



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Pyridoxal 5'-phosphate for the treatment of pyridoxamine 5'-phosphate oxidase deficiency

On 15 October 2014, orphan designation (EU/3/14/1347) was granted by the European Commission to Great Ormond Street Hospital Foundation Trust, United Kingdom, for pyridoxal 5'-phosphate for the treatment of pyridoxamine 5'-phosphate oxidase deficiency.

What is pyridoxamine 5'-phosphate oxidase deficiency?

Pyridoxamine 5'-phosphate oxidase deficiency is a hereditary disease affecting children. It is caused by a defect in the *PNPO* gene needed to produce an enzyme known as pyridoxine 5'-phosphate oxidase. This enzyme is required to transform pyridoxine (or vitamin B6) into its active form pyridoxamine 5'-phosphate (PLP), which is essential for brain function. Children with the disease lack PLP and this leads to various symptoms, which normally appear shortly after birth, including irritability, inflammation of the lips, conjunctivitis (inflammation of the membrane that lines the eye and the inside of the eyelids), seizures (fits) as well as other neurological symptoms.

Pyridoxamine 5'-phosphate oxidase deficiency is a life-threatening disease due to seizures.

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

At the time of designation, pyridoxamine 5'-phosphate oxidase deficiency affected less than 0.02 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 1,000 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, no satisfactory methods of treatment were authorised in the EU for pyridoxamine 5'-phosphate oxidase deficiency. Products containing PLP (the active form of vitamin B6)

*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).



were given to patients, however existing formulations were for use by mouth only and not appropriate for use in infants.

How is this medicine expected to work?

This medicine is made of PLP to be given by injection. It is expected to work by replacing the missing PLP in patients with pyridoxamine 5'-phosphate oxidase deficiency, thus improving the symptoms of the disease.

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.

At the time of submission, clinical trials with the medicine in patients with pyridoxamine 5'-phosphate oxidase deficiency had not started.

At the time of submission, the medicine was not authorised anywhere in the EU for pyridoxamine 5'-phosphate oxidase deficiency 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 4 September 2014 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:

Great Ormond Street Hospital for Children, NHS Foundation Trust
Great Ormond Street
London WC1N 3JH
United Kingdom
Tel. +44 (0)207 4059 200
E-mail: e.footitt@ucl.ac.uk

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	Pyridoxal 5'-phosphate	Treatment of pyridoxamine 5'-phosphate oxidase deficiency
Bulgarian	пиридоксал 5'-фосфат	Лечение на пиридоксамин 5'-фосфат оксидаза дефицит
Croatian	Piridoksal-5'-fosfat	Liječenje nedostatka piridoksamin 5'-fosfat oksidaze
Czech	Pyridoxal 5'-vápenatý	Zacházení pyridoxamine 5'-fosfát oxidázy nedostatek
Danish	Pyridoxal 5'-phosphat	Behandling af pyridoxamin 5'-fosfat oxidase mangel
Dutch	Pyridoxal-5'-fosfaat	Behandeling van pyridoxamine 5'-fosfaat oxidase deficiëntie
Estonian	5'-püridoksaalfosfaat	Püridoksamiin 5'-fosfaadi oksüdaasi puudulikkusse ravi
Finnish	5'-Pyridoksaalifosfaati	Pyridoxamiini 5'-fosfaatti oksidaasi puuteen hoito
French	5'-Phosphate de pyridoxal	Traitement du déficit en pyridoxamine 5'-phosphate oxydase
German	5'-Pyridoxalphosphat	Behandlung von Pyridoxamin 5'-Phosphat-Oxidase-mangel
Greek	πυριδοξάλη 5'- φωσφορική	Θεραπεία έλλειψης της πυριδοξαμίνης 5'- φωσφορικής οξειδάσης
Hungarian	Piridoxál-5'-foszfát	Piridoxamin 5'-foszfát-oxidáz hiány kezelésére
Italian	Piridossal 5'-fosfato	Trattamento di piridossamina 5'-fosfato ossidasi carenza
Latvian	Piridoksāl 5'-fosfāts	Piridoksamīna 5'-fosfāta oksidāzes deficīta ārstēšana
Lithuanian	Piridoksal 5'-fosfatas	Piridoksamino 5'-fostafo oksidazės stokos gydymas pyridoxamine 5'-fosfatas oksidazės trukumas
Maltese	Pyridoxal 5'-phosphate	Kura ta' nuqqas ta' pyridoxamine 5'-phosphate oxidase
Polish	5'-pirydoksalu fosforan	Leczenie niedoboru oksydazy 5'-fosforanu pirydoksaminy
Portuguese	5'-Fosfato piridoxal	Tratamento da deficiência de piridoxamina 5'- fosfato oxidase
Romanian	Piridoxal 5'-fosfat	Tratamentul pyridoxamine 5'-fosfato oxidase deficienția
Slovak	Pyridoxal 5'-fosfát	Liečba nedostatku pyridoxamin 5'-fosfát oxidázy
Slovenian	5'-piridoksalfosfat	Zdravljenje pomanjkanja piridoksamin 5'-fosfatne oksidaze
Spanish	Piridoxal 5'-fosfato	Tratamiento de la deficiencia de piridoxamina 5'-fosfato oxidasa
Swedish	5'-Pyridoxalfosfat	Behandling av pyridoxamin 5'-fosfatoxidase-brist
Norwegian	5'-Pyridoksalfosfat	Behandling av pyridoksamin 5'-fosfat-oxidase-mangel
Icelandic	Pýridoxal 5'-fosfat	Meðhöndlun á pýridoxamín 5'-fosfat oxidasa skorti

¹ At the time of designation