



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**

#### **apomorphine hydrochloride (inhalation use) for the treatment of off-periods in Parkinson's disease not responding to oral treatment**

On 16 February 2006, orphan designation (EU/3/06/349) was granted by the European Commission to Vectura Group plc, United Kingdom, for apomorphine hydrochloride (inhalation use) for the treatment of off-periods in Parkinson's disease not responding to oral treatment.

#### **What are off-periods in Parkinson's disease not responding to oral treatment?**

Parkinson's disease results from progressive damage to the nerves 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.

Oral treatment with a dopamine precursor (absorbed through the intestines) is effective 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 of the Parkinson's disease will appear (off periods). Therefore, as the disease progresses, the action of oral treatment with dopamine precursors and other available therapies will gradually shorten.

Off-periods in Parkinson's disease not responding adequately to oral treatment is chronically debilitating, due to progressive severe neurological damage.

#### **What are the methods of treatment available?**

At the time of submission of the application for the orphan drug designation, apomorphine (for injection or subcutaneous use) was authorised in the European Union for the treatment of off-periods in Parkinson's disease not responding adequately to other existing oral therapies.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that apomorphine hydrochloride (inhalation use) might be of potential significant benefit for the treatment of off-periods in Parkinson's disease not responding adequately to oral treatment because of the different way of administration compared to the existing injectable drug. Inhalation use could lead to a better absorption profile and thus provide a better control of the "off periods". Additionally, a less invasive treatment might represent a contribution to the patient care. These assumptions will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

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

According to the information provided by the sponsor, off-periods in Parkinson's disease not responding to oral treatment were considered to affect about 161,000 persons in the European Union.

**How is this medicinal product expected to act?**

Apomorphine is a dopamine agonist. Dopamine agonists, as the dopamine itself, are able to directly stimulate the dopamine receptors (binding site of dopamine molecule) of the nerves in the brain that normally would be stimulated by the natural dopamine. The brain 'believes it is receiving dopamine, which in turn reduces the symptoms of Parkinson's disease.

**What is the stage of development of this medicinal product?**

The effects of apomorphine hydrochloride (inhalation use) were evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials in patients with off-periods in Parkinson's disease not responding to oral treatment were initiated.

Apomorphine hydrochloride (inhalation use) was not authorised anywhere worldwide for off-periods in Parkinson's disease or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 11 January 2006 a positive opinion recommending the grant of the above-mentioned designation.

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Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

**For more information:**

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\*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 (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

Patients' associations contact points:

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

<b>Language</b>	<b>Active Ingredient</b>	<b>Indication</b>
English	Apomorphine hydrochloride (inhalation use)	Treatment of off-periods in Parkinson's disease not responding to oral treatment
Czech	Apomorfin hydrochlorid (inhalační podání)	Léčba Parkinsonovy choroby neodpovídající na perorální medikaci
Danish	Apomorphinhydrochlorid (til inhalation)	Behandling af off-perioder i Parkinsons sygdom som ikke responderer på oral behandling
Dutch	Apomorfinehydrochloride (inhalatie)	Behandeling van OFF-perioden bij de ziekte van Parkinson die niet reageren op orale therapie
Estonian	Apomorfiinvesinikkloriid (inhalatsiooniks)	Suukaudsele ravile mittealluva Parkinsoni haiguse väljalülitamise perioodide ravi
Finnish	Apomorfiinihydrokloridi (inhalaatiokäyttöön)	Parkinsonin taudin sellaisen "off"-jaksojen hoito, jotka eivät vastaa oraalihoitoon
French	Chlorhydrate d'apomorphine (voie inhalée)	Traitement des périodes "OFF" de la maladie de Parkinson ne répondant pas aux traitements par voie orale
German	Apomorphinhydrochlorid (zur Inhalation)	Behandlung von "Off-Zeiten" bei Morbus Parkinson, wenn der Patient auf orale Therapien nicht anspricht
Greek	Υδροχλωρική απομορφίνη (Χρήση δια εισπνοής)	Θεραπεία για τις περιόδους "OFF" της νόσου του Πάρκινσον μη ανταποκρινόμενης σε άλλες υπάρχουσες στοματικές αγωγές .
Hungarian	Apomorfin hidroklorid (inhalációs alkalmazás)	Orális kezeléssre rezisztens Parkinson-kór off-periódusának kezelése
Italian	Apomorfina cloridrato (uso inalatorio)	Trattamento degli periodi-off in pazienti affetti da morbo di Parkinson, i quali non rispondano adeguatamente alle terapie orali esistenti
Latvian	Apomorfīna hidrohlorīds (inhalācijām)	Parkinsona slimības off periodu ārstēšanai, ja perorālā ārstēšana nav efektīva
Lithuanian	Apomorfino hidrokloridas (inhaliuoti)	Parkinsono ligos sustingimo periodų, nepasiduodančių gydymui <i>per os</i> , gydymas
Polish	Chlorowodorek apomorfiny (podanie wziewne)	Leczenie fazy „off” choroby Parkinsona nie ustępujących po leczeniu doustnym
Portuguese	Cloridrato de Apomorfina (via inalatoria)	Tratamento dos períodos "off" da doença de Parkinson que não responda a terapêuticas - por via oral
Slovak	Apomorfíniumchlorid (inhalačné použitie)	Liečba off fázy Parkinsonovej choroby, ktorá neodpovedá na perorálnu liečbu
Slovenian	Apomorfínijev hidroklorid (za inhaliranje)	Zdravljenje off-obdobja pri Parkinsonovi bolezni, ki se ne odziva na peroralno zdravljenje
Spanish	Clorhidrato de apomorfina (via inhalatoria)	Tratamiento de los períodos "OFF" en la enfermedad de Parkinson que no responden al tratamiento por vía oral
Swedish	Apomorfinhydroklorid (användning för inhalation)	Behandling av off-perioder hos patienter med Parkinsons sjukdom som inte svarar på peroral behandling

Norwegian	Apomorfínhydroklorid (bruk til inhalasjon)	Behandling av ”off”-perioder ved Parkinsons sykdom som ikke responderer på oral behandling
Icelandic	Apómorfín-hýdróklóríð (til innöndunar)	Meðferð á off-tímabilum í Parkinson sjúkdómi sem svara ekki meðferð í inntöku