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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant thymidine phosphorylase encapsulated in autologous erythrocytes for the treatment of mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) due to thymidine phosphorylase deficiency

On 15 April 2011, orphan designation (EU/3/11/856) was granted by the European Commission to St George's University of London, United Kingdom, for recombinant thymidine phosphorylase encapsulated in autologous erythrocytes for the treatment of mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) due to thymidine phosphorylase deficiency.

What is mitochondrial neurogastrointestinal encephalomyopathy (MNGIE)?

Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is an inherited disease caused by defects in a gene responsible for the production of an enzyme called 'thymidine phosphorylase'. This enzyme controls the amount of certain compounds, such as thymidine, found in the genetic material of cells.

Patients with the disease do not have enough of the thymidine phosphorylase enzyme and therefore are unable to break down thymidine, causing it to build up in the cells, where it destroys a type of DNA called 'mitochondrial DNA'. The disruption of mitochondrial DNA leads to the symptoms of the disease, although the exact way in which this happens is not known.

The disease affects many parts of the body, particularly the digestive system, where it causes problems such as nausea (feeling sick), abdominal pain (stomach ache), diarrhoea and weight loss, and the nervous system, where it causes symptoms such as weakness, numbness and tingling sensations. Symptoms can appear at any time from birth but usually start during the second decade of life, and worsen with time.

MNGIE is a debilitating disease that is long lasting and life threatening due to its effects on gut movement and on the nervous system including the brain.

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

At the time of designation, MNGIE affected less than 0.01 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of fewer than 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).

What treatments are available?

At the time of submission of the application for orphan drug designation, no satisfactory methods had been authorised in the EU for the treatment of patients affected by the condition. Patients were given treatments to help alleviate their symptoms and genetic counselling (discussion of the risks of passing the condition on to children). In some patients, allogeneic stem-cell transplantation was used. This is a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow.

How is this medicine expected to work?

'Recombinant thymidine phosphorylase encapsulated in autologous erythrocytes' is intended to be an enzyme replacement therapy for patients with MNGIE. It is expected to replace the patient's missing enzyme, thereby reducing the build up of thymidine and slowing down or curing the disease.

The medicine is made by a method known as 'recombinant DNA technology': it is made by a cell that has received a gene, which makes the cell able to produce the thymidine phosphorylase enzyme. The enzyme is then enclosed within red blood cells (erythrocytes) taken from the patient's own blood. When the medicine is injected into the patient, the accumulated thymidine diffuses from the blood into the erythrocytes, where it is broken down by the enzyme.

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, no clinical trials with the medicine in patients with MNGIE had been started.

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 January 2011 recommending the granting of this designation.

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[*]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 506,300,000 (Eurostat 2011).

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:

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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	Recombinant thymidine phosphorylase encapsulated in autologous erythrocytes	Treatment of mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) due to thymidine phosphorylase deficiency
Bulgarian	Рекомбинатна тимидин фосфорилаза, енкапсулирана в автоложни еритроцити	Лечение на митохондриална невргстроинтестинална енцефаломиопатия (MNGIE), в резултат на дефицит на тимидин фосфорилаза
Czech	Rekombinantní thymidinfosforyláza zapouzdřená v autologních erytrocytech	Léčba mitochondriální neurogastrointestinální encefalomyopatie (MNGIE) způsobená nedostatkem thymidinfosforylázy
Danish	Rekombinant thymidin phosphorylase indkapslet i autologe erytrocytter	Behandling af mitokondriel neurogastrointestinal encefalomyopati (MNGIE) på grund af thymidin phosphorylase mangel
Dutch	Recombinant thymidine fosforylase geïncapsuleerd in autologe erythrocyten	Behandeling van mitochondriale neurogastrointestinale encephalomyopathie (MNGIE) ten gevolge van thymidine fosforylase deficiëntie
Estonian	Autoloogsetes erütrotsüütides kapseldatud rekombinantne tümidiinfosforülaas.	Tümidiinfosforülaasi defitsiidist tingitud mitokondrialse neurogastrointestinaalse entsefalopaatia (MNGIE) ravi
Finnish	Rekombinantti tymidiinifosforylaasi autologisiin punasoluihin kapseloituna	Tymidiinifosforylaasin puutoksesta johtuvan mitokondriaalisen neurogastrointestinaalisen enkefalomyopatian (MNGIE) hoito
French	Recombinaison de la thymidine phosphorylase encapsulée dans les érythrocytes autologous	Traitement des encéphalomyopathies neurogastrointestinales mitochondriales (MNGIE) due à un déficit en thymidine phosphorylase
German	Rekombinante Thymidinphosphorylase eingekapselt in autologe Erythrozyten	Behandlung der Mitochondrialen Neurogastrointestinal Enzephalopathie (MNGIE) aufgrund eines Thymidinphosphorylasemangels
Greek	Ανασυνδυασμένη φωσφορυλάση θυμιδίνης εντός αυτόλογων ερυθροκυττάρων	Θεραπεία της μιτοχονδριακής νευρογαστρεντερικής εγκεφαλομυοπάθειας (MNGIE) λόγω ανεπάρκειας θυμιδινικής φωσφορυλάσης.
Hungarian	Autológ vörösvérsejtekbe enkapszulált rekombináns timidin foszforiláz	Timidin foszforiláz hiány okozta mitokondriális neurogasztrointesztinális enkefalomyopáthia (MNGIE) kezelésére
Italian	Timidina fosforilasi ricombinante incapsulata in eritrociti autologhi	Trattamento della encefalomiopatia mitocondriale neurogastrointestinale (MNGIE) da carenza di timidina fosforilasi
Latvian	Autologos eritrocītos iekapsulēta rekombinantā timidīnfosforilāze	Timidīna fosforilāzes deficīta izraisītas Mitohondriju neirogastrointestinālās encefalomiopātijas (MNGIE) ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	Į autologinius eritrocitus inkapsuliuota rekombinantinė timidino fosforilazė	Mioneurogastrointestininės encefalopatijos (MNGIE) dėl timidino fosforilazės stokos (mitochondriopatijos) gydymas
Maltese	Thymidine phosphorylase rikombinanti inkapsulat f'eritroċiti awtologi	Kura ta' enċefalomijopatija newrogastrointestinali mitokondrijali (MNGIE) minħabba nuqqas ta' thymidine phosphorylase
Polish	Rekombinowana fosforylaza tymidynowa zamknięta w autologicznych erttrocytach	Leczenie zespołu mitochondrialnej encefalomiopatii dotyczącej układu nerwowego, żołądka i jelit (MNGIE) spowodowanego niedoborem fosforylazy tymidynowej
Portuguese	Timidina Fosforilase recombinante encapsulada em eritrócites autólogos	Tratamento de encephalomyopathy neurogastrointestinal mitocondrial (MNGIE), devido à deficiência de timidina fosforilase
Romanian	Timidin-fosforilaza recombinantă încapsulată în eritrocite autologe	Tratamentul encephalomyopathy neurogastrointestinal mitocondrial (MNGIE), din cauza deficitului de timidin fosforilaza
Slovak	Rekombinantná thymidínfosforyláza enkapsulovaná v autológnych erytrocytoch	Liečba mitochondriálnej neurogastrointestinálnej encefalomyopatie (MNGIE) spôsobenej nedostatkom thymidínfosforylázy
Slovenian	Rekombinantna timidin fosforilaza inkapsulirana v avtologih eritrocitiv	Zdravljenje mitohondrijske neurogastrointestinanel encefalomiopatije (MNGIE) zaradi pomanjkanja timidin fosforilaze
Spanish	Timidina fosforilasa recombinante encapsulada en eritrocitos autólogos	Tratamiento del síndrome de encefalomiopatía neurogastrointestinal mitocondrial (MNGIE) debido a la deficiencia de timidina fosforilasa
Swedish	Rekombinant tymidinfosforylas inkapslat i autologa erytrocyter	Behandling av mitokondriell neurogastrointestinal encefalomyopati (MNGIE) på grund av tymidinfosforylas brist
Norwegian	Rekombinant tymidin fosforylase innkapslet i autologe erytrocytter	Behandling av mitokondrie-neurogastrointestinal encefalomyopati (MNGIE) på grunn av tymidinfosforylase-mangel
Icelandic	Raðbrigða týmidín fosfórýlasi hylkjað í samgena rauðkornum	Meðferð á hvatbera neurogastrointestinal encephalomyopathy (MNGIE) vegna týmidínfosfórýlasa skorts