



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Pegylated recombinant phenylalanine ammonia lyase for the treatment of hyperphenylalaninaemia

On 28 January 2010, orphan designation (EU/3/09/708) was granted by the European Commission to BioMarin Europe Ltd, United Kingdom, for pegylated recombinant phenylalanine ammonia lyase for the treatment of hyperphenylalaninaemia.

What is hyperphenylalaninaemia?

Hyperphenylalaninaemia is high levels of phenylalanine in the blood. Phenylalanine is an amino acid, one of the building blocks of proteins, and comes from the diet. Hyperphenylalaninaemia mainly occurs in patients with a genetic disorder called phenylketonuria (PKU). Patients with this disorder cannot convert phenylalanine into tyrosine (another amino acid). This causes a build-up of phenylalanine in the blood, which causes problems with the brain and nervous system.

Hyperphenylalaninaemia is a long-term debilitating disease that leads to mental retardation if left untreated.

What is the estimated number of patients affected by the condition?

At the time of designation, hyperphenylalaninaemia affected approximately 1.7 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 86,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of designation, one product was authorised in the EU for the treatment of hyperphenylalaninaemia. In addition, patients were advised to follow a lifelong strict diet low in phenylalanine-containing foods (such as meat, fish, eggs, nuts, legumes and corn) to reduce phenylalanine intake.

*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 27), Norway, Iceland and Liechtenstein. This represents a population of 504,800,000 (Eurostat 2009).



The sponsor has provided sufficient information to show that pegylated recombinant phenylalanine ammonia lyase might be of significant benefit for patients with hyperphenylalaninaemia because it works in a different way to existing treatment and because early studies indicate that it might improve the outcome of patients who do not respond to existing treatment. These assumptions 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?

Hyperphenylalaninaemia is mainly caused by the lack of phenylalanine hydroxylase (PAH), an enzyme that converts phenylalanine into tyrosine.

Pegylated recombinant phenylalanine ammonia lyase is a bacterial enzyme that can break down phenylalanine in a similar way to PAH. In the body, it is expected to replace the missing PAH. This is expected to stop the accumulation of phenylalanine in the body, relieving the symptoms of the disease.

Pegylated recombinant phenylalanine ammonia lyase is made by a method known as 'recombinant DNA technology': it is made by a bacterium that has received a gene (DNA) that makes it able to produce phenylalanine ammonia lyase. The enzyme has also been modified by a process called 'pegylation', meaning that it has been attached to a chemical called polyethylene glycol.

What is the stage of development of this medicine?

The effects of pegylated recombinant phenylalanine ammonia lyase have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with hyperphenylalaninaemia were ongoing.

At the time of submission, pegylated recombinant phenylalanine ammonia lyase was not authorised anywhere in the EU for hyperphenylalaninaemia 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 5 November 2009 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 Community) 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

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Translations of the active ingredient and indication in all official EU languages, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Pegylated recombinant phenylalanine ammonia lyase	Treatment of hyperphenylalaninaemia
Bulgarian	Рекомбинантна фенилаланин амоняк-лиаза, свързана с ПЕГ(полиетиленгликол)-вериги	Лечение на хиперфенилаланинемия
Czech	Rekombinovaná pegylovaná fenylalaninamoniumlyasa	Léčba hyperfenylalaninémie
Danish	Pegylet recombinant fenylalaninammoniaklyase	Behandling af hyperfenylalaninæmi
Dutch	Gepegyleerd recombinant fenylalanine-ammonialyase	Behandeling van hyperfenylalaninemie
Estonian	Pegüleeritud rekombinantne fenüülalaniinammooniumlääs	Hüperfenüülalanineemia ravi
Finnish	Pegyloitu yhdistelmäfenyyilalaniiniammoniakki-lysaasi	Hyperfenyyilalaninemian hoito
French	Lyase phénylalanine-ammoniaque recombinante pegylée	Traitement de l'hyperphénylalaninémie
German	Pegylierte rekombinante Phenylalanin-Ammoniaklyase	Behandlung von Hyperphenylalaninämie
Greek	Πεγκυλιωμένη ανασυνδυασμένη λύαση αμμωνίας - φαινυλαλανίνης	Θεραπεία της υπερφαινυλαλανιναιμίας
Hungarian	Pegilált rekombináns fenilalanin-ammonia-liáz	Hyperphenylalaninaemia kezelése
Italian	Fenilalanina ammonio liasi ricombinante pegilata	Trattamento dell'iperfenilalaninemia
Latvian	Pegilēta rekombinētā fenilalanīna amonija liāze	Hiperfenilalaninēmijas ārstēšana
Lithuanian	Pegiliuota rekombinantinė fenilalanino amonio liazė	Hiperfenilalaninemijos gydymas
Maltese	Phenylalanine ammonia lyase rikombinanti pegilat	Kura ta' l-iperfenilalaninimja
Polish	Rekombinowana pegylowana amoniakoliza fenylalaninowa	Leczenie hiperfenyloalaninemii
Portuguese	Recombinante pegilado da fenilalanina amónia liase	Tratamento da hiperfenilalaninemia
Romanian	Fenilalanină amoniac liază recombinantă pegilată	Tratamentul hiperfenilalaninemiei
Slovak	Pegylovaná rekombinantná fenylalanín amónium lyáza	Liečba hyperfenylalaninémie
Slovenian	Pegilirana rekombinantna fenilalanin amonij liaza	Zdravljenje hiperfenilalaninemije
Spanish	Fenilalanina amoníaco-liasa recombinante pegilada	Tratamiento de la hiperfenilalaninemia
Swedish	Pegylerad rekombinant fenylalanin-ammoniaklyas	Behandling av hyperfenylalaninemi
Norwegian	Pegylert rekombinant fenylalaninammoniumlyase	Behandling av hyperfenylalaninemi
Icelandic	Pegýleraður raðbrigða fenýlalanín ammóníaklýasi	Meðferð við fenýlalaníndreyra