16 January 2017
EMA/753055/2017

Public summary of opinion on orphan designation

(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide for the treatment of paroxysmal nocturnal haemoglobinuria

On 12 December 2017, orphan designation (EU/3/17/1946) was granted by the European Commission to FGK Representative Service GmbH, Germany, for (2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide (also known as ACH-0144471) 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 (haemolysis), leading to the release into the urine of a large amount of haemoglobin (the protein found in red blood cells that carries oxygen around the body). 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 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 515,700,000 (Eurostat 2017).

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What treatments are available?

At the time of designation, 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. Other methods such as blood transfusions and treatment with medicines 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. This is because preliminary data have shown that the medicine can reduce the number of transfusions in a form of the disease associated with another condition (aplastic anaemia) that cannot be treated with eculizumab.

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?

In patients with PNH, proteins of the immune system called complement proteins damage the patients' own blood cells.

The medicine blocks a complement protein called factor D. Blocking this protein is expected to help prevent complement proteins from damaging blood cells, thereby relieving 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 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 31 October 2017 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	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide	Treatment of paroxysmal nocturnal haemoglobinuria
Bulgarian	(2S,4R)-1-(2-(3-ацетил-5-(2-метилпиримидин-5-ил)-1H-индазол-1-ил)ацетил)-N-(6-бромопиридин-2-ил)-4-флуоропиролидин-2-карбоксамид	Лечение на пароксизмална нощна хемоглобинурия
Croatian	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidin-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridin-2-il)-4-fluoropirrolidin-2-carboksamid	Liječenje paroksizmalne noćne hemoglobinurije
Czech	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide	K léčbě paroxysmální noční hemoglobinurie
Danish	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamid	Behandling af paroksysmatisk nocturn hæmoglobinuria
Dutch	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide	Behandeling van paroxismale nachtelijke hemoglobinurie
Estonian	(2S,4R)-1-(2-(3-atsetüül-5-(2-metüülpürimidiin-5-üül)-1H-indazool-1-üül)atsetüül)-N-(6-bromopüridiin-2-üül)-4-fluoropürrolidiin-2-karboksamiid	Paroksüsmaalse öise hemoglubinuuria ravi
Finnish	(2S,4R)-1-(2-(3-asetyyli-5-(2-metyylipyrimid-5-yyli)-1H-indatsol-1-yyli)asetyyli)-N-(6-bromopyridin-2-yyli)-4-fluoropyrrolidiini-2-karboksamidi	Paroksysmaalisen nokturnaalisen hemoglobinurian hoito
French	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide	Traitement de l'hémoglobinurie paroxystique nocturne
German	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamid	Behandlung von paroxysmaler nächtlicher Hämoglobinurie

[1] At the time of designation

Language	Active ingredient	Indication
Greek	(2S,4R)-1-(2-(3-ακετυλ-5-(2-μεθυλπυριμιδινο-5-υλ)-1Η-ινδαζολ-1-υλ)ακετυλ)-Ν-(6-βρωμοπυριδινο-2-υλ)-4-φθοροπυρολιδινο-2-καρβοξαμιδη	Θεραπεία της παροξυσμικής νυκτερινής αιμοσφαιρινουρίας
Hungarian	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidin-2-carboxamid	Paroxysmalis nocturnalis haemoglobinuria kezelése
Italian	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidinе-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridinе-2-yl)-4-fluoropyrrolidine-2-carboxamide	Trattamento dell'emoglobinuria parossistica notturna
Latvian	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidīn-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridīn-2-il)-4-fluoropirrolidīn-2-karboksamīds	Paroksismālas nakts hemoglobinūrijas ārstēšana
Lithuanian	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidin-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridin-2-il)-4-fluoropirolidino-2-karboksamidas	Priepuolinės naktinės hemoglobinurijos gydymas
Maltese	(2S,4R)-1-(2-(3-aċetil-5-(2-metilpirimidina-5-il)-1H-indażol-1-il)aċetil)-N-(6-bromopiridina-2-il)-4-fluworopirrolidina-2-karbossammid	Kura ta' l-emoglobinurja parossistika ta' billejl
Polish	(2S,4R)-1-(2-(3-acetylo-5-(2-metylpyrimidynо-5-yl)-1H-indazol-1-yl)acetylo)-N-(6-bromopyridynо-2-yl)-4-fluoropyrolidyno-2-karboksamid	Leczenie napadowej nocnej hemoglobinurii
Portuguese	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidin-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridin-2-il)-4-fluoropirrolidina-2-carboxamida	Tratamento da hemoglobinúria paroxística nocturna
Romanian	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidin-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridin-2-il)-4-fluoropirolidin-2-carboxamidă	Tratamentul hemoglobinuriei paroxistice nocturne
Slovak	(2S,4R)-1-(2-(3-acetyl-5-(2-metylpyrimidín-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridín-2-yl)-4-fluoropyrolidín-2-karboxamid	Liečba paroxyzmálnej nočnej hemoglobinúrie
Slovenian	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidin-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridin-2-il)-4-fluoropirrolidin-2-karboxamid	Zdravljenje paroksizmalne nočne hemoglobinurije
Spanish	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidinа-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridina2-yl)-4-fluoropirrolidina-2-carboxamida	Tratamiento de la hemoglobinuria paroxística nocturna
Swedish	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidin-2-carboxamid	Behandling av paroxysmal nattlig hemoglobinuri
Norwegian	(2S,4R)-1-(2-(3-acetyl-5-(2-metylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidin-2-karboksamid	Behandling av paroksysmal nattlig hemoglobinuri

Language	Active ingredient	Indication
Icelandic	(2S,4R)-1-(2-(3-acetýl-5-(2-methýlpýrimídín-5-ýl)-1H-indazól-1-ýl)acetýl)-N-(6-brómópýridín-2-ýl)-4-flúórópýrrólídín-2-carboxamíð	Meðferð fyrir paroxysmal nætur blóðrauðamigu