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EMEA/COMP/245/04

COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

**PUBLIC SUMMARY OF
POSITIVE OPINION FOR ORPHAN DESIGNATION
OF**

**5'CTG CCA CGT TCT CCT GC-(2' methoxy)A-(2' methoxy)C-(2'methoxy)C-3'
for the treatment of myasthenia gravis**

On 21 June 2004, orphan designation (EU/3/04/203) was granted by the European Commission to PPD Global Ltd, United Kingdom, for 5'CTG CCA CGT TCT CCT GC (2' methoxy)A (2' methoxy)C-(2'methoxy)C-3' for the treatment of myasthenia gravis.

What is myasthenia gravis?

Myasthenia gravis is an autoimmune disease affecting muscular function. This disease is caused by abnormal antibodies produced by the patient's own immune system. These antibodies link and block specific proteins (acetylcholine receptors) on the surface of the muscles, thereby interfering with muscular contraction. Acetylcholine is a chemical substance produced by motor neurons, that activates specific receptors on muscles to trigger contraction. In most patients, the abnormal antibody production is associated with abnormalities of a gland in the chest called the thymus, which is part of the immune system. Myasthenia gravis is characterized by painless muscle weakness. The muscles weaken more rapidly than normally. In addition, the symptoms typically worsen towards the end of the day and after exercise. When the diaphragm, the muscle that assists breathing, becomes weak, myasthenic crisis can occur and emergency room hospitalisation is required. In most patients, blood tests can detect the antibodies that cause myasthenia gravis. Electromyography (EMG) is a very sensitive method to assess the changes in muscle electrical activity caused by myasthenia. Sometimes an injection of the drug edrophonium hydrochloride can also be given (the Tensilon test), which causes a swift but brief improvement in most patients' muscle weakness. This test helps in the diagnosis of myasthenia.

What are the methods of treatment available?

Acetylcholine is broken down in the body by enzymes called cholinesterases. This action can be blocked by anticholinesterase drugs such as pyridostigmine. This drug can control myasthenia in some patients but many others need additional treatment. Surgical removal of the thymus gland (thymectomy) is performed in patients when myasthenia is due to a thymus tumour (thymoma), and can also help some other patients, especially those who develop myasthenia before the age of about 45. Drugs such as prednisolone (a steroid hormone) and azathioprine that suppress the immune system are often used in patients with disabling weakness, especially those who cannot have, or fail to respond to a thymectomy. When rapid improvement is needed, for example in case of severe weakness causing breathing or swallowing problems, patients can undergo plasma exchange, which removes antibodies from the blood. Another option is an infusion of intravenous immunoglobulin. The benefits of these emergency treatments only last for a few weeks. 5'CTG CCA CGT TCT CCT GC (2' methoxy)A (2' methoxy)C-(2'methoxy)C-3' is a new type of drug which might be of potential significant benefit for the treatment of myasthenia gravis due to its new mechanism of action. The assumption 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, myasthenia gravis was considered to affect about 60,000 persons in the European Union at the time the application was made.

How is this medicinal product expected to act?

The medicinal product is expected to act by degrading the genetic material that produces the cholinesterases. Therefore it is expected that the symptoms of muscle weakness are attenuated.

What is the stage of development of this medicinal product?

The effects of 5'CTG CCA CGT TCT CCT GC (2' methoxy)A (2' methoxy)C-(2'methoxy)C-3' were evaluated in experimental models.

At the time of submission of the application for orphan designation, one clinical trial in patients with myasthenia was completed.

5'CTG CCA CGT TCT CCT GC (2' methoxy)A (2' methoxy)C-(2'methoxy)C-3' was not marketed anywhere worldwide for myasthenia gravis at the time of submission.

Orphan designation of 5'CTG CCA CGT TCT CCT GC (2' methoxy)A (2' methoxy)C-(2'methoxy)C-3' was granted in the United States for the treatment of myasthenia gravis.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 14 May 2004 a positive opinion recommending the grant of the above-mentioned designation.

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.

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

Language	Active Ingredient	Indication
English	5'-CTG CCA CGT TCT CCT GC-(2' methoxy)A-(2' methoxy)C-(2' methoxy)C-3'	Treatment of myasthenia gravis
Czech	5'-CTG CCA CGT TCT CCT GC-(2' methoxy)A-(2' methoxy)C-(2' methoxy)C-3'	Léčba myasthenie gravis
Danish	5'-CTG CCA CGT TCT CCT GC-(2' methoxy)A-(2' methoxy)C-(2' methoxy)C-3'	Behandling af myasthenia gravis
Dutch	5'-CTG CCA CGT TCT CCT GC-(2' methoxy)A-(2' methoxy)C-(2' methoxy)C-3'	Behandeling van myasthenia gravis
Estonian	5'-CTG CCA CGT TCT CCT GC-(2' methoxy)A-(2' methoxy)C-(2' methoxy)C-3'	Myasthenia Gravis ravi.
Finnish	5'-CTG CCA CGT TCT CCT GC-(2' metoksi)A-(2' metoksi)C-(2' metoksi)C-3'	Myasthenia graviksen hoito
French	5'-CTG CCA CGT TCT CCT GC-(2' methoxy)A-(2' methoxy)C-(2' methoxy)C-3'	Traitement de la myasthénie
German	5'-CTG CCA CGT TCT CCT GC-(2' methoxy)A-(2' methoxy)C-(2' methoxy)C-3'	Behandlung der Myasthenia Gravis
Greek	5'-CTG CCA CGT TCT CCT GC-(2' μεθοξυ)A-(2' μεθοξυ)C-(2' μεθοξυ)C-3'	Θεραπεία της βαρειάς μυασθένειας
Hungarian	5'-CTG CCA CGT TCT CCT GC-(2' methoxy)A-(2' methoxy)C-(2' methoxy)C-3'	Myasthenia gravis kezelése
Italian	5'-CTG CCA CGT TCT CCT GC-(2' metossi)A-(2' metossi)C-(2' metossi)C-3'	Trattamento della miastenia grave
Latvian	5'-CTG CCA CGT TCT CCT GC-(2' methoxy)A-(2' methoxy)C-(2' methoxy)C-3'	Myasthenia gravis ārstēšanai
Lithuanian	5'-CTG CCA CGT TCT CCT GC-(2' metoksi)A-(2' metoksi)C-(2' metoksi)C-3'	Didžiosios miastenijos gydymas
Maltese	5'-CTG CCA CGT TCT CCT GC-(2' methoxy)A-(2' methoxy)C-(2' methoxy)C-3'	Treatment of myasthenia gravis
Polish	5'-CTG CCA CGT TCT CCT GC-(2' metoksy)A-(2' metoksy)C-(2' metoksy)C-3'	Leczenie miastении
Portuguese	5'-CTG CCA CGT TCT CCT GC-(2' metoxi)A-(2' metoxi)C-(2' metoxi)C-3'	Tratamento da miastenia gravis
Slovak	5'-CTG CCA CGT TCT CCT GC-(2' metoxy)A-(2' metoxy)C-(2' metoxy)C-3'	Liečba myasthenie gravis
Slovenian	5'-CTG CCA CGT TCT CCT GC-(2' metoksi)A-(2' metoksi)C-(2' metoksi)C-3'	Zdravljenje miasteniije gravis
Spanish	5'-CTG CCA CGT TCT CCT GC-(2' metoxi)A-(2' metoxi)C-(2' metoxi)C-3'	Tratamiento de la miastenia gravis
Swedish	5'-CTG CCA CGT TCT CCT GC-(2' methoxy)A-(2' methoxy)C-(2' methoxy)C-3'	Behandling av myasthenia gravis
Norwegian	5'-CTG CCA CGT TCT CCT GC-(2' metoksy)A-(2' metoksy)C-(2' metoksy)C-3'	Behandling av myasthenia gravis
Icelandic	5'-CTG CCA CGT TCT CCT GC-(2' metoxy)A-(2' metoxy)C-(2' metoxy)C-3'	Meðferð við vöðvaslensfári