7 March 2013
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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

1-[(2-chloro-4-methoxyphenoxy)methyl]-4-[(2,6-dichlorophenoxy)methyl]benzene for the prevention of poliomyelitis in patients with immunodeficiencies deemed at risk

On 17 July 2012, orphan designation (EU/3/12/1021) was granted by the European Commission to ProPhase Development Ltd, United Kingdom, for 1-[(2-chloro-4-methoxyphenoxy)methyl]-4-[(2,6-dichlorophenoxy)methyl]benzene for the prevention of poliomyelitis in patients with immunodeficiencies deemed at risk.

The sponsorship was transferred to ViroDefense Ltd, United Kingdom, in January 2013.

What is poliomyelitis?

Poliomyelitis (also known as polio) is a viral disease caused by the poliovirus. In the vast majority of cases (more than 95%), infection with the virus does not result in any symptoms or may cause mild symptoms from which the patient will recover completely. However, in the most severe form of poliovirus infection (less than 1% of cases), the virus reaches the nervous system where it attacks the nerve cells involved in movement, leading to muscle weakness and paralysis.

Although vaccines are available for preventing poliomyelitis and have been used to eradicate the disease in the EU, patients with immunodeficiencies (weakened immune systems) may be at risk. This is because some vaccines contain live (although weakened) viruses, which these patients may not be able to clear from their bodies. These patients may also be exposed to viruses that are shed into the environment by other people who have been vaccinated.

Poliomyelitis is debilitating in the long term because it can cause meningitis (inflammation of the meninges) and encephalitis (inflammation of the brain tissue), pain, paralysis and muscle wasting. It is also life-threatening with a death rate of up to 15% in patients with the acute paralytic forms of the disease.

What is the estimated number of patients with immunodeficiencies considered to be at risk?

At the time of designation, the number of patients with immunodeficiencies considered to be at risk was approximately 0.00008 in 10,000 people in the European Union (EU). This was equivalent to a

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total of around 4 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 methods of prevention are available?

At the time of orphan designation no satisfactory methods of prevention of poliomyelitis were available specifically for patients with immunodeficiencies deemed at risk.

How is this medicine expected to work?

The medicine works by integrating itself into the capsid (or outer shell) of the poliovirus. Once inside the capsid it is expected to prevent the virus from 'uncoating', which is the process by which the virus releases its genetic material from the capsid to infect other cells.

By preventing the uncoating of the virus, the medicine is expected to prevent the virus from spreading and causing disease. The medicine may be used for early treatment of infection or in patients who have been vaccinated against the disease but were subsequently exposed to the virus.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with immunodeficiencies deemed at risk had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the prevention of poliomyelitis in patients with immunodeficiencies deemed at risk. Orphan designation of the medicine had been granted in the United States of America for treatment of poliovirus infection.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 June 2012 recommending the granting of this designation.

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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.

*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 (EU 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 509,000,000 (Eurostat 2012).

For more information

Sponsor's contact details:

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The Catalyst, Suite G17
University of York
Baird Lane
York 010 5GA
United Kingdom
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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	1-[(2-Chloro-4-methoxyphenoxy)methyl]-4-[(2,6-dichlorophenoxy)methyl]benzene	Prevention of poliomyelitis in patients with immunodeficiencies deemed at risk
Bulgarian	1-[(2-хлоро-4-метокси феноксu) метил]-4-[(2, бензен дихлор феноксu) метил] benzene	Превенция на полиомиелит при рискови пациенти с имунен дефицит.
Czech	1 - [(2-chlor-4-methoxy fenoxy) methyl] -4 - [(2,6 - dichlor fenoxy) methyl] benzen	Prevence poliomyelitidy u rizikových pacientů s imunodeficitem
Danish	1-[(2-Chlor-4-methoxy phenoxy) methyl] -4-[(2,6-dichlor-phenoxy) methyl] benzen	Forebyggelse af poliomyelitis i risikopatienter med immundefekter
Dutch	1 - [(2 - Chloor -4 - methoxy fenoxy) methyl] -4 - [(2,6 - dichloor fenoxy) methyl] benzeen	Preventie van poliomyelitis in patiënten met immunodeficiënties beschouwd als risicohoudend.
Estonian	1-[(2-Kloro-4-metoksüfenoksü) metüül] -4-[(2,6-dikloro fenoksü) metüül] benseen	Poliomüeliidi ennetuseks immuunpuudulikkusega patsientidel, kel suurenenud risk.
Finnish	1-[(2-kloori-4-metoksifenoksi) metyyli]-4-[(2,6-dikloorifenoksi) metyyli] bentseeni	Poliomyeliitin ehkäisy, kun potilaalla on immuunivajavuustilasta johtuva polioriski
French	1-[(2-Chloro-4- méthoxy phénoxy) méthyl]-4-[(2,6-dichloro phénoxy) méthyl] benzène	Prévention de la poliomyélite chez les patients immunodéprimés
German	1-[(2-Chloro-4-methoxy phenoxy) methyl]-4-[(2,6-dichloro phenoxy) methyl] Benzol	Poliomyelitisprävention in Riskopatienten mit Immundefizienz
Greek	1-[(2-χλωρο-4-μεθοξυ φαινοξυ) μεθυλο] -4-(2,6-διχλωρο φαινοξυ) μεθυλο]βενζόλιο	Πρόληψη της πολιομυελίτιδας σε ασθενείς υψηλού κινδύνου με ανοσοανεπάρκεια
Hungarian	1-[(2-klór -4- metoxifenoxi) metil] -4-[(2,6-diklór fenoxi) metil]-benzol	Polyomyelitis megelőzése immunhiányos, a fertőzésnek kitett betegeknél
Italian	1 - [(2 - Cloro -4 - fenossi metossi) metil] -4 - [(2,6 - dicloro fenossi) metil] benzene	Prevenzione della poliomielite in pazienti immunodeficienti a rischio
Latvian	1 - [(2 - Hlor -4 - metoksi fenoksi) metil] -4 - [(2,6 - dihlor fenoksi) metil] benzols	Poliomielīta profilakse riska pacientiem ar imunodeficītu
Lithuanian	1 - [(2-chlor - 4 - metoksifenoksi) metil] -4 - [(2,6 - dichlorfenoksi) metil] benzenas	Poliomielito prevencija pacientams su galima imunodeficito rizika
Maltese	1-[(2-Chloro-4-methoxyphenoxy)methyl]-4-[(2,6-dichlorophenoxy)methyl]benzene	Prevenzjoni tal-poljomelite f'pazjenti b'nuqqasijiet immunitarji kkunsidrati f'riskju
Polish	1- [(2-chloro-4-metoksy-fenoksy)metylo]-4-[(2,6-dichloro-fenoksy)metylo]benzene	Zapobieganie polio u pacjentów z ryzykiem niedoboru odporności
Portuguese	1-[(2-Cloro-4-metoxifenoxi)metil]-4-[(2,6-diclorofenoxi)metil]benzeno	Prevenção da poliomielite em doentes com immunodeficiência considerados em risco
Romanian	1 - [(2 - cloro -4 - metoxi fenoxi) metil] -4 - [(2,6 - dicloro fenoxi) metil] benzen	Profilaxia poliomielitei la pacienţii imunodeprimaţi încadraţi într-o clasă de risc

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	1 - [(2 - chlór -4 - metoxy fenoxy) metyl] - 4 - [(2,6 - dichlór fenoxy) metyl] benzén	Prevencia poliomyelitídy u rizikových pacientov s imunodeficitom
Slovenian	1 - [(2 - kloro -4 - metoksi fenoksi) metil] - 4 - [(2,6 - dikloro fenoksi) metil] benzen	Preprečevanje poliomielitisa pri pacientih z zvečanim tveganjem zaradi zmanjšane imunske odpornosti
Spanish	1 - [(2 - cloro -4 - fenoxi metoxi) metil] -4 - [(2,6 - dicloro fenoxi)-metil] benceno	Prevención de la poliomielitis en pacientes immunodeprimidos conisderados de riesgo
Swedish	1 - [(2 -kloro-4-metoxifenoxi)metyl] -4- [(2,6-diklorofenoxi)metyl]bensen	Förebyggande av poliomyelit hos riskpatienter med immundefekter