



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

5-bromo-N-(prop-2-yn-1-yl)-2-(1H-1,2,4-triazol-1-yl)pyrimidine-4,6-diamine for the treatment of Huntington's disease

On 16 December 2014, orphan designation (EU/3/14/1392) was granted by the European Commission to Palobiofarma S.L., Spain, for 5-bromo-N-(prop-2-yn-1-yl)-2-(1H-1,2,4-triazol-1-yl)pyrimidine-4,6-diamine 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 diagnosed 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 511,100,000 (Eurostat 2014).



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 the medicine might be of significant benefit for patients with Huntington's disease because early studies in experimental models of the condition show that the medicine improves movement and brain function. 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 is expected to work in patients with Huntington's disease by blocking the action of an enzyme called phosphodiesterase-10 (PDE-10), which is involved in regulating certain compounds called 'cyclic nucleotides' within specific brain cells, where they play a role in controlling normal function. In patients with Huntington's disease, the activity of certain cyclic nucleotides is thought to be reduced. By blocking PDE-10, the medicine is expected to restore the activity of cyclic nucleotides, thus limiting the extent of the damage and improving the symptoms of the 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 had not started.

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 13 November 2014 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:

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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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	5-bromo-N-(prop-2-yn-1-yl)-2-(1H-1,2,4-triazol-1-yl)pyrimidine-4,6-diamine	Treatment of Huntington's disease
Bulgarian	5-бромо-N-(проп-2-ин-1-ил)-2-1H-1,2,4-триазол-1-ил)пиримидин-4,6-диамин	Лечение на болест на Хънтингтон
Croatian	5-brom-N-(prop-2-in-1-il)-2-1H-1,2,4-triazol-1-il)pirimidin-4,6-diamin	Liječenje Huntingtonove bolesti
Czech	5-brom-N-(prop-2-yn-1-yl)-2-1H-1,2,4-triazol-1-yl)pyrimidin-4,6-diamin	Léčba Huntingtonovy nemoci
Danish	5-brom-N-(prop-2-yn-1-yl)-2-1H-1,2,4-triazol-1-yl) pyrimidin-4,6-diamin	Behandling af Huntington's sygdom
Dutch	5-broom-N-(prop-2-yn-1-yl)-2-1H-1,2,4-triazol-1-yl)pyrimidine-4,6-diamine	Behandeling van de ziekte van Huntington
Estonian	5-bromo-N-(prop-2-üün-1-üül)-2-1H-1,2,4-triasool-1-üül)pürimidiin-4,6-diamiin	Huntington'i tõve ravi
Finnish	5-bromi-N-(prop-2-yn-1-yyli)-2-1H-1,2,4-triatsol-1-yyli)pyrimidiini-4,6-diamiini	Huntingtonin taudin hoito
French	5-bromo-N-(prop-2-yn-1-yl)-2-1H-1,2,4-triazole-1-yl)pyrimidine-4,6-diamine	Traitement de la maladie d'Huntington
German	5-Brom-N-(prop-2-yn-1-yl)-2-1H-1,2,4-triazol-1-yl)pyrimidin-4,6-diamin	Behandlung der Huntington Erkrankung
Greek	5-βρωμο-N-(προπ-2-υν-1-υλ)-2-(1H-1,2,4-τριαζολ-1-υλ) πυριμιδίνη-4,6-διαμίνη	Θεραπεία της νόσου Huntington
Hungarian	5-brómo-N-(prop-2-in-1-il)-2-1H-1,2,4-triazol-1-il)-pirimidin-4,6-diamin	Huntington kór kezelése
Italian	5-bromo-N-(prop-2-yn-1-yl)-2-1H-1,2,4-triazol-1-yl) pirimidina-4,6-diammina	Trattamento della malattia di Huntington
Latvian	5-brom-N-(prop-2-īn-1-il)-2-1H-1,2,4-triazol-1-il)pirimidīn-4,6-diamīns	Hantingtona slimības ārstēšanai
Lithuanian	5-bromo-N-(prop-2-in-1-il)-2-1H-1,2,4-triazol-1-il)pirimidino-4,6-diaminas	Huntington'o ligos gydymas
Maltese	5-bromo-N-(prop-2-yn-1-yl)-2-(1H-1,2,4-triazol-1-yl)pyrimidine-4,6-diamine	Kura tal-marda ta' Huntington
Polish	5-bromo-N-(prop-2-yn-1-ylo)-2-1H-1,2,4-triazol-1-ilo)pirymidyno-4,6-diamina	Leczenie płasawicy Huntingtona
Portuguese	5-bromo-N-(prop-2-in-1-il)-2-1H-1,2,4-triazol-1-il)pirimidina-4,6-diamina	Tratamento da doença de Huntington
Romanian	5-bromo-N-(prop-2-in-1-il)-2-1H-1,2,4-triazol-1-il)pirimidin-4,6-diamină	Tratamentul bolii Huntington
Slovak	5-bróm-N-(prop-2-yn-1-yl)-2-1 H-1,2,4-triazol-1-yl)pyrimidin-4,6-diamín	Liečba Huntingtonovej choroby

¹ At the time of designation

Language	Active ingredient	Indication
Slovenian	5-bromo-N-(prop-2-in-1-il)-2-1H-1,2,4-triazol-1-il)pirimidin-4,6-diamin	Zdravljenje Huntingtonove bolezni
Spanish	5-bromo-N-(prop-2-in-1-il)-2-1H-1,2,4-triazol-1-il)pirimidina-4,6-diamina	Tratamiento de la enfermedad de Huntington
Swedish	5-brom-N-(prop-2-yn-1-yl)-2-1H-1,2,4-triazol-1-yl)pyrimidin-4,6-diamin	Behandling av Huntingtons sjukdom
Norwegian	5-brom-N-(prop-2-yn-1-yl)-2-1H-1,2,4-triazol-1-yl)pyrimidin-4,6-diamin	Behandling av Huntingtons sykdom
Icelandic	5-brómó-N-(próp-2-ýn-1-ýl)-2-1H-1,2,4-tríasól-1-ýl)pýrimídín-4,6-díamín	Meðferð við Huntingtons sjúkdómi