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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Levodopa/carbidopa (gastroenteral use) for the treatment of advanced idiopathic Parkinson's disease with severe motor fluctuations and not responding to oral treatment

First publication	3 March 2009
Rev.1: sponsor's name change	15 March 2011
Rev.2: transfer of sponsorship	3 May 2013

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.

On 10 May 2001, orphan designation (EU/3/01/035) was granted by the European Commission to NeoPharma Production AB, Sweden, for levodopa / carbidopa (gastroenteral use) for the treatment of advanced idiopathic Parkinson's disease with severe motor fluctuations and not responding to oral treatment.

The sponsorship was transferred to Solvay Pharmaceuticals GmbH, Germany, in March 2006.

The sponsor changed name to Abbott Products GmbH in November 2010.

The sponsorship was transferred to AbbVie Ltd, United Kingdom, in February 2013.

What is advanced idiopathic Parkinson's disease with severe motor fluctuations and not responding to oral treatment?

Parkinson's disease results from progressive damage to the nerve cells in the area of the brain responsible for controlling muscle tone and movement. The damaged cells are those needed to produce a neurotransmitter (chemical messenger in the brain that transmits information from one nerve cell to another) called dopamine. Patients with Parkinson's disease have low levels of dopamine. Parkinson's disease occurs primarily, but not exclusively, in the elderly. The symptoms of Parkinson's disease are bradykinesia (slowness and poverty of movement), muscular rigidity, resting tremor and an impairment of postural balance. The cause of Parkinson's disease is not known in the vast majority of the cases (idiopathic).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

Oral treatment with a dopamine precursor called levodopa is effective in the early stages of the disease. The brain still has the ability to store dopamine precursor and transform it into dopamine. As the disease progresses, the brain loses this ability to store or use its reserves of dopamine precursor. In practice, hours after taking the oral treatment, the characteristic symptoms such as motor fluctuations will re-appear (off periods). Therefore, as the disease progresses, the action of oral treatment with dopamine precursors will gradually shorten. Advanced idiopathic Parkinson's disease with severe motor fluctuations and not responding to oral treatment is progressive and chronically debilitating.

What is the estimated number of patients affected by the condition?

At the time of designation, advanced idiopathic Parkinson's disease with severe motor fluctuations and not responding to oral treatment affected approximately 2.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 91,000 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 the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of submission of the application for the orphan drug designation, several medicinal products, such as levodopa and apomorphine were authorised for the treatment of Parkinson's disease. However, in spite of these authorised oral treatments, there was a subset of advanced Parkinson's disease patients who did not respond satisfactorily to the available treatments and there were no satisfactory authorised methods available for these patients, at the time of designation.

How is this medicine expected to work?

Levodopa is the naturally occurring precursor of dopamine. It is converted to dopamine in the cells. Dopamine is a neurotransmitter, a chemical used for transmitting signals from the nervous system to the body. Levodopa is given to increase the production of dopamine in the brain to reduce the symptoms of Parkinson's disease. In order to maintain high levels of levodopa in the brain, levodopa is given with another substance called carbidopa which prevents the breakdown of levodopa. This particular medicinal product will be administered as a suspension into the duodenum (the first section of the small intestine) using a surgically placed permanent tube. This way, the product is expected to be delivered at a steady rate, resulting in stable plasma concentrations and decreasing the symptoms of advanced idiopathic Parkinson's disease with severe motor fluctuations and not responding to oral treatment.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, clinical trials in patients with advanced idiopathic Parkinson's disease with severe motor fluctuations and not responding to oral treatment were ongoing.

Levodopa/carbidopa was not authorised anywhere in the world for advanced idiopathic Parkinson's disease with severe motor fluctuations and not responding to oral treatment, at the time of submission. Orphan designation of levodopa/carbidopa was granted in the United States in January 2000 for the treatment of late stage Parkinson's disease.

[*]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.
At the time of designation, this represented a population of 378,800,000 (Eurostat 2001).

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 20 March 2001 recommending the granting of this designation.

Update: Levodopa/Carbidopa (Duodopa) was designated as an orphan drug in Australia in April 2006.

Levodopa/Carbidopa (Gastroenteral use) (Duodopa intestinal gel) is authorised via Mutual Recognition in the European Union for the treatment of advanced levodopa-responsive Parkinson's disease with severe motor fluctuations and hyper-/dyskinesia when available combinations of Parkinson medicinal products have not given satisfactory results.

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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:

AbbVie Ltd
Vanwall Business Park
Vanwall Road
Maidenhead, Berks, SL6 4XE
United Kingdom
Telephone: +441628 644 501
Telefax: +44 1628 672 624
E-mail: orphandrugs.enquiries@abbvie.com

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	Levodopa and Carbidopa (Gastroenteral use)	Treatment of advanced idiopathic Parkinson's disease with severe motor fluctuations and not responding to oral treatment
Bulgarian	Леводопа/Карбидопа (гастроентерално приложение)	Лечение на напреднала идиопатична болест на Паркинсон с тежки моторни флуктуации и неотговаряща на перорално лечение
Czech	Levodopa/Carbidopa (gastroenterální aplikace)	Léčba idiopatické Parkinsonovy choroby se silnými motorickými fluktuacemi a neodpovídajícími na perorální medikaci
Danish	Levodopa og Carbidopa (gastrointestinal anvendelse)	Behandling af fremskreden idiopatisk Parkinsons sygdom med svære motoriske fluktuationer og som ikke responderer på oral behandling
Dutch	Levodopa en carbidopa (gastro-enteraal gebruik)	Behandeling van gevorderde idiopathische ziekte van Parkinson met ernstige motorische fluctuaties en niet reagerend op orale behandeling.
Estonian	Levodopa/Karbidopa (gastroenteraalseks kasutamiseks)	Tugeva motoorse kõikumisega ja suukaudsele ravile mittealluva kaugelearenenud idiopaatilise Parkinsoni haiguse ravi
Finnish	Levodopa ja Carbidopa (Gastroenteraaliseen käyttöön)	Pitkälle kehittyneen idiopaattisen Parkinsonin taudin hoito, johon liittyy vakavia motorisia vaihteluita ja johon oraalinen hoito ei tehoa.
French	Lévodopa et Carbidopa (administration gastro-entérale)	Traitement de la forme évoluée de la maladie de Parkinson idiopathique accompagnée de fluctuations motrices sévères et ne répondant pas au traitement par voie orale
German	Levodopa und Carbidopa (gastroenterale Applikation)	Zur Behandlung des fortgeschrittenen idiopathischen Parkinson-Syndroms mit schweren motorischen Fluktuationen und nicht ansprechend auf orale Therapie
Greek	Λεβοντόπα και καρβιντόπα (γαστροεντερική χρήση)	Θεραπεία της ιδιοπαθούς νόσου του Parkinson προχωρημένου σταδίου που παρουσιάζει σοβαρές κινητικές διακυμάνσεις και δεν αποκρίνεται σε δια του στόματος φαρμακευτική αγωγή.
Hungarian	Levodopa/Carbidopa (Gasztroenterális alkalmazás)	Orális kezelésre rezisztens súlyos motoros fluktuációval kísért előrehaladott idiopathiás Parkinson-kór
Italian	Levodopa e Carbidopa (uso gastrointestinale)	Trattamento del morbo di Parkinson idiopatico in fase avanzata con fluttuazioni motorie severe e che non risponde al trattamento orale

[1] At the time of transfer of transfer of sponsorship

Language	Active Ingredient	Indication
Latvian	Levodopa/ Carbidopa (gastroenterālai lietošanai)	Progresējušas idiopātiskas Parkinsona slimības ar nopietnām motorām svārstībām, ārstēšanai, ja perorāla ārstēšana nav efektīva
Lithuanian	Levodopa/Karbidopa (gastroenterinis vartojimas)	Progresuojančios idiopatinės Parkinsono ligos su sunkia motorine fliuktuacija gydymas, nepasiduodant gydymui per os
Maltese	Levodopa/Carbidopa (Użu gastroenterali)	Kura tal-marda ta' Parkinson idjopatika avvanzata b'varjazzjonijiet motorji severi u li ma tirrispondix għal kura li tittieħed mill-ħalq.
Polish	Lewodopa/Karbidopa (zastosowanie dojelitowe)	Leczenie zaawansowanej, idiopatycznej choroby Parkinsona z ciężkimi fluktuacjami ruchowymi nieodpowiadające na leczenie doustne
Portuguese	Levodopa e Carbidopa (uso gastrointestinal)	Tratamento da doença de Parkinson idiopática em estado avançado com fluctuações motoras severas e que não reagem ao tratamento oral
Romanian	Levodopa/Carbidopa (uz gastroenteral)	Tratamentul bolii Parkinson idiopatice avansate cu fluctuaţii motorii severe şi care nu răspunde la tratamentul oral
Slovak	Levodopa/Karbidopa (gastrointestinálne použitie)	Liečba pokročilého štádia idiopatickej Parkinsonovej choroby s ťažkými motorickými fluktuáciami, ktorá neodpovedá na perorálnu liečbu
Slovenian	Levodopa/karbidopa (gastroenteralna uporaba)	Zdravljenje napredovane idiopatske Parkinsonpve bolezni s hudimi spremembami motorike, ki se ne odziva na peroralno zdravljenje
Spanish	Levodopa y Carbidopa (Vía gastroenteral)	Tratamiento de la enfermedad de Parkinson idiopática en estado avanzado con fluctuaciones motoras severas y que no responde al tratamiento oral.
Swedish	Levodopa och Karbidopa	Behandling av avancerad idiopatisk Parkinsons sjukdom med svåra motoriska fluktuationer och som ej svarar på oral behandling