19 May 2015
EMA/COMP/205588/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Phenol, 4-[2-(aminomethyl)-4-thiazolyl]-2,6-bis(1,1-dimethylethyl) monohydrochloride for the treatment of Huntington's disease

On 24 April 2015, orphan designation (EU/3/15/1481) was granted by the European Commission to Ipsen Pharma, France, for phenol, 4-[2-(aminomethyl)-4-thiazolyl]-2,6-bis(1,1-dimethylethyl) monohydrochloride 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 defects 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 approximately 0.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 41,000 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, the treatments authorised in the EU for Huntington's disease were aimed at relieving the symptoms of the disease. In some Member States, haloperidol, pimozide, tetrabenazine

*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 512,900,000 (Eurostat 2015).

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and tiapride were 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 this medicine might be of significant benefit for patients with Huntington's disease because early studies in experimental models indicate that the medicine may reduce brain damage, and improve movement as well as survival. 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?

In Huntington's disease, the abnormal huntingtin protein interferes with several cell processes that ultimately lead to the death of nerve cells, such as the transmission of signals and the normal functioning of mitochondria (structures located inside cells, which produce the energy necessary for cells to function).

This medicine is expected to work in Huntington's disease in different ways: by neutralising oxygen free radicals, which are toxic substances that accumulate in mitochondria when they are not functioning normally; by reducing inflammation by blocking enzymes known as cyclooxygenases; and by reducing overstimulation of brain cells by the neurotransmitter (nerve signalling molecule) glutamate, which can lead to injury and cell death. These actions are expected to protect brain cells from degenerating in patients with Huntington's disease.

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, clinical trials with the medicine in patients with Huntington's disease were ongoing.

At the time of submission, the medicine 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 19 March 2015 recommending the granting of this designation.

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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	Phenol, 4-[2-(aminomethyl)-4-thiazolyl]-2,6-bis(1,1-dimethylethyl)monohydrochloride	Treatment of Huntington's disease
Bulgarian	Фенол, 4-[2-(аминометил)-4-тиазолил]-2,6-бис(1,1-диметилетил)монохидрохлорид	Лечение на болест на Хънтингтон
Croatian	Fenol, 4-[2-(aminometil)-4-tiazolil]-2,6-bis(1,1-dimetiletil)klorid	Liječenje Huntingtonove bolesti
Czech	Fenol, 4-[2-(aminometyl)-4-thiazolyl]-2,6-bis(1,1-dimetyletyl)monohydrochlorid	Léčba Huntingtonovy nemoci
Danish	Phenol, 4-[2-(aminomethyl)-4-thiazolyl]-2,6-bis(1,1-dimethylethyl)monohydrochlorid	Behandling af Huntington's sygdom
Dutch	Fenol, 4-[2-(aminomethyl)-4-thiazolyl]-2,6-bis(1,1-dimethylethyl)monohydrochloride	Behandeling van de ziekte van Huntington
Estonian	Fenool, 4-[2-(aminometüül)-4-tiasolüül]-2,6-bis(1,1-dimetüületüül)vesinikkloriid	Huntington'i tõve ravi
Finnish	Fenoli, 4-[2-(aminometyyli)-4-tiatsolyyli]-2,6-bis(1,1-dimetyylietyyli)monohydrokloridi	Huntingtonin taudin hoito
French	Monochlorydrate de phénol, 4-[2-(aminométhyl)-4-thiazolyl]-2,6-bis(1,1-diméthyléthyl)	Traitement de la maladie d'Huntington
German	Phenol, 4-[2-(Aminomethyl)-4-Thiazolyl]-2,6-bis(1,1-Dimethylethyl)Monohydrochlorid	Behandlung der Huntington Erkrankung
Greek	Φαινόλη, 4-[2-(αμινομεθύλ)-4-θειαζόλυλ]-2,6-δι(1,1-διμεθυλαιθυλ)μονοϋδροχλωρική	Θεραπεία της νόσου Huntington
Hungarian	Fenol, 4-[2-(aminometil)-4-tiazol]-2,6-bisz(1,1-dimetiletil)hidroklorid	Huntington kór kezelése
Italian	Fenolo, 4-[2-(aminometil)-4-tiazolil]-2,6-bis(1,1-dimetiletile)monoidrocloruro	Trattamento della malattia di Huntington
Latvian	Fenol, 4-[2-(aminometil)-4-tiazolil]-2,6-bis(1,1-dimetiletil)monohidrohlorīds	Hantingtona slimības ārstēšanai
Lithuanian	Fenolis, 4-[2-(aminometil)-4-tiazolil]-2,6-bis(1,1-dimetiletil)monohidrochloridas	Huntington'o ligos gydymas
Maltese	Phenol, 4-[2-(aminomethyl)-4-thiazolyl]-2,6-bis(1,1-dimethylethyl)monohydrochloride	Kura tal-marda ta' Huntington
Polish	Fenol, monohydrochlorek 4-[2-(aminometyl)-4-tiazolyl]-2,6-bis(1,1-dimetyletylu)	Leczenie pląsawicy Huntingtona
Portuguese	Monocloridrato de 4-[2-(aminometil)-4-tiazolil]-2,6-bis(1,1-dimetiletil)fenólico	Tratamento da doença de Huntington
Romanian	Fenol, 4-[2-(aminometil)-4-tiazolil]-2,6-bis(1,1-dimetiletil)monoclorhidrat	Tratamentul bolii Huntington
Slovak	Fenol, 4-[2-(aminometyl)-4-thiazolyl]-2,6-bis(1,1-dimetyletyl)monohydrochlorid	Liečba Huntingtonovej choroby

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	4-[2-(aminometil)-4-tiazolil]-2,6-bis(1,1-dimetiletil) fenol monohidroklorid	Zdravljenje Huntingtonove bolezni
Spanish	Fenol, 4-[2-(aminometil)-4-tiazolil]-2,6-bis(1,1-dimetiletil)monohidrocloruro	Tratamiento de la enfermedad de Huntington
Swedish	Fenol, 4-[2-(aminometyl)-4-tiazolyl]-2,6-bis(1,1-dimetyletyl)monohydroklorid	Behandling av Huntingtons sjukdom
Norwegian	Fenol, 4-[2-(aminometyl)-4-tiazolyl]-2,6-bis(1,1-dimetyletyl)monohydroklorid	Behandling av Huntingtons sykdom
Icelandic	Fenól, 4-[2-(amínómetýl)-4-tíasólýl]-2,6-bis(1,1-dímetýletýl)mónóhýdróklóríð	Meðferð við Huntingtons sjúkdómi