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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Lithium citrate tetrahydrate (in reverse-micelle formulation) for the treatment of Huntington's disease

On 28 January 2010, orphan designation (EU/3/09/706) was granted by the European Commission to Medesis Pharma, France, for lithium citrate tetrahydrate (in reverse-micelle formulation) for the treatment of Huntington's disease.

What is Huntington's disease?

Huntington's disease is a hereditary disease that causes brain cells to die. This leads to symptoms such as involuntary jerky movements, behavioural problems and dementia (loss of intellectual function). The disease is usually first noticed between 35 and 45 years of age, and gets worse over time.

Huntington's disease is caused by abnormalities in the gene responsible for the production of a protein called huntingtin. The gene abnormalities result in an abnormal form of the protein being produced, which causes damage to the cells in specific areas of the brain.

Huntington's disease is a debilitating and life-threatening condition because it causes severe behavioural and mental problems, a progressive loss of the ability to move and potentially life-threatening complications.

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

At the time of designation, Huntington's disease affected between 0.4 and 0.8 in 10,000 people in the European Union (EU)*. This is equivalent to a total of between 20,000 and 40,000 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, the treatments authorised in the EU were aimed at relieving the symptoms of the disease. In some Member States, tetrabenazine, haloperidol, pimozide and tiapride were

*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).

7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
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authorised for the abnormal involuntary movements that occur in Huntington's disease. In addition, benzodiazepines were used for anxiety, and antidepressants and lithium to treat depression and mood swings.

The sponsor has provided sufficient information to show that lithium citrate tetrahydrate (in reverse-micelle formulation) might be of significant benefit for patients with Huntington's disease because early studies in experimental models indicate that it might improve the treatment of patients with this condition. Furthermore, it is a new formulation of lithium, which allows the use of very low doses of lithium, therefore reducing its well-known side effects. 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?

Lithium has been used as a mood stabiliser for several decades. Recent studies indicate that it might also be used in neurodegenerative diseases, such as Huntington's disease, in which cells of the brain are lost. However, the exact way that lithium works in these diseases is currently unknown. It is thought to interact with several receptors in the brain to prevent cell death.

In lithium citrate tetrahydrate (in reverse-micelle formulation), the lithium is trapped in small particles called 'micelles' that are 'reversed', meaning that the inside is water-soluble and the outside is oil-soluble. The medicine is to be given 'transmucosally', through mucous membranes in the mouth, in the cavity between the cheek and gum. The reverse micelles are expected to cross cell membranes and to carry lithium directly into the brain cells, reducing the amount of free lithium circulating in the body.

What is the stage of development of this medicine?

The effects of lithium citrate tetrahydrate (in reverse-micelle formulation) have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the designated product in patients with Huntington's disease had been started.

At the time of submission, lithium citrate tetrahydrate (in reverse-micelle formulation) was not authorised anywhere in the EU for Huntington's disease 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

Sponsor's contact details:

Medesis Pharma
L'Orée des Mas
Avenue du Golf
34670 Baillargues
France
Telephone: +33 4 67 03 03 99
Telefax: +33 4 67 72 26 21
E-mail: jc-maurel@medesispharma.com

Patient associations' contact points

HDA - The Huntington's Disease Association
1 London Bridge
London SE1 9BG
United Kingdom
Telephone: +44 207 022 1950
Telefax: +44 207 022 1953
E-mail: info@hda.org.uk

Association Huntington France
44 rue du Château des Rentiers
75013 Paris
France
Telephone: +33 1 53 60 08 79
Telefax: +33 1 53 60 08 99
E-mail: huntingtonfrance@wanadoo.fr

Deutsche Huntington-Hilfe e.V.
Börsenstr. 10
47051 Duisburg
Germany
Telephone: +49 203 22915
Telefax: +49 203 22925
E-mail: dhh@dhh-ev.de

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

Language	Active ingredient	Indication
English	Lithium citrate tetrahydrate (in reverse-micelle formulation)	Treatment of Huntington's disease
Bulgarian	литиев цитрат тетрахидрат (във формула с обратен мицел)	Лечение на болест на Хънтингтон
Czech	Lithium citrát tetrahydrát (v formě inverzních micel)	Léčba Huntingtonovy nemoci
Danish	Lithiumcitrat tetrahydrat (i et præparat af omvendte miceller)	Behandling af Huntington's sygdom
Dutch	Lithiumcitraat-tetrahydraat (in een formulering van omgekeerde micellen)	Behandeling van de ziekte van Huntington
Estonian	Liitiumtsitraattetrahüdraat (pöördmitsellivalmistises)	Huntington'i tõve ravi
Finnish	Litiumsitraatti tetrahydraatti (käänteisiä misellejä sisältävässä valmisteessa)	Huntingtonin taudin hoito
French	Citrate de lithium tétrahydraté (dans une formulation de micelles inverses)	Traitement de la maladie d'Huntington
German	Tetrahydriertes Lithiumcitrat (in einer Inversmizellen-Formulierung)	Behandlung der Huntington Erkrankung
Greek	τετραϋδρικό κιτρικό λίθιο (σε διάλυμα αναστρόφων μικκυλίων)	Θεραπεία της νόσου Huntington
Hungarian	Tetrahidratált lithium - citrát (forditott micella-képletben)	Huntington kór kezelése
Italian	Citrato di litio tetraidrato (in formulazione di micelle inverse)	Trattamento della malattia di Huntington
Latvian	Litija citrāta tetrahidrāts (preparātā, kas satur reversīvās micellas)	Hantingtona slimības ārstēšana
Lithuanian	Ličio citrato tetrahidratas (atvirkščiai suformuotos micelės)	Huntington'o ligos gydymas
Maltese	Lithium citrate tetrahydrate (f'formulazzjoni ta' micelle bil-kuntrarju)	Kura tal-marda ta' Huntington
Polish	Litu cytrynian czterowodny (w postaci miceli odwróconych)	Leczenie pląsawicy Huntingtona
Portuguese	Citrato de lítio tetrahidratado (em formulação de micelas invertidas)	Tratamento da doença de Huntington
Romanian	Citrat de litiu tetrahidrat (într-o formulare de micelii inversate)	Tratamentul bolii Huntington
Slovak	Tetrahydrát citranu lítneho (v prípravku s reverznými micelami)	Liečba Huntingtonovej choroby
Slovenian	Tetrahidratni litijev citrat (v formulaciji reverznih micel)	Zdravljenje Huntingtonove bolezni
Spanish	Citrato de litio tetrahidrato (en una formulación de micelas inversas)	Tratamiento de la enfermedad de Huntington
Swedish	Litiumcitrat tetrahydrat (i en sammansättning av omvända miceller)	Behandling av Huntingtons sjukdom
Norwegian	Litiumsitrattetrahydrat (i en formuleringmed inverterte miceller)	Behandling av Huntingtons sykdom
Icelandic	Litíum sítrat tetrahýdrat (í andhverfri ördropasamsetningu)	Meðferð við Huntingtons sjúkdómi