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 idebenone for the treatment of Friedreich's ataxia

On 20 November 2001, orphan designation (EU/3/01/062) was granted by the European Commission to Laboratoires Takeda, France, for idebenone for the treatment of Friedreich's ataxia**.**

What is Friedreich's ataxia?
Friedreich's ataxia is an inherited (genetic) disease of the nervous system and muscles. Genes located on structures called chromosomes carry the genetic information that determines the characteristics of each individual. In humans, each cell has 23 pairs of chromosomes. For each pair one chromosome is inherited from the mother and the other from the father. In Friedreich's ataxia there is an abnormality in a gene carried by the pair number 9 and responsible for the production of a protein called "frataxin". For a patient to be affected of Friedreich's ataxia both chromosomes on the pair number 9 should be affected. Frataxin plays a major role in iron metabolism and its absence would produce the accumulation of iron and other substances that finally would injure the cells, in particula those of the nervous system.
Friedreich's ataxia is characterised by difficulties to coordinate movements. The symptoms develop progressively and are mainly due to the neurological alterations. They mainly concern the ability to walk, gait disturbances, speech problems, cardiac function (cardiomyopathy) and are sometimes associated to diabetes.
Friedreich's ataxia is chronically debilitating and life threatening due to the progression of symptoms, severe neurological and cardiac complications and short life expectancy.

What are the methods of treatment available?
No satisfactory methods exist that were authorised at the time of application.

What is the estimated number of patients affected by the condition*
According to the information provided by the sponsor, Friedreich's ataxia was considered to affect less than 27,000 persons in the European Union.

How is this medicinal product expected to act?
Mitochondria are structures located inside the cells, which produce the energy necessary for the cell functioning, through a process named "cellular respiration". This process is realised by a complex of different molecules that need oxygen to produce energy. During this process, toxic oxygen free radicals can be produced and they should be neutralised by other substances in order not to be harmful for the cell. One of the hypotheses for Friedreich's ataxia is that due to the frataxin protein deficit, the iron overload in the mitochondria, could lead to the formation of an excess of toxic oxygen free radicals. Idebenone is expected to act as a reactive oxygen scavenger. That means that it can naturally accept and

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link oxygen molecules and therefore have an antioxidant effect. By binding these reactive oxygen molecules idebenone can thereby prevent cellular damage.

What is the stage of development of this medicinal product?
The effects of idebenone have been evaluated in experimental models.
At the time of submission of the application for orphan designation, clinical trials in patients with Friedreich's ataxia were ongoing.

Idebenone was not marketed anywhere worldwide for Friedreich's ataxia 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 7 September 2001 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.

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*Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001) and may differ from the true number of patients affected by the condition. This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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Translations of the active ingredient and indication in all EU languages

Language	Active Ingredient	Indication
English	Idebenone	Treatment of Friedreich's ataxia
Danish	Idebenone	Behandling af Friedreichs ataksi
Dutch	Idebenone	Behandeling van de ataxie van Friedreich
Finnish	Idebenoni	Friedreich-ataksian hoito
French	Idebenone	Traitement de l'ataxie de Friedreich
German	Idebenon	Therapie der Friedreichschen Ataxie
Greek	Ιδεβενονη	Θεραπεία της αταξίας Friedreich
Italian	Idebenone	Trattamento dell'atassia di Friedreich
Potuguese	Idebenona	Tratamento da ataxia de Friedreich
Spanish	Idebenona	Tratamiento de la ataxia de Friedreich
Swedish	Idebenon	Behandling av Friedreichs ataxi