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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Synthetic 15-amino-acid macrocyclic peptide acylated with a polyethyleneglycol palmitoylated linker for the treatment of paroxysmal nocturnal haemoglobinuria

On 14 October 2016, orphan designation (EU/3/16/1762) was granted by the European Commission to Ra Europe Limited, United Kingdom, for synthetic 15-amino-acid macrocyclic peptide acylated with a polyethyleneglycol palmitoylated linker 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 caused by 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).

*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 red blood 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 with blood-thinning compounds to prevent clotting 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 preliminary data suggest that it can be used in patients for whom Soliris does not work. In addition, patients may be able to take the medicine themselves, as it would be injected under the skin and not into a vein. 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 is expected to work by attaching to and blocking the C5 complement protein, one of the proteins of the 'complement system', which is part of the body's defence system. In patients with PNH, the complement system causes damage to the patients' own blood cells which lack proteins on their surface that would normally protect them. By blocking the C5 complement protein, this medicine is expected to prevent the complement system 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 this 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 PNH were 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 8 September 2016 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, 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	Synthetic-15-amino acid macrocyclic peptide acylated with a polyethyleneglycol palmitoylated linker	Treatment of paroxysmal nocturnal haemoglobinuria
Bulgarian	Синтетичен макроцикличен пептид с 15 аминокиселини, ацетилиран чрез линкер, палмитилиран с полиетиленгликол	Лечение на пароксизмална нощна хемоглобинурия
Croatian	Sintetički makrociklički peptid s 15 aminokiselina aciliran polietilenglikol palmitoiliranom vezom	Liječenje paroksizmalne noćne hemoglobinurije
Czech	Syntetický 15aminokyselinový a makrocyklický peptid acylovaný s polyethylenglykolovým palmitovaným linkerem	K léčbě paroxysmální noční hemoglobinurie
Danish	Syntetisk 15-aminosyre makrocyklisk peptid acyleret med en polyethylenglycol palmitoyleret linker	Behandling af paroksysmatisk nocturn hæmoglobinuria
Dutch	Synthetische 15-aminozuur macrocyclische peptide geacyleerd met een polyethyleenglycol gepalmitoyleerde linker	Behandeling van paroxismale nachtelijke hemoglobinurie
Estonian	Sünteetiline 15-aminohappeline makrotsükliline peptiid, mis on atsetüleeritud polüetüleenglükooli palmitüleeritud sidujaga	Paroksüsmaalse öise hemoglubinuuria ravi
Finnish	Synteettinen 15 aminohapon makrosyklinen peptidi, joka on asyloitu palmitoidulla polyeteeniglykolilinkkerillä	Paroksysmaalisen nokturnaalisen hemoglobinurian hoito
French	Peptide macrocyclique synthétique de 15 acides aminés, acylé avec un lieur palmitoylé couplé au polyéthylène glycol	Traitement de l'hémoglobinurie paroxystique nocturne
German	Synthetisches makrozyklisches Peptid aus 15 Aminosäuren, acyliert mit einem mit Polyethylenglykol palmitoylierten Linker	Behandlung von paroxysmaler nächtlicher Hämoglobinurie
Greek	Συνθετικό μακροκυκλικό πεπτίδιο 15 αμινοξέων ακυλιωμένο με έναν παλμιτοϋλιωμένο συνδέτη πολυαιθυλενογλυκόλης	Θεραπεία της παροξυσμικής νυκτερινής αιμοσφαιρινουρίας
Hungarian	Szintetikus, 15 aminosavból álló makrociklikus peptid, mely polietilén-glikol palmitoilált linkerével van acilálva	Paroxysmalis nocturnalis haemoglobinuria kezelése
Italian	Peptide macrociclico di sintesi di 15 aminoacidi acilato con un linker polietilenglicol-palmitoilato	Trattamento dell'emoglobinuria parossistica notturna
Latvian	Sintētisks 15 aminoskābju makrociklisks peptīds, kas acilēts ar polietilēnglikola palmitoilētu saistītāju	Paroksismālas nakts hemoglobinūrijas ārstēšana
Lithuanian	Sintetinis 15 aminorūgščių makrociklinis peptidas, acilintas polietilenglikolio palmitato rišikliu	Priepuolinės naktinės hemoglobinurijos gydymas

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	Peptid makroċikliku sintetiku bi ħmistax-il aċidu amino aċilat b'polyethyleneglycol palmitoylated linker	Kura ta' l-emoglobinurja parossistika ta' billejl
Polish	Syntetyczny, acylowany, 15-aminokwasowy makrocykliczny peptyd, z polietylenoglikolowo-palmitoilowanym łącznikiem	Leczenie napadowej nocnej hemoglobinurii
Portuguese	Péptido macrocíclico sintético de 15 aminoácidos acilado com um ligante polietileneglicol palmitoilado	Tratamento da hemoglobinúria paroxística nocturna
Romanian	Peptidă sintetică macrociclică formată din 15 aminoacizi acilată cu un ligand palmitoilat din polietilenglicol	Tratamentul hemoglobinuriei paroxistice nocturne
Slovak	Syntetický 15-aminokyselinový makrocyklický peptid acylovaný polyetylénglykolovým palmitoylovaným linkerom	Liečba paroxyzmálnej nočnej hemoglobinúrie
Slovenian	Sintetični makrociklični 15-aminokislinski peptid aciliran s povezovalcem iz palmitoiliranega polietilenglikola	Zdravljenje paroksizmalne nočne hemoglobinurije
Spanish	Péptido macrocíclico sintético de 15 aminoácidos acilado con un ligante de polietilenglicol palmitoilado	Tratamiento de la hemoglobinuria paroxística nocturna
Swedish	Syntetisk makrocyklisk peptid på 15 aminosyror acylerad med en polyetylenglykolpalmitoylerad länksubstans	Behandling av paroxysmal nattlig hemoglobinuri
Norwegian	Syntetisk makrosyklisk peptid (15 aminosyrer) acylert med et palmitoylert polyetylenglykolbindeledd	Behandling av paroksysmal nattlig hemoglobinuri
Icelandic	Tilbúið 15 amínósýru hringtengt stórsameindapeptíð asýlerað með pólýetýlenglýkól-palmítóýluðum tengli	Meðferð fyrir paroxysmal nætur blóðrauðamigu