



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

31 March 2016
EMA/COMP/63648/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Methyl 3-((2R)-2-hydroxy-4-((((S)-1-methoxy-1-oxopropan-2-yl) amino)(phenoxy)phosphoryl)oxy)-3,3-dimethylbutanamido)propanoate for the treatment of pantothenate-kinase-associated neurodegeneration

On 17 February 2016, orphan designation (EU/3/16/1612) was granted by the European Commission to Retrophin Europe Limited, Ireland, for methyl 3-((2R)-2-hydroxy-4-((((S)-1-methoxy-1-oxopropan-2-yl) amino)(phenoxy)phosphoryl)oxy)-3,3-dimethylbutanamido)propanoate for the treatment of pantothenate-kinase-associated neurodegeneration.

What is pantothenate-kinase-associated neurodegeneration?

Pantothenate-kinase-associated neurodegeneration (PKAN) is an inherited disease caused by a mutation (change) in the gene that produces an enzyme called pantothenate kinase-2. This enzyme is needed by brain cells for the first step in producing coenzyme A, which is essential for them to function. Patients with the disease cannot produce pantothenate kinase-2, resulting in gradual brain damage. Symptoms of PKAN usually appear in childhood and include severe dystonias (painful muscle spasms) and Parkinson-like effects such as rigidity and slow movement, as well as loss of sight and impaired swallowing.

PKAN is a long-term debilitating and life-threatening disease due to complications of severe muscle spasms that can affect swallowing and lead to pneumonia (infection of the lungs) and malnutrition.

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

At the time of designation, PKAN affected less than 0.03 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 1,500 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?

No satisfactory methods of treatment for PKAN were authorised in the EU at the time of orphan designation. Patients received supportive therapy including muscle-relaxant medicines and Parkinson medicines to deal with the symptoms.

How is this medicine expected to work?

The enzyme pantothenate kinase-2 converts pantothenate (also called vitamin B5) from food into phosphopantothenate. This is the first of several steps in the production of the essential substance coenzyme A. Because patients with PKAN lack functioning pantothenate kinase-2, the cells cannot produce normal levels of phosphopantothenate that they need to produce coenzyme A.

This medicine provides a source of phosphopantothenate in a form that can be absorbed by cells. This allows brain cells to make the coenzyme A they need, thereby improving the symptoms of the condition.

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, a clinical trial with this medicine in healthy volunteer had been completed and clinical trials in patients with PKAN were planned.

At the time of submission, the medicine was not authorised anywhere in the EU for PKAN. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 21 January 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	Methyl 3-((2R)-2-hydroxy-4-((((S)-1-methoxy-1-oxopropan-2-yl) amino)(phenoxy)phosphoryl)oxy)-3,3-dimethylbutanamido)propanoate	Treatment of pantothenate-kinase-associated neurodegeneration
Bulgarian	Метил 3-((2R)-2-хидрокси-4-((((S)-1-метокси-1-оксопропан-2-ил) амино)(фенокси)фосфорил)окси)-3,3-диметилбутанамидо)пропаноат	Лечение на пантотенат киназа-асоциирана невродегенерация
Croatian	Metil 3-((2R)-2-hidroksi-4-((((S)-1-metoksi-1-oksopropan-2-il) amino)(fenoksi)fosforil)oksi)-3,3-dimetilbutanamido)propanoat	Liječenje neurodegeneracije povezane s pantotenat kinazom
Czech	Methyl 3-((2R)-2-hydroxy-4-((((S)-1-methoxy-1-oxopropan-2-yl) amino)(fenoxy)fosforyl)oxy)-3,3-dimethylbutanamido)propanoát	Léčba neurodegenerace asociované s pantotenátkinázou
Danish	Methyl 3-((2R)-2-hydroxy-4-((((S)-1-methoxy-1-oxopropan-2-yl) amino)(phenoxy)phosphoryl)oxy)-3,3-dimethylbutanamido)propanoat	Behandling af Hallervorden-Spatz sygdom
Dutch	Methyl-3-((2R)-2-hydroxy-4-((((S)-1-methoxy-1-oxopropan-2-yl) amino)(fenoxy)fosforyl)oxy)-3,3-dimethylbutanamido)propanoat	De behandeling van pantothenaatkinase-geassocieerde neurodegeneratie
Estonian	Metüül-3-((2R)-2-hüdroksü-4-((((S)-1-metoksü-1-oksopropan-2-üül) amino)(fenoksü)fosforüül)oksü)-3,3-dimetüülbutaanamido)propanoat	Pantotenaat kinaasiga seotud neurodegeneratsiooni ravi
Finnish	Metyyli 3-((2R)-2-hydroksi-4-((((S)-1-metoksi-1-oksopropan-2-yyli) amino)(fenoksi)fosforyyli)oksi)-3,3-dimetyylibutanamido)propanoatti	Pantotenaattikinaasiin liittyvän neurodegeneraation hoito
French	Méthyle 3-((2R)-2-hydroxy-4-((((S)-1-méthoxy-1-oxopropane-2-yl) amino)(phénoxy)phosphoryl)oxy)-3,3-diméthylbutanamido)propanoate	Traitement de la neuro-dégénérescence associée à pantothénate kinase
German	Methyl 3-((2R)-2-hydroxy-4-((((S)-1-methoxy-1-oxopropan-2-yl) amino)(phenoxy)phosphoryl)oxy)-3,3-dimethylbutanamido)propanoat	Behandlung der Pantothenatkinase-assoziierten Neurodegeneration
Greek	Μεθυλο 3-((2R)-2-υδροξυ-4-((((S)-1-μεθοξυ-1-οξοπροπανο-2-υλο) αμινο)(φαινοξυ)φωσφορυλ)οξυ)-3,3-διμεθυλοβουταναμιδο)προπανοϊκό άλας	Θεραπεία της σχετιζόμενης με την παντοθενική κινάση νευροεκφύλισης

¹ At the time of designation

Language	Active ingredient	Indication
Hungarian	Metil-3-((2R)-2-hidroxi-4-((((S)-1-metoxi-1-oxopropán-2-il)-amino)(fenoxi)-foszforil)-oxi)-3,3-dimetilbutánamid)-propanoát	Pantotenát-kináz asszociált neurodegeneráció kezelése
Italian	Metil 3((2R)-2-idrossi-4-((((S)-1-metossi-1-ossopropan-2-il) ammino)(fenossi)fosforil)ossi)-3,3-dimetilbutanammide)propanoato	Trattamento della neurodegenerazione associata alla pantotenato chinasi
Latvian	Metil 3-((2R)-2-hidroksi-4-((((S)-1-metoksi-1-oksopropān-2-il) amino)(fenoksi)fosforil)oksi)-3,3-dimetilbutānamīda)propanāts	Ar pantotenāta kināzi saistītas neiroleģenerācijas ārstēšana
Lithuanian	Metil 3-((2R)-2-hidroksi-4-((((S)-1-metoksi-1-oksopropan-2-il) amino)(fenoksi)fosforil)oksi)-3,3-dimetilbutanamido)propanoatas	Su pantotenato kinaze siejamos neurodegeneracijos gydymas
Maltese	Methyl 3-((2R)-2-hydroxy-4-((((S)-1-methoxy-1-oxopropan-2-yl) amino)(phenoxy)phosphoryl)oxy)-3,3-dimethylbutanamido)propanoate	Kura ta' newrodegenerazzjoni assoċjata ma' pantothenate kinase
Polish	3-((2R)-2-hydroksy-4-((((S)-1-metoksy-1-oksopropan-2-ylo) amino)(fenoksy)fosforyl)oksy)-3,3-dimetylobutanamido)propionian metylu	Leczenie neurodegeneracji związanej z kinazą pantotenu
Portuguese	Propanoato de metil 3-((2R)-2-hidroxi-4-((((S)-1-metoxi-1-oxopropan-2-il) amino)(fenoxi)fosforil)oxi)-3,3-dimetilbutanamida)	Tratamento da neurodegeneração associada à deficiência em pantotenato cinase
Romanian	Metil 3-((2R)-2-hidroxi-4-((((S)-1-metoxi-1-oxopropan-2-il) amino)(fenoxi)fosforil)oxi)-3,3-dimetilbutanamido)propanoat	Tratamentul neurodegenerenței asociate cu pantotenat-kinaza
Slovak	Metyl 3-((2R)-2-hydroxy-4-((((S)-1-metoxi-1-oxopropán-2-yl) amino)(fenoxy)fosforyl)oxy)-3,3-dimetylbutanamido)propanoát	Liečba neurodegenerácie asociovanej s pantotenát-kinázou
Slovenian	Metil 3-((2R)-2-hidroksi-4-((((S)-1-metoksi-1-oksopropan-2-il) amino)(fenoksi)fosforil)oksi)-3,3-dimetilbutanamido)propanoat	Zdravljenje nevrodegeneracije, povezane s pantotenat kinazo
Spanish	Metil 3-((2R)-2-hidroxi-4-((((S)-1-metoxi-1-oxopropan-2-il) amino)(fenoxi)fosforil)oxi)-3,3-dimetilbutanamido)propanoato	Tratamiento de la neurodegeneración asociada al pantotenato quinasa
Swedish	Metyl 3-((2R)-2-hydroxi-4-((((S)-1-metoxi-1-oxopropan-2-yl) amino)(fenoxi)fosforyl)oxi)-3,3-dimetylbutanamido)propanoat	Behandlingen av pantotenatkinas-associerad neurodegeneration
Norwegian	Metyl 3-((2R)-2-hydroksy-4-((((S)-1-metoksy-1-oksopropan-2-yl) amino)(fenoksy)fosforyl)oksy)-3,3-dimetylbutanamid)propanoat	Behandling av pantotenatkinase-assosiert nevrodegenerering

Language	Active ingredient	Indication
Icelandic	Metýl-3-((2R)-2-hýdroxý-4-(((S)-1-metoxý-1-oxóprópan-2-ýl) amínó)(fenoxý)fosfórýl)oxý)-3,3-dímetýlbútanamíð)própanóat	Meðferð við pantótenatakínasatengdri taugahrönnun

Withdrawn