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EMA/COMP/451043/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-[4-(1-methyl-4-pyridin-4-yl-1H-pyrazol-3-yl)-phenoxyethyl]-quinoline succinic acid for the treatment of Huntington's disease

On 14 July 2016, orphan designation (EU/3/16/1691) was granted by the European Commission to Pfizer Limited, United Kingdom, for 2-[4-(1-methyl-4-pyridin-4-yl-1H-pyrazol-3-yl)-phenoxyethyl]-quinoline succinic acid 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 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 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 513,700,000 (Eurostat 2016).

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 suggest that it can improve aspects of the condition that are currently not sufficiently managed with authorised treatments, such as motivation and pursuit of goals. 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?

This medicine works by blocking the action of an enzyme called PDE10a and as a result it increases the amount of certain substances in the brain that are important for the normal functioning of brain cells. By blocking the action of the enzyme, the medicine is expected to improve activity of brain cells and the symptoms of 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. 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 16 June 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	2-[4-(1-methyl-4-pyridin-4-yl-1H-pyrazol-3-yl)-phenoxy-methyl]-quinoline succinic acid	Treatment of Huntington's disease
Bulgarian	2-[4-(1-метил-4-пиридин-4-ил-1H-пиразол-3-ил)-феноксиметил]-хинолин сукцинова киселина	Лечение на болест на Хънтингтон
Croatian	2-[4-(1-metil-4-piridin-4-il-1H-pirazol-3-il)-fenoksimetil]-kinolin sukcinatna kiselina	Liječenje Huntingtonove bolesti
Czech	2-{[4-(1-methyl-4-pyridin-4-yl-1H-pyrazol-3-yl)phenoxy]methyl}chinolin-sukcinát	Léčba Huntingtonovy nemoci
Danish	2-[4-(1-methyl-4-pyridin-4-yl-1H-pyrazol-3-yl)-phenoxy-methyl]-quinolin-butandisyre	Behandling af Huntington's sygdom
Dutch	2-[4-(1-methyl-4-pyridine-4-yl-1H-pyrazool-3-yl)-fenoxy-methyl]-chinoline succinaatzuur	Behandeling van de ziekte van Huntington
Estonian	2-[4-(1-metüül-4-püridiin-4-üül-1H-pürasool-3-üül)-fenoksümetüül]-kinoliin suksiinhape	Huntington'i tõve ravi
Finnish	2-[4-(1-metyyli-4-pyridiini-4-yyli-1H-pyratsoli-3-yyli)-fenoksimetyyli]-kinoliinimeripihkahappo	Huntingtonin taudin hoito
French	2-[4-(1-méthyl-4-pyridine-4-yl-1H-pyrazole-3-yl)-phénoxy-méthyl]-quinoléine acide succinique	Traitement de la maladie d'Huntington
German	2-[4-(1-Methyl-4-pyridin-4-yl-1H-pyrazol-3-yl)-phenoxy-methyl]-chinolin Bernsteinsäure	Behandlung der Huntington Erkrankung
Greek	2-[4-(1-μέθυλ-4-πυριδίν-4-υλ-1H-πυραζόλ-3-υλ)-φαινομεθοξύ]-κινολίνη σουκινικό οξύ	Θεραπεία της νόσου Huntington
Hungarian	2-[4-(1-metil-4-piridin-4-il-1H-pirazol-3-il)-fenoximetil]-quinolin szukcin-sav	Huntington kór kezelése
Italian	2-[4-(1-metil-4-piridina-4-il-1H-pirazol-3-il)-fenossimetil]-chinolina acido succinico	Trattamento della malattia di Huntington
Latvian	2-[4-(1-metil-4-piridīn-4-il-1H-pirazol-3-il)-fenoksimetil]-hinolīna dzintarskābe	Hantingtona slimības ārstēšanai
Lithuanian	2-[4-(1-metil-4-piridin-4-il-1H-pirazol-3-il)-fenoksimetil]-kvinolino sukcininė rūgštis	Huntington'o ligos gydymas
Maltese	2-[4-(1-methyl-4-pyridin-4-yl-1H-pyrazol-3-yl)-phenoxy-methyl]-quinoline succinic acid	Kura tal-marda ta' Huntington
Polish	Bursztynian 2-(4-(1-metylo-4-pirydyn-4-ylo-1H-pirazol-3-ylo)-fenoksymetylo)chinoliny	Leczenie płasawicy Huntingtona
Portuguese	Ácido 2-[4-(1-metil-4-piridin-4-il-1H-pirazol-3-il)-fenoximetil]-quinolina sucínico	Tratamento da doença de Huntington
Romanian	2-[4-(1-metil-4-piridin-4-il-1H-pirazol-3-il)-fenoximetil]-chinolină acid succinic	Tratamentul bolii Huntington
Slovak	2-[4-(1-metyl-4-pyridín-4-yl-1H-pyrazol-3-yl)-fenoxy-metyl]-chinolín kyseliny jantárovej	Liečba Huntingtonovej choroby

¹ At the time of designation

Language	Active ingredient	Indication
Slovenian	2-[4-(1-metil-4-piridin-4-il-1H-pirazol-3-il)-fenoksimetil]-kinolin sukčinska kislina	Zdravljenje Huntingtonove bolezni
Spanish	Ácido succínico de 2-[4-(1-metil-4-(piridin-4-il)-1H-pirazol-3-il)-fenoximetil]quinolina	Tratamiento de la enfermedad de Huntington
Swedish	2-[4-(1-metyl-4-pyridin-4-yl-1H-pyrazol-3-yl)-fenoximetyl]-kinolin-succinylsyra	Behandling av Huntingtons sjukdom
Norwegian	2-[4-(1-metyl-4-pyridin-4-yl-1H-pyrazol-3-yl)-fenoksymetyl]-kinolin-1,4-butandisyre	Behandling av Huntingtons sykdom
Icelandic	2-[4-(1-metýl-4-pýridín-4-ýlý-1H-pýrazól-3-ýl)-fenoxýmetýl]-quínólín-súccínicsýra	Meðferð við Huntingtons sjúkdómi