5 August 2020
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Public summary of opinion on orphan designation

(4-{(2S,4S)-4-Ethoxy-1-[(5-methoxy-7-methyl-1H-indol-4-yl)methyl]piperidin-2-yl}benzoic acid-hydrogen chloride(1/1)) for the treatment of paroxysmal nocturnal haemoglobinuria

On 4 June 2020, orphan designation EU/3/20/2281 was granted by the European Commission to Novartis Europharm Limited, Ireland, for (4-{(2S,4S)-4-ethoxy-1-[(5-methoxy-7-methyl-1H-indol-4-yl)methyl]piperidin-2-yl}benzoic acid-hydrogen chloride(1/1)) (also known as LNP023) 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 in red blood cells that carries oxygen around the body). Because haemoglobin is red, the passing of red urine, particularly in the mornings, is usually the most obvious sign of the disease. Patients may also feel very tired and develop blood clots (thromboses) in veins and excess bleeding. 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, paroxysmal nocturnal haemoglobinuria affected approximately 0.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 21,000 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, Soliris (eculizumab) and Ultomiris (ravilizumab) were authorised in the EU for the treatment of PNH. Patients were also treated with hematopoietic stem cell transplantation, a

*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, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
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procedure where the patient's bone marrow is replaced to form new bone marrow that produces healthy cells. Other methods such as blood transfusions and treatment with medicines to prevent clotting were used to improve symptoms.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with paroxysmal nocturnal haemoglobinuria. This is because preliminary data support improved reduction of haemolysis, when the medicine is combined with available treatments. 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 PNH, red blood cells lack a protein on their surface which leaves them open to being broken down by the complement system, part of the immune system (the body's defences). The medicine blocks the activity of a protein called complement factor B. It is expected that this action will prevent breakdown of red blood cells and so reduce 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 paroxysmal nocturnal haemoglobinuria were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of paroxysmal nocturnal haemoglobinuria or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 23 April 2020, 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.

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	(4-{(2S,4S)-4-ethoxy-1-[(5-methoxy-7-methyl-1H-indol-4-yl)methyl]piperidin-2-yl}benzoic acid-hydrogen chloride(1/1))	Treatment of paroxysmal nocturnal haemoglobinuria
Bulgarian	(4-{(2S,4S)-4-етокси-1-[(5-метокси-7-метил-1H-индол-4-ил)метил]пиперидин-2-ил}бензоева киселина-хидроген хлорид(1/1))	Лечение на пароксизмална нощна хемоглобинурия
Croatian	(4-{(2S,4S)-4-etoksi-1-[(5-metoksi-7-metil-1H-indol-4-il)metil]piperidin-2-il}benzojeva kiselina-klorovodik(1/1))	Liječenje paroksizmalne noćne hemoglobinurije
Czech	Hydrochlorid kyseliny 4-{(2S,4S)-4-ethoxy-1-[(5-methoxy-7-methyl-1H-indol-4-yl)methyl]piperidin-2-yl}benzoové (1/1)	K léčbě paroxysmální noční hemoglobinurie
Danish	(4-{(2S,4S)-4-ethoxy-1-[(5-methoxy-7-methyl-1H-indol-4-yl)methyl]piperidin-2-yl}benzoesyre-hydrogenchlorid(1/1))	Behandling af paroksysmatisk nocturn hæmoglobinuria
Dutch	(4-{(2S,4S)-4-ethoxy-1-[(5-methoxy-7-methyl-1H-indol-4-yl)methyl]piperidine-2-yl}benzoëzuur-waterstof chloride(1/1))	Behandeling van paroxismale nachtelijke hemoglobinurie
Estonian	(4-{(2S,4S)-4-etoksü-1-[(5-metoksü-7-metüül-1H-indool-4-üül)metüül]piperidiin-2-üül} bensoehappe vesinikkloriid (1/1))	Paroksüsmaalse öise hemoglubinuuria ravi
Finnish	(4-{(2S,4S)-4-etoksi-1-[(5-metoksi-7-metyyli-1H-indoli-4-yl)metyyli]piperidiini-2-yl}bentsoehappo-hydrogeenikloridi (1/1))	Paroksysmaalisen nokturnaalisen hemoglobinurian hoito
French	(4-{(2S,4S)-4-ethoxy-1-[(5-méthoxy-7-méthyl-1H-indol-4-yl)méthyl]pipéridine-2-yl}acide benzoïque-chlorure d'hydrogène(1/1))	Traitement de l'hémoglobinurie paroxystique nocturne
German	(4-{2S,4S)-4-Ethoxy-1-[(5-Methoxy-7-Methyl-1H-Indol-4-yl}methyl]Piperidin-2-yl}Benzoesäurehydrogenchlorid (1/1))	Behandlung von paroxysmaler nächtlicher Hämoglobinurie
Greek	(4-{(2S,4S)-4-αιθοξυ-1-[(5-μεθοξυ-7-μεθυλ-1H-ινδολ-4-υλ)μέθυλ]πιπεριδίνο-2-υλ}βενζοϊκό οξύ-υδροχλώριο(1/1))	Θεραπεία της παροξυσμικής νυκτερινής αιμοσφαιρινουρίας
Hungarian	4-{(2S,4S)-4-etoxi-1-[(7-metil-5-metoxi-1H-indol-4-il)metil]piperidin-2-il}benzoesav—(hidrogén-klorid) (1/1)	Paroxysmalis nocturnalis haemoglobinuria
Italian	(4-{(2S,4S)-4-etossi-1-[(5-metossi-7-metil-1H-indol-4-yl)metil]piperidina-2-yl}acido benzoico-idrogeno cloruro (1/1))	Trattamento dell'emoglobinuria parossistica notturna

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	(4-{(2S,4S)-4-etoksi-1-[(5-metoksi-7-metil-1H-indol-4-il)metil]piperidīn-2-il}benzoskābes hidrogēnhlorīds(1/1))	Paroksismālas nakts hemoglobinūrijas ārstēšana
Lithuanian	(4-{(2S,4S)-4-etoksi-1-[(5-metoksi-7-metil-1H-indol-4-il)metil]piperidin-2-il}benzoinė rūgštis - vandenilio chloridas (1/1))	Priepuolinės naktinės hemoglobinurijos gydymas
Maltese	(4-{(2S,4S)-4-etossi-1-[(5-metossi-7-metil-1H-indol-4-il)metil]piperidin-2-yl}aċidu benżojku-klorur tal-idroġenu(1/1))	Kura ta' l-emoglobinurja parossistika ta' billejl
Polish	4-{(2S, 4S)-4-etoksy-1-[(5-metoksy-7-metylo-1H-indol-4-ilo) metylo] piperydyn-2-ylo} benzoesowy kwas solny (1/1))	Leczenie napadowej nocnej hemoglobinurii
Portuguese	Ácido (4-{(2*S*,4*S*)-4-etoxi-1-[(5-metoxi-7-metil-1H-indol-4-il)metil]piperidin-2-il}benzoico – ácido clorídrico (1/1))	Tratamento da hemoglobinúria paroxística nocturna
Romanian	(4-{(2S,4S)-4-etoxi-1-[(5-metoxi-7-metil-1H-indol-4-il)metil]piperidin-2-yl}acid benzoic-clorura de hydrogen (1/1))	Tratamentul hemoglobinuriei paroxistice nocturne
Slovak	Hydrochlorid kyseliny 4-{(2S,4S)-4-etoxy-1-[(5-metoxy-7-metyl-1H-indol-4-yl)metyl]piperidín-2-yl} benzoovej (1/1)	Liečba paroxyzmálnej nočnej hemoglobinúrie
Slovenian	(4-{(2S,4S)-4-etoksi-1-[(5 metoksi-7-metil-1H-indol-4-il)metil]piperidin-2 il}benzojska kislina-vodikov klorid(1/1))	Zdravljenje paroksizmalne nočne hemoglobinurije
Spanish	(4-{(2S,4S)-4-etoxi-1-[(5-metoxi-7-metil-1H-indol-4-il)metil]piperidin-2-il}ácido benzoico-cloruro de hidrógeno(1/1))	Tratamiento de la hemoglobinuria paroxística nocturna
Swedish	(4-{(2S,4S)-4-etoxi-1-[(5-metoxi-7-metyl-1H-indol-4-yl)metyl]piperidin-2-yl}bensoesyra-väteklorid(1/1))	Behandling av paroxysmal nattlig hemoglobinuri
Norwegian	(4-{(2*S*,4*S*)-4-etoksy-1-[(5-metoksy-7-metyl-1H-indol-4-yl)metyl]piperidin-2-yl}benzosyre-hydrogenklorid (1/1))	Behandling av paroksysmal nattlig hemoglobinuri
Icelandic	(4-{(2S,4S)-4-etoxý-1-[(5-metoxý-7-metýl-1H-indól-4-yl)metýl]píperídín-2-ýl}bensósýru-vetnisklóríð (1/1))	Meðferð við blóðrauðamigu sem kemur í köstum að nóttu til