25 May 2011
EMA/COMP/209/2004 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Apomorphine (oromucosal use) for the treatment of off-periods in Parkinson's disease not responding adequately to other existing therapies

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in February 2005 on request of the sponsor.

On 5 December 2001, orphan designation (EU/3/01/072) was granted by the European Commission to Orion Corporation, Finland, for apomorphine (oromucosal use) for the treatment of off-periods in Parkinson's disease not responding adequately to other existing therapies.

What are off-periods in Parkinson's disease not responding adequately to other existing therapies?

Parkinson's disease is a degenerative disorder of the central nervous system. Patients with Parkinson's disease suffer from muscle rigidity, resting tremor, slowing of physical movement (bradykinesia) and, in extreme cases, complete loss of movement (akinesia). Parkinson's disease results from progressive damage to the nerves in the area of the brain responsible for controlling muscle tone and movement. Nerves that would normally produce the neurotransmitter called dopamine (chemical messenger in the brain that transmits information from one nerve cell to another) do not function properly. Patients with Parkinson's disease have depleted levels of dopamine.

Oral treatment with dopamine precursor is used in the early stages of the disease. The brain still has the ability to store the 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. Off-periods in Parkinson's disease not responding adequately to other existing therapies is a progressive and chronically debilitating condition.

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

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

At the time of designation, off-periods in Parkinson's disease not responding adequately to other existing therapies affected approximately 0.35-0.48 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 13,000-18,000 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 application for the orphan drug designation, several medicinal products, such as levodopa and apomorphine were authorised for the treatment of Parkinson's disease. Specifically, apomorphine hydrochloride administered subcutaneously was authorised in the European Union for the treatment of refractory motor fluctuations in Parkinsons' disease. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that sublingual apomorphine (administered and absorbed under the tongue) might be of potential significant benefit for the treatment of the condition, as it might be major contribution to patient care. Sublingual apomorphine could lead to a better absorption of the drug and thus provide a better control of the off-periods. The assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

Apomorphine is a dopamine agonist. Dopamine agonists directly stimulate the dopamine receptors (binding site of dopamine molecule) of the nerves in the brain that normally would be stimulated by dopamine and the brain reacts as if it is receiving dopamine. In patients with off-periods, the treatment could easily be administered under the tongue (oromucosal) that would rapidly relieve off-periods, and thus help reducing the symptoms of Parkinson's disease.

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 off-periods in Parkinson's disease not responding adequately to other existing therapies were ongoing.

This medicinal product was not marketed anywhere worldwide for the treatment of off-periods in Parkinson's disease not responding adequately to other existing therapies, at the time of submission. Orphan designation of apomorphine was granted in the United States for use as rescue treatment for early morning motor dysfunction in late-stage Parkinson's disease. However, the product was later withdrawn from the orphan drug registry in the United States.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 September 2001 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 based on data from the European Union. This represents a population of 377,000,000 (Eurostat 2001).

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:

Orion Corporation
Orionintie 1,
FIN-02200 Espoo
Finland
Telephone: +358 10 426 1

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	Apomorphine (oromucosal use)	Treatment of off-periods in Parkinson´s disease not responding to other oral treatment
Danish	Apomorphin (Til anvendelse i mundhulen)	Behandling af "off-perioder" ved Parkinson's sygdom, der ikke responderer på andre behandlinger
Dutch	Apomorfine (Oromucosaal gebruik)	Behandeling van OFF-perioden bij de ziekte van Parkinson die niet reageren op andere orale therapie
Finnish	apomorfiini (Suuonteloon)	Off-vaiheiden hoito Parkinson-potilailla, jotka eivät ole hyötyneet muusta oraalisestahoidosta
French	Apomorphine (Voie buccale)	Traitement des périodes off de la maladie de Parkinson ne répondant pas aux autres traitements par voie orale
German	Apomorphin (Anwendung in der Mundhöhle)	Behandlung von "Off-Zeiten" bei Morbus Parkinson, wenn der Patient auf andere orale Therapien nicht anspricht
Greek	Απομορφίνη (στοματική χρήση)	Θεραπεία για τις περιόδους "OFF" της νόσου του Πάρκινσον μη ανταποκρινόμενης σε άλλες υπάρχουσες στοματικές αγωγές .
Italian	Apomorfina (Per mucosa orale)	Trattamento degli periodi-off in pazienti affetti da morbo di Parkinson, i quali non rispondano adeguatamente alle altre terapie orali esistenti
Portuguese	Apomorfina (Uso bucal/Via sublingual)	Tratamento de período de inactividade na doença de Parkinson que não tenha respondido a outras terapêuticas orães
Spanish	Apomorfina (Vía bucofáringea)	Tratamiento de los períodos "OFF" en la enfermedad de Parkinson que no responden a otras terapias por vía oral
Swedish	Apomorfin (Användning i munhålan)	Behandling av off-perioder hos patienter med Parkinsons sjukdom som inte svarar på annan peroral behandling

[1] At the time of designation