23 September 2014
EMA/COMP/452195/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamide) for the treatment of paroxysmal nocturnal haemoglobinuria

On 22 August 2014, orphan designation (EU/3/14/1327) was granted by the European Commission to Amyndas Pharmaceuticals S.A., Greece, for S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamide) for the treatment of paroxysmal nocturnal haemoglobinuria.

What is paroxysmal nocturnal haemoglobinuria?

Paroxysmal nocturnal haemoglobinuria is a condition in which there is excessive breakdown of the patient's 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 anaemia (low levels of red blood cells) such as tiredness and shortness of breath and 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).

Paroxysmal nocturnal haemoglobinuria 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, paroxysmal nocturnal haemoglobinuria affected approximately 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 5,000 people*, and

*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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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 paroxysmal nocturnal haemoglobinuria. 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 can improve the symptoms in a small percentage of patients.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with paroxysmal nocturnal haemoglobinuria as it works differently to currently authorised treatment, and early studies in experimental models showed that it may be effective also in patients who do not respond to current treatment. 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 works by attaching to the C3 protein in the blood. This protein is part of a group of proteins known as the 'complement system', which normally helps the immune system to fight infections but which in patients with paroxysmal nocturnal haemoglobinuria also attacks red blood cells. By attaching to this protein, the medicine is expected to block or reduce the destruction of the red blood cells and thereby 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, no clinical trials with the medicine in patients with paroxysmal nocturnal haemoglobinuria had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for paroxysmal nocturnal haemoglobinuria 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	S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamide)	Treatment of paroxysmal nocturnal haemoglobinuria
Bulgarian	S3,S13-цикло(D-тиролзил-L-изолевкил-L-цистеинил-L-валил-1-метил-L-триптофил-L-глутаминил-L-аспартил-L-триптофил-N-метил-L-глицил-L-аланил-L-хистидил-L-агринил-L-цистеинил-N-метил-L-изолевкинамид)	Лечение на пароксизмална нощна хемоглобинурия
Croatian	S3,S13-ciklo(D-tirozil-L-izoleucil-L-cisteinil-L-valil-1-metil-L-triptofil-L-glutaminil-L-aspartil-L-triptofil-N-metil-L-glicil-L-alanil-L-histidil-L-arginil-L-cisteinil-N-metil-L-izoleucinamid)	Liječenje paroksizmalne noćne hemoglobinurije
Czech	S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamide)	K léčbě paroxysmální noční hemoglobinurie
Danish	S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamid)	Behandling af paroksysmatisk nocturn hæmoglobinuria
Dutch	S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamide)	Behandeling van paroxismale nachtelijke hemoglobinurie
Estonian	S3,S13-tsüklo(D-türolsüül-L-isoleutsüül-L-tsüsteinüül-L-valüül-1-metüül-L-trüptofüül-L-glutaminüül-L-aspartüül-L-trüptofüül-N-metüül-L-glütsüül-L-alanüül-L-histidüül-L-arginüül-L-tsüsteinüül-N-meüül-L-isoleutsinamiid)	Paroksüsmaalse öise hemoglubinuuria ravi
Finnish	S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamide)	Paroksysmaalisen nokturnaalisen hemoglobinurian hoito

[1] At the time of designation

Language	Active ingredient	Indication
French	S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamide)	Traitement de l'hémoglobinurie paroxystique nocturne
German	S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamide)	Behandlung von paroxysmaler nächtlicher Hämoglobinurie
Greek	S3,S13-κυκλο(D-τυρολσυλ-L-ισολευκυλ-L-κυστεϊνυλ-L-βαλυλ-1-μεθυλ-L-τρυπτοφυλ-L-γλουταμινυλ-L-ασπαρτυλ-L-τρυπτοφυλ-N-μεθυλ-L-γλυκυλ-L-αλανυλ-L-ιστιδυλ-L-αργινυλ-L-κυστενυλ-N-μεθυλ-L-ισολευκιναμίδιο)	Θεραπεία της παροξυσμικής νυκτερινής αιμοσφαιρινουρίας
Hungarian	S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamide)	Paroxysmalis nocturnalis haemoglobinuria
Italian	S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamide)	Trattamento dell'emoglobinuria parossistica notturna
Latvian	S3,S13-ciklo(D-tirolzil-L-izoleicil-L-cisteīnil-L-valil-1-metil-L-triptofil-L-glutamīnil-L-aspartil-L-triptofil-N-metil-L-glicil-L-alanil-L-histidil-L-arginil-L-cisteīnil-N-metil-L-izoleicīnamīds)	Paroksismālas nakts hemoglobinūrijas ārstēšana
Lithuanian	S3,S13-ciklo(D-tirolzil-L-izoleucil-L-cisteinil-L-valil-1-metil-L-triptofil-L-glutaminil-L-aspartil-L-triptofil-N-metil-L-glicil-L-alanil-L-histidil-L-arginil-L-cisteinil-N-metil-L-izoleucinamidas)	Priepuolinės naktinės hemoglobinurijos gydymas
Maltese	S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamide)	Kura ta' l-emoglobinurja parossistika ta' billejl
Polish	S3,S13-cyklo(D-tyrozyl-L-izoleucyl-L-cysteinyl-L-walil-1-metyl-L-tryptofanyl-L-glutaminyl-L-aspartyl-L-tryptofanyl-N-metyl-L-glicyl-L-alanyl-L-histydyl-L-arginyl-L-cysteinyl-N-metyl-L-izoleucynamid)	Leczenie napadowej nocnej hemoglobinurii
Portuguese	S3,S13-ciclo(D-tirolsil-L-isoleucil-L-cisteinil-L-valil-1-metil-L-triptofil-L-glutaminil-L-aspartil-L-triptofil-N-metil-L-glicil-L-alanil-L-histidil-L-arginil-L-cisteinil-N-metil-L-isoleucinamida)	Tratamento da hemoglobinúria paroxística nocturna

Language	Active ingredient	Indication
Romanian	S3,S13-ciclo(D-tirolzil-L-izoleucil-L-cisteinil-L-valil-1-metil-L-triptofil-L-glutaminil-L-aspartil-L-triptofil-N-metil-L-glicil-L-alanil-L-histidil-L-arginil-L-cisteinil-N-metil-L-izoleucinamidă)	Tratamentul hemoglobinuriei paroxistice nocturne
Slovak	S3,S13-cyklo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-metyl-L-tryptofyl-L-glutaminyl-L-aspartyl-L-tryptofyl-N-metyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-metyl-L-izoleucínamid)	Liečba paroxyzmálnej nočnej hemoglobinúrie
Slovenian	S3,S13-ciklo(D-tirosil-L-izoleucil-L-cisteinil-L-valil-1-metil-L-triptofil-L-glutaminil-L-aspartil-L-triptofil-N-metil-L-glicil-L-alanil-L-histidil-L-arginil-L-cisteinil-N-metil-L-izoleucinamid)	Zdravljenje paroksizmalne nočne hemoglobinurije
Spanish	S3,S13-ciclo(D-tirolsil-L-isoleucil-L-cisteinil-L-valil-1-metil-L-triptofil-L-glutaminil-L-aspartil-L-triptofil-N-metil-L-glicil-L-alanil-L-histidil-L-arginil-L-cisteinil-N-metil-L-isoleucinamida	Tratamiento de la hemoglobinuria paroxística nocturna
Swedish	S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-metyl-L-tryptofyl-L-glutaminyl-L-aspartyl-L-tryptofyl-N-metyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-metyl-L-isoleucinamid)	Behandling av paroxysmal nattlig hemoglobinuri
Norwegian	S3,S13-syklo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-metyl-L-tryptofyl-L-glutaminyl-L-aspartyl-L-tryptofyl-N-metyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-metyl-L-isoleucinamid)	Behandling av paroksysmal nattlig hemoglobinuri
Icelandic	S3,S13-cýcló(D-týrólsýl-L-ísóleucýl-L-cýsteinýl-L-valýl-1-methýl-L-trýptóphýl-L-glútaminýl-L-aspartýl-L-trýptóphýl-N-methýl-L-glýcýl-L-alanýl-L-histidýl-L-arginýl-L-cýsteinýl-N-methýl-L-ísóleucínamíð)	Meðferð fyrir paroxysmal nætur blóðrauðamigu