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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Fc- and CDR-modified humanised monoclonal antibody against C5 for the treatment of paroxysmal nocturnal haemoglobinuria

On 30 May 2016, orphan designation (EU/3/16/1661) was granted by the European Commission to Alexion Europe SAS, France, for Fc- and CDR-modified humanised monoclonal antibody against C5 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 less than 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 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).

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

[*]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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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 result in a greater reduction in the breakdown of red blood cells compared with Soliris. 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?

The medicine is a monoclonal antibody, a protein designed to attach specifically to the C5 protein in the blood. C5 protein is part of a group of proteins known as the 'complement system', which normally help the immune system to fight infections. In patients with PNH this system is overactive and also attacks red blood cells. By attaching to C5 protein, the medicine is expected to block its effect and so reduce the destruction of red blood cells. This is expected to reduce the patient's symptoms.

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 this medicine in patients with PNH were ongoing.

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 21 April 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	Fc- and CDR-modified humanised monoclonal antibody against C5	Treatment of paroxysmal nocturnal haemoglobinuria
Bulgarian	Fc- и CDR-модифицирано хуманизирано моноклонално антитяло срещу C5	Лечение на пароксизмална нощна хемоглобинурия
Croatian	Humanizirano monoklonsko protutijelo protiv C5 s modificiranim Fc fragmentom i CDR regijom	Liječenje paroksizmalne noćne hemoglobinurije
Czech	Humanizovaná monoklonální protilátka vůčiC5 s modifikovanými Fc a CRD oblastmi	K léčbě paroxysmální noční hemoglobinurie
Danish	Fc- og CDR-modificeret humaniseret monoklonalt antistof mod C5	Behandling af paroksysmatisk nocturn hæmoglobinuria
Dutch	Fc- en CDR-gewijzigd gehumaniseerd monoklonaal antilichaam tegen C5	Behandeling van paroxismale nachtelijke hemoglobinurie
Estonian	Fc-ga ja CDR-iga modifitseeritud C5-vastane humaniseeritud monoklonaalne antikeha	Paroksüsmaalse öise hemoglubinuuria ravi
Finnish	Fc- ja CDR-muokattu humanisoitu monoklonaalinen C5-vasta-aine	Paroksysmaalisen nokturnaalisen hemoglobinurian hoito
French	Anticorps monoclonal contre le C5 à parties Fc et CDR modifiées	Traitement de l'hémoglobinurie paroxystique nocturne
German	Fc- und CDR-modifizierter humanisierter monoklonaler Antikörper gegen C5	Behandlung von paroxysmaler nächtlicher Hämoglobinurie
Greek	Fc- και CDR-τροποποιημένο ανθρωποποιημένο μονοκλωνικό αντίσωμα έναντι του C5	Θεραπεία της παροξυσμικής νυκτερινής αιμοσφαιρινουρίας
Hungarian	C5 elleni Fc- és CDR-módosított, humanizált, monoklonális antitest	Paroxysmalis nocturnalis haemoglobinuria
Italian	Anticorpo monoclonale anti C5 umanizzato, FC e CDR-modificato	Trattamento dell'emoglobinuria parossistica notturna
Latvian	Fc un CDR modificēta humanizēta monoklonāla antiviela pret C5	Paroksismālas nakts hemoglobinūrijas ārstēšana
Lithuanian	Humanizuotas monokloninis modifikuotų Fc ir CDR sričių antikūnas prieš C5	Priepuolinės naktinės hemoglobinurijos gydymas
Maltese	Antikorp monoklonali umanizzat kontra C5, b'Fc u CDR modifikati	Kura ta' l-emoglobinurja parossistika ta' billejl
Polish	Humanizowane przeciwciało monoklonalne specyficzne względem C5, modyfikowane w regionach CDR oraz Fc	Leczenie napadowej nocnej hemoglobinurii
Portuguese	Anticorpo monoclonal humanizado contra a C5, modificado em Fc e CDR	Tratamento da hemoglobinúria paroxística nocturna
Romanian	Anticorp monoclonal umanizat anti-C5, cu porţiunile Fc şi CDR modificate	Tratamentul hemoglobinuriei paroxistice nocturne

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Humanizovaná monoklonálna protilátka proti C5 s modifikovanými Fc a CRD oblasťami	Liečba paroxyzmálnej nočnej hemoglobinúrie
Slovenian	Humanizirano monoklonsko protitelo proti C5, modificirano s Fc in CDR	Zdravljenje paroksizmalne nočne hemoglobinurije
Spanish	Anticuerpo monoclonal humanizado contra C5 modificado en el Fc y CDR	Tratamiento de la hemoglobinuria paroxística nocturna
Swedish	Humaniserad Fc- och CDR-modifierad monoklonal antikropp riktad mot C5	Behandling av paroxysmal nattlig hemoglobinuri
Norwegian	Fc- og CDR-modifisert humanisert monoklonalt antistoff mot C5	Behandling av paroksysmal nattlig hemoglobinuri
Icelandic	Fc- og CDR-breytt manngert einstofna mótefni gegn C5	Meðferð fyrir paroxysmal nætur blóðrauðamigu