



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13 December 2016
EMA/676430/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Particles comprised of methacrylic acid based co-polymer, cross-linked with a bi-functional cross-linker, purified to bind L-phenylalanine and L-phenylalanine containing peptides, for the treatment of hyperphenylalaninaemia

On 18 November 2016, orphan designation (EU/3/16/1784) was granted by the European Commission to MipSalus ApS, Denmark, for particles comprised of methacrylic acid based co-polymer, cross-linked with a bi-functional cross-linker, purified to bind L-phenylalanine and L-phenylalanine containing peptides (also called PHE-MIP) 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 disability if left untreated.

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

At the time of designation, hyperphenylalaninaemia affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 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).



What treatments are available?

At the time of designation, the medicine Kuvan (sapropterin) was authorised in the EU for the treatment of hyperphenylalaninaemia of certain causes. In addition, patients were advised to follow a lifelong strict diet low in phenylalanine-containing foods (which include meat, fish, eggs, nuts, legumes and corn) to reduce phenylalanine intake.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with hyperphenylalaninaemia because experimental results suggest it could be useful to patients in whom the existing approved medicine cannot be used. 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 consists of particles of a long plastic-like substance (a polymer) that is not digested or absorbed by the body. The polymer has been designed to attach selectively to phenylalanine or protein fragments that contain phenylalanine. When the medicine is given with food, it is expected to attach to the phenylalanine from food proteins as they are broken down in the gut, preventing the amino acid from being absorbed. The medicine and its attached phenylalanine will then pass out of the body in the stools, helping to keep levels of phenylalanine in the body from rising.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

No clinical trials with the medicine in patients with hyperphenylalaninaemia had been started.

At the time of submission, the medicine 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 6 October 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Particles comprised of methacrylic acid based co-polymer, cross-linked with a bi-functional cross-linker, purified to bind L-phenylalanine and L-phenylalanine containing peptides	Treatment of hyperphenylalaninaemia
Bulgarian	Пречистени частици, съставени от кополимер базиран на метакрилова киселина, свързан с би-функционален крос-линкер, предназначен за свързване на L-фенилаланин и пептиди съдържащи L-фенилаланин	Лечение на хиперфенилаланинемия
Croatian	Čestice sastavljena od ko-polimera baziranog na metakrilnoj kiselini, križno vezanog s bi-funkcionalnim poprečnim poveziivačem, pročišćen da bi vezao L-fenilalanin i peptide koji sadrže L-fenilalanin	Liječenje hiperfenilalaninemije
Czech	Částice sestávající z metakrylové kyseliny na ko-polymeru, křížene vázané s bifunkčním kříženou vazební molekulou, čištěné k vazbě L-fenylalaninu a L-fenylalaninu obsahující peptidy	Léčba hyperfenylalaninémie
Danish	Partikler sammensat af methacrylsyre-baseret copolymer, krydlinket med en bi-funktionel krydlinker, som er purificeret til at binde L-phenylalanine og L-phenylalanine-indeholdende peptider	Behandling af hyperfenylalaninæmi
Dutch	Deeltjes bestaande uit een methacryliczuur gebaseerd co-polymeer, kruisverbonden met een bi-functioneel "cross-linker", gezuiverd om L-fenylalanine en L-fenylalanine bevattende peptide te binden	Behandeling van hyperfenylalaninemie
Estonian	Puhastatud osakesed, mis sisaldavad metakrüülhappel baseeruvaid co-polümeere, on ühendatud bifunktsionaalse ristühendajaga, ja on võimelised liitma L-fenüülalaniini ja L-fenüülalaniini sisaldavaid peptiide	Hüperfenüülalanineemia ravi
Finnish	Partikkelit sisältäen metakryylihaposta peräisin olevan kopolymeerin, silloitettuna bifunktionaalisen silloitusrakenteen avulla, puhdistettuna sitoutuakseen L-fenyylialaniiniin ja L-fenyylialaniinia sisältäviin peptideihin	Hyperfenyylialaninemian hoito

¹ At the time of designation

Language	Active ingredient	Indication
French	Particules comprenant un co-polymère à base d'acide méthacrylique, liées transversalement par un ligand bi-fonctionnel, purifié pour lier des peptides contenant L-phénylalanine et L-phénylalanine	Traitement de l'hyperphénylalaninémie
German	Partikel bestehend aus einem Methacrylsäure Co-Polymer, die mit einem bi-funktionalem Crosslinker verbunden sind, und purifiziert sind um L-Phenylalanin und Peptide mit L-Phenylalanin zu binden	Behandlung von Hyperphenylalaninämie
Greek	Σωματίδια αποτελούμενα από συμπολυμερές μεθακρυλικής βάσης, διασυνδεδεμένο με ένα συνδέτη διπλής λειτουργίας, παρασκευασμένο να προσδένει L-φαινυλαλανίνη και πεπτιδία που περιέχουν L-φαινυλαλανίνη	Θεραπεία της υπερφαινυλαλανιναιμίας
Hungarian	L-fenilalanint és L-fenilalanint tartalmazó peptideket megköttő tisztított, bi-funkcionális térhálósítóval térhálósított, metakrilsav alapú co-polimerből álló részecskék	Hyperphenylalaninaemia kezelése
Italian	Particelle contenenti un co-polimero su based di acid metacrilico, cross-linked con un cross-linker bi-funzionale, purificato per legare L-fenilalanina e peptidi contenenti L-fenilalanina	Trattamento dell'iperfenilalaninemia
Latvian	Dalīņas, kas sastāv no metakrīlskābes bāzes polimēra, kas šķerssaitēts ar bifunkcionālu saistvielu un attīrīts, lai saistītos ar L-fenilalanīnu un L-fenilalanīnu saturošiem peptīdiem	Hiperfenilalaninēmijas ārstēšana
Lithuanian	Dalelės, sudarytos iš metakrilinės rūgšties pagrindo ko-polimero, kryžmai sujungtos bifunkcine kryžmine jungtimi, išgrynintos surišti L-fenilalaniną ir L-fenilalaniną, turinčius peptidus	Hiperfenilalaninemijos gydymas
Maltese	Partikoli magħmula minn aċidu metakriliku bbażat fuq kopolimer, inkroċjat ma' inkroċjatur bifunzjonali, ippurifikat biex jgħaqqad L-fenilalanin u L-fenilalanin li fih il-peptidi	Il-kura ta' iperfenilalaninemija
Polish	Cząstki złożone z ko-polimeru opartego na kwasie metakrylowym, zsięciowane dwufunkcyjnym mostkiem, oczyszczone tak aby wiązać L-fenyloalaninę oraz peptydy zawierające L-fenyloalaninę	Leczenie hiperfenyloalaninemii
Portuguese	Partículas compostas por um copolímero à base de ácido metacrílico, com ligação cruzada a um agente de ligação bi-funcional, purificadas para se ligarem a L-fenilalanina e a péptidos contendo L-fenilalanina	Tratamento da hiperfenilalaninemia

Language	Active ingredient	Indication
Romanian	Particule alcătuite dintr-un co-polimer pe bază de acid metacrilic, legat încrucișat cu un cross-linker bifuncțional, purificat pentru a lega L-fenilalanina și peptide ce contin L-fenilalanina	Tratamentul hiperfenilalaninemieii
Slovak	Častice pozostávajúce z kopolyméru kyseliny metakrylovej previazané s bi-funkčným "cross-linkerom", purifikované na viazanie L-fenylalanínu a peptidov obsahujúcich L-fenylalanín	Liečba hyperfenylalaninémie
Slovenian	Delci, sestavljeni iz kopolimera na osnovi metakrilne kisline, prečno povezane s prečiščenim mrežnim povezovalcem, ki veže L-fenilalanin in L-fenilalanin vsebujoče peptide	Zdravljenje hiperfenilalaninemije
Spanish	Partículas compuestas de co-polimeros del ácido metacrílico reticulado con un reticulante bi-funcional purificado que se unen a la L-fenilalanina y péptidos que contienen L-fenilalanina.	Tratamiento de la hiperfenilalaninemia
Swedish	Partiklar bestående av (en) metakrylsyrabaserad sampolymer, tvärbunden med ett bifunktionellt tvärbindningsmedel, uppenad för att binda L-fenylalanin och L-fenylalanininnehållande peptider.	Behandling av hyperfenylalaninemi
Norwegian	Partikler som består av metakrylsyrebaserte kopolymerer, kryssbundet med en bifunksjonell kryssbinder, rensset til å binde L-fenylalanin og peptider som inneholder L-fenylalanin	Behandling av hyperfenylalaninemi
Icelandic	Agnir sem samanstanda af methakrylík sýru byggðri co-fjölliðu, kross-bundin með tvívirku kross-tengi hreinsuðu til að binda L-fenýlalanín sem inniheldur peptíð	Meðferð við fenýlalaníndreyra