European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of 6-chloro-2,3,4,9-tetrahydro-1*H*-carbazole-1-carboxamide for the treatment of Huntington's disease

On 28 October 2009, orphan designation (EU/3/09/681) was granted by the European Commission to Siena Biotech SpA, Italy, for 6-chloro-2,3,4,9-tetrahydro-1*H*-carbazole-1-carboxamide 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 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 6-chloro-2,3,4,9-tetrahydro-1*H*-carbazole-1-carboxamide might be of significant benefit for patients with Huntington's disease because it works in a different way to existing treatments and because early studies in experimental models indicate that it might improve the treatment of patients with this condition. These assumptions will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

[*]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).

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How is this medicine expected to work?
6-chloro-2,3,4,9-tetrahydro-1*H*-carbazole-1-carboxamide is expected to work by blocking the activity of an enzyme called SirT1, which is thought to be involved in controlling the removal of the abnormal huntingtin protein. The medicine is thought to work by increasing the removal of the protein, thus reducing its levels in the brain cells. This is expected to prevent damage to the brain cells and therefore potentially slow down the progression of the disease.

What is the stage of development of this medicine?
The effects of 6-chloro-2,3,4,9-tetrahydro-1*H*-carbazole-1-carboxamide 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, 6-chloro-2,3,4,9-tetrahydro-1*H*-carbazole-1-carboxamide was not authorised anywhere in the EU 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 2 September 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.

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

Language	Active ingredient	Indication
English	6-chloro-2,3,4,9-tetrahydro-1H-carbazole-1-carboxamide	Treatment of Huntington's disease
Bulgarian	6-хлоро-2,3,4,9-тетрахидро-1Н-карбазол-1-карбоксамид	Лечение на болест на Хънтингтон
Czech	6-chloro-2,3,4,9-tetrahydro-1H-karbazol-1-karboxamid	Léčba Huntingtonovy nemoci
Danish	6-chlor-2,3,4,9-tetrahydro-1H-carbazol-1-carboxamid	Behandling af Huntington's sygdom
Dutch	6-chloor-2,3,4,9-tetrahydro-1H-carbazool-1-carboxamide	Behandeling van de ziekte van Huntington
Estonian	6-kloro-2, 3, 4, 9-tetrahüdro-1H-karbasool-1-karboksamiid	Huntington'i tõve ravi
Finnish	6-kloori-2,3,4,9-tetrahydro-1H-karbatsoli-1-karboksamidi	Huntingtonin taudin hoito
French	6-chloro-2,3,4,9-tétrahydro-1H-carbazole-1-carboxamide	Traitement de la maladie d'Huntington
German	6-Chlor-2,3,4,9-tetrahydro-1H-carbazol-1-carboxamid	Behandlung der Huntington Erkrankung
Greek	6-Χλωρο-2,3,4,9-τετραϋδρο-1Η-καρβαζόλη-1-καρβοξαμίδη	Θεραπεία της νόσου Huntington
Hungarian	6-klór-2,3,4,9-tetrahidro-1H-karbazol-1-karboxamid	Huntington kór kezelése
Italian	6-Cloro-2,3,4,9-tetraidro-1H-carbazol-1-carbossammide	Trattamento della malattia di Huntington
Latvian	6 hlor-2,3,4,9-tetrahidro-1H karbozol-1-karboksamīds	Hantingtona slimības ārstēšanai
Lithuanian	6-chloro-2,3,4,9-tetrahidro-1H-karbazol-1-karboksamidas	Huntington'o ligos gydymas
Maltese	6-chloro-2,3,4,9-tetrahydro-1H-carbazole-1-carboxamide	Kura tal-marda ta' Huntington
Polish	6-chloro-2,3,4,9-tetrahydro-1H-karbozolo-1-karboksyamid	Leczenie pląsawicy Huntingtona
Portuguese	6-cloro-2,3,4,9-tetrahidro-1H-carbazole-1-carboxamida	Tratamento da doença de Huntington
Romanian	6-Cloro-2,3,4,9-tetrahidro-1H-carbazol-1-carboxamidă	Tratamentul bolii Huntington
Slovak	6-chloro-2,3,4,9-tetrahydro-1H-karbazol-1-karboxamid	Liečba Huntingtonovej choroby
Slovenian	6-kloro-2,3,4,9-tetrahidro-1H-karbazol-1-karboksamid	Zdravljenje Huntingtonove bolezni
Spanish	6-Cloro-2,3,4,9-tetrahidro-1H-carbazol-1-carboxamida	Tratamiento de la enfermedad de Huntington
Swedish	6-klor-2,3,4,9-tetrahydro-1H-karbazol-1-karboxamid	Behandling av Huntingtons sjukdom
Norwegian	6-klor-2,3,4,9-tetrahydro-*1H*-karbazol-1-karboksamid	Behandling av Huntingtons sykdom
Icelandic	6-klóró-2,3,4,9-tetrahýdró-1H-karbasól-1-karboxamíð	Meðferð við Huntingtons sjúkdómi