13 April 2015
EMA/COMP/628335/2008 Rev.4
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2,3,4,5 tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridinyl)ethyl]-1H-pyrido[4,3-b]indole dihydrochloride for the treatment of Huntington's disease

First publication	16 February 2009
Rev.1: sponsor's change of address	6 April 2011
Rev.2: sponsor's name and address change	5 April 2013
Rev.3: sponsor's change of address	10 March 2015
Rev.4: withdrawal from the Community Register	13 April 2015

Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in February 2015 on request of the Sponsor.

On 20 January 2009, orphan designation (EU/3/08/597) was granted by the European Commission to Innovative Drug European Associates Limited, United Kingdom, for 2,3,4,5 tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridinyl)ethyl]-1H-pyrido[4,3-b]indole dihydrochloride for the treatment of Huntington's disease.

In December 2012, Innovative Drug European Associates Limited changed name to IDEA Innovative Drug European Associates Limited.

What is Huntington's disease?

Huntington's disease is a hereditary disease where the cells (neurons) of specific areas of the brain (the so-called basal ganglia and cerebral cortex) degenerate. When activated, normal neurons release several substances known as neurotransmitters. Once released, neurotransmitters activate or inhibit the target cells in the different body organs. In Huntington's disease, because of extensive degeneration of neurons, the nervous system cannot regulate properly the target organs anymore. This leads to symptoms typical of Huntington's, such as involuntary movements, behavioural

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disturbances and mental deterioration. The disease progresses over time and is long-lasting with 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 was equivalent to a total of between 20,000 and 40,000 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 submission of the orphan drug designation application, some products were authorised for the symptomatic treatment of the Huntington's disease. In some member states, tetrabenazine, haloperidol, pimozide, and tiapride were authorised.

The sponsor has provided sufficient information to show that 2,3,4,5 tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridinyl)ethyl]-1H-pyrido[4,3-b]indole dihydrochloride might be of potential significant benefit for the patients because its new mechanism of action could lead to an improvent of the overall outcome of the patients. 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?

The mechanism of action of 2,3,4,5 tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridinyl)ethyl]-1H-pyrido[4,3-b]indole dihydrochloride is not fully understood. However, this medicinal product is expected to have a neuroprotective effect (protect neurons from degenerating) in patients with Huntington's disease.

What is the stage of development of this medicine?

The effects of 2,3,4,5 tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridinyl)ethyl]-1H-pyrido[4,3-b]indole dihydrochloride have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with Huntington's disease were ongoing.

At the time of submission, 2,3,4,5 tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridinyl)ethyl]-1H-pyrido[4,3-b]indole dihydrochloride was not authorised anywhere in the world for Huntington's disease or designated as 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 2008 recommending the granting of this designation.

[*]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.
At the time of designation, this represented a population of 504,800,000 (Eurostat 2009).

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	2,3,4,5 tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridyl)ethyl]-1H-pyrido[4,3-b]indole dihydrochloride	Treatment of Huntington's disease
Bulgarian	2,3,4,5 тетрахидро-2,8-диметил-5-[2-(6-метил-3-пиридил)етил]-1Н- пиридо [4,3-b] индол дихидрохлорид	Лечение на болест на Хънтингтон
Czech	2,3,4,5 tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridyl)etyl]-1H-pyrido[4,3-b]indol dihydrochlorid	Léčba Huntingtonovy nemoci
Danish	2,3,4,5 tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridyl)ethyl]-1H-pyrido[4,3-b]indol dihydroklorid	Behandling af Huntington's sygdom
Dutch	2,3,4,5 tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridyl)ethyl]-1H-pyrido[4,3-b]indol dihydrochloride	Behandeling van de ziekte van Huntington
Estonian	2,3,4,5 tetrahüdro-2,8-dimetüül-5-[2-(6-metüül-3-püridüül)etüül]-1H-pürido [4,3-b]indool dihüdrokloriid	Huntington'i tõve ravi
Finnish	2,3,4,5 tetrahydro-2,8-dimetyyli-5-[2-(6-metyyli-3-pyridyyli)etyyli]-1H-pyrido[4,3-b]indoli dihydrokloridi	Huntingtonin taudin hoito
French	2,3,4,5 tétrahydro-2,8-diméthyl-5-[2-(6-méthyl-3-pyridyl)éthyl]-1H-pyrido[4,3-b]indole dichlorhydrate	Traitement de la maladie d'Huntington
German	2,3,4,5 tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridyl)ethyl]-1H-pyrido[4,3-b]indol dihydrochlorid	Behandlung der Huntington Erkrankung
Greek	2,3,4,5 τετραϋδρο-2,8-διμεθυλο-5-[2-(6-μεθυλ-3-πυριδυλο)αιθυλ]-1Η-πυριδο [4,3-b] ινδόλη Διυδροχλωριδιακή	Θεραπεία της νόσου Huntington
Hungarian	2,3,4,5 tetrahidro-2,8-dimetil-5-[2-(6-metil-3-piridil)etil]-1H-pirido[4,3-b]indol dihidroklorid	Huntington kór kezelése
Italian	2,3,4,5 tetraidro-2,8-dimetil-5-[2-(6-metil-3-piridil)etil]-1H-pirido[4,3-b]indolo dicloridrato	Trattamento della malattia di Huntington
Latvian	2,3,4,5 tetrahidro-2,8-dimetil-5-[2-(6-metil-3-piridil)etila]-1H-pirido[4,3-b]indola dihidrohlorīds	Hantingtona slimības ārstēšanai
Lithuanian	2,3,4,5-tetrahidro-2,8-dimetil-5-[2-(6-metil-3-piridil)etil]-1H-pirido[4,3-b]indolo dihidrochloridas	Huntington'o ligos gydymas

[1] At the time of designation

Language	Active Ingredient	Indication
Maltese	2,3,4,5 tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridyl)ethyl]-1H-pyrido[4,3-b]indole dihydrochloride	Kura tal-marda ta' Huntington
Polish	2,3,4,5 tetrahydro-2,8-dimetylo-5-[2-(6-metylo-3-pyridyl)etyl]-1H-pirydo [4,3-b]indol dichlorowodorek	Leczenie pląsawicy Huntingtona
Portuguese	2,3,4,5 tetrahidro-2,8-dimetil-5-[2-(6-metil-3-piridil)etil]-1H-pirido[4,3-b]indole dihidrocloreto	Tratamento da doença de Huntington
Romanian	2,3,4,5 tetrahidro-2,8-dimetil-5-[2-(6-metil-3-piridil)etil]-1H-pirido[4,3-b]indol diclorhidrat	Tratamentul bolii Huntington
Slovak	2,3,4,5 tetrahydro-2,8-dimetyl-5-[2-(6-metyl-3-pyridyl)etyl]-1H-pyrido[4,3-b]indol dihydrochlorid	Liečba Huntingtonovej choroby
Slovenian	2,3,4,5 tetrahidro-2,8-dimetil-5-[2-(6-metil-3-piridil)etil]-1H-pirido[4,3-b]indol dihidroklorid	Zdravljenje Huntingtonove bolezni
Spanish	2,3,4,5 tetrahidro-2,8-dimetil-5-[2-(6-metil-3-piridil)etil]-1H-pirido[4,3-b]indol dihidrocloruro	Tratamiento de la enfermedad de Huntington
Swedish	2,3,4,5 tetrahydro-2,8-dimetyl-5-[2-(6-metyl-3-pyridyl)etyl]-1H-pyrido[4,3-b]indol dihydroklorid	Behandling av Huntingtons sjukdom
Norwegian	2,3,4,5 tetrahydro-2,8-dimetyl-5-[2-(6-metyl-3-pyridyl)etyl]-1H-pyrido[4,3-b]indol dihydroklorid	Behandling av Huntingtons sykdom.
Icelandic	2,3,4,5 tetrahýdró-2,8-dimethýl-5-[2-(6-metýl-3-pýridýl)etýl]-1H-pýrídó [4,3-b]indól díhýdróklóríð	Meðferð við Huntingtons sjúkdómi