived from the saliva of the *Ornithodoros moubata* tick	Treatment of paroxysmal nocturnal haemoglobinuria
Bulgarian	Рекомбинантен протеин, извлечен от слюнката на кърлеж *Ornithodoros moubata*	Лечение на пароксизмална нощна хемоглобинурия
Croatian	Rekombinantni protein dobiven iz sline krpelja *Ornithodoros* moubata	Liječenje paroksizmalne noćne hemoglobinurije
Czech	Rekombinantní protein odvozený ze slin klíštěte *Ornithodoros moubata*	K léčbě paroxysmální noční hemoglobinurie
Danish	Rekombinant protein afledt af saliva fra flåten *Ornithodoros moubata*	Behandling af paroksysmatisk nocturn hæmoglobinuria
Dutch	Recombinant eiwit afgeleid van het speeksel van de *Ornithodoros moubata*-teek	Behandeling van paroxismale nachtelijke hemoglobinurie
Estonian	Puugi *Ornithodoros moubata* süljest saadud rekombinantne valk	Paroksüsmaalse öise hemoglubinuuria ravi
Finnish	*Ornithodoros moubata*-punkin syljestä peräisin oleva rekombinanttiproteiini	Paroksysmaalisen nokturnaalisen hemoglobinurian hoito
French	Protéine recombinante dérivée de la salive de tique *Ornithodoros moubata*	Traitement de l'hémoglobinurie paroxystique nocturne
German	Rekombinantes Protein, gewonnen aus dem Speichel der Zecke *Ornithodoros moubata*	Behandlung von paroxysmaler nächtlicher Hämoglobinurie
Greek	Ανασυνδυασμένη πρωτεΐνη προερχόμενη από σίελο του ακάρεως *Ornithodoros moubata*	Θεραπεία της παροξυσμικής νυκτερινής αιμοσφαιρινουρίας
Hungarian	*Ornithodoros moubata* kullancs nyálából nyert rekombináns fehérje	Paroxysmalis nocturnalis haemoglobinuria
Italian	Proteina ricombinante derivata dalla saliva della zecca *Ornithodoros moubata*	Trattamento dell'emoglobinuria parossistica notturna
Latvian	Rekombinants proteīns, kas iegūts no *Ornithodoros moubata* ērču siekalām	Paroksismālas nakts hemoglobinūrijas ārstēšana
Lithuanian	Rekombinantinis baltymas, išgautas iš erkės *Ornithodoros moubata* seilių	Priepuolinės naktinės hemoglobinurijos gydymas
Maltese	Proteina rikombinanti mnissla mill-bżieq tal-qurdiena *Ornithodoros moubata*	Kura ta' l-emoglobinurja parossistika ta' billejl
Polish	Rekombinowane białko wyprowadzone ze śliny kleszcza *Ornithodoros moubata*	Leczenie napadowej nocnej hemoglobinurii
Portuguese	Proteína recombinante derivada da saliva da carraça *Ornithodoros moubata*	Tratamento da hemoglobinúria paroxística nocturna
Romanian	Proteină recombinantă obţinută din saliva căpuşei *Ornithodoros moubata*	Tratamentul hemoglobinuriei paroxistice nocturne
Slovak	Rekombinantný proteín odvodený zo slín kliešťa *Ornithodoros moubata*	Liečba paroxyzmálnej nočnej hemoglobinúrie

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Rekombinantni protein, pridobljen iz sline klopa *Ornithodoros moubata*	Zdravljenje paroksizmalne nočne hemoglobinurije
Spanish	Proteína recombinante derivada de la saliva de la garrapata *Ornithodoros moubata*	Tratamiento de la hemoglobinuria paroxística nocturna
Swedish	Rekombinant protein framställt från saliven hos *Ornithodoros moubata*-fästing	Behandling av paroxysmal nattlig hemoglobinuri
Norwegian	Rekombinant protein fremstilt fra spytt fra flåtten *Ornithodoros moubata*	Behandling av paroksysmal nattlig hemoglobinuri
Icelandic	Raðbrigða prótein unnið úr munnvatni blóðmítilsins *Ornithodoros moubata*	Meðferð fyrir paroxysmal nætur blóðrauðamigu