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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

5-[1-(2,6-dichlorobenzyl)piperidin-4-ylmethoxy]quinazoline-2,4-diamine dihydrochloride for the treatment of 5q spinal muscular atrophy

First publication	18 June 2013
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Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 7 June 2013, orphan designation (EU/3/13/1136) was granted by the European Commission to Repligen Sweden AB, Sweden, for 5-[1-(2,6-dichlorobenzyl)piperidin-4-ylmethoxy]quinazoline-2,4-diamine dihydrochloride for the treatment of 5q spinal muscular atrophy.

The sponsorship was transferred to Pfizer Limited, United Kingdom, in September 2013.

What is 5q spinal muscular atrophy?

5q spinal muscular atrophy is an inherited disease that affects the motor neurons (nerves from the brain and spinal cord that control muscle movements). Patients with the disease lack a protein called 'survival motor neuron' (SMN), which is essential for the normal functioning and survival of motor neurons. Without this protein, the motor neurons deteriorate and eventually die. This causes the muscles to fall into disuse, leading to muscle wasting (atrophy) and weakness. The disease is linked to a defect on chromosome 5q and is usually diagnosed in the first year of life.

5q spinal muscular atrophy is a long-term debilitating and life-threatening disease because it causes breathing problems and paralysis that worsens over time.

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

At the time of designation, 5q spinal muscular atrophy affected approximately 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 10,000 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 designation, no satisfactory methods were authorised in the EU for the treatment of 5q spinal muscular atrophy. Patients received supportive treatment to help them and their families cope with the symptoms of the disease. This included chest physiotherapy and physical aids to support muscular function, and ventilators to help with breathing.

How is this medicine expected to work?

Patients with 5q spinal muscular atrophy lack *SMN* genes of which there are two types, *SMN1* and *SMN2*. Many patients lack *SMN1* but have *SMN2*, which normally produces low levels of the SMN protein.

This medicine is expected to increase the level of the SMN protein produced by *SMN2*, thereby increasing the survival of motor neurons. It is expected to do this by blocking DcpS (scavenger decapping enzyme), the enzyme that is responsible for the low protein yield through its action in cutting the genetic material involved in protein synthesis.

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, clinical trials with the medicine in patients with 5q spinal muscular atrophy were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for 5q spinal muscular atrophy. Orphan designation had been granted in the United States of America for spinal muscular atrophy.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 17 April 2013 recommending the granting of this designation.

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[*]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. This represents a population of 509,000,000 (Eurostat 2013).

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:

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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	5-[1-(2,6-dichlorobenzyl)piperidin-4-ylmethoxy]quinazoline-2,4-diamine dihydrochloride	Treatment of 5q spinal muscular atrophy
Bulgarian	5-[1-(2,6-дихлоробензил)пиперидин-4-илметокси]квиназолин-2,4-диамин дихидрохлорид	Лечение на 5q спинална мускулна атрофия
Croatian	5-[1-(2,6-diklorobenzil) piperidin-4-ilmetoksi] kinazolin-2,4-diamin dihidroklorid	Liječenje spinalne mišićne atrofije 5q
Czech	5-[1-(2,6-dichlorobenzyl)piperidin-4-ylmethoxy]quinazolin-2,4-diamin dihydrochlorid	Léčba 5q spinální muskulární atrofie
Danish	5-[1-(2,6-dichlorobenzyl)piperidin-4-ylmethoxy]quinazolin-2,4-diamin dihydrochlorid	Behandling af 5q spinal muskelatrofi
Dutch	5-[1-(2,6-dichloorbenzyl)piperidine-4-ylmethoxy]quinazoline-2,4-diamine-dihydrochloride	Behandeling van 5q spinale spieratrofie
Estonian	5-[1-(2,6-diklorobensüül)piperidiin-4-üülmetoksü]kinasoliin-2,4-diamiindihüdrokloriid	5q spinaalse lihasatroofia ravi
Finnish	5-[1-(2,6-diklorobentsyyli)piperidin-4-yylimetoksi]kinatsolin-2,4-diamiinidihydrokloridi	Selkärangan 5q lihassurkastuman hoito
French	Dichlorydrate de 5-[1-(2,6-dichlorobenzyl)pipéridine-4-ylméthoxy]quinazoline-2,4-diamine	Traitement de l'amyotrophie spinale 5q
German	5-[1-(2,6-Dichlorobenzyl)piperidin-4-ylmethoxy]Quinazolin-2,4-Diamin-Dihydrochlorid	Behandlung der 5q spinalen Muskelatrophie
Greek	Διϋδροχλωρική 5-[1-(2,6-διχλωροβενζυλο)πιπεριδιν-4-υλμεθοξυ]κιναζολιν-2,4-διαμίνη	Θεραπεία της νωτιαίας μυϊκής ατροφίας (5q)
Hungarian	5-[1-(2,6-diklórbenzil)piperidin-4-ilmetoxi]quinazolin-2,4-diamin dihidroklorid	5q spinális izomatrophia kezelése
Italian	5-[1-(2,6-diclorobenzil)piperidina-4-ilmetossi] quinazolina-2,4-diamina dicloridrato	Trattamento dell'atrofia muscolare spinale 5q
Latvian	5-[1-(2,6-dihlorbenzil)-piperidīn-4-ilmetoksi]hinazolīn-2,4-diamīna dihidrohlorīds	5q spinālas muskuļu atrofijas ārstēšana

[1] At the time of transfer of sponsorship

Language	Active ingredient	Indication
Lithuanian	5-[1-(2,6-dichlorbenzil)piperidino-4-ilmetoksi]chinazolino-2,4-diamino dihidrochloridas	Spinalinės raumenų atrofijos gydymas, esant 5q delecijoms
Maltese	5-[1-(2,6-dichlorobenzyl)piperidin-4-ylmethoxy]quinazoline-2,4-diamine dihydrochloride	Kura tal-atrofija muskolari spinali 5q
Polish	Dichlorowodorek 5-[1-(2,6-dichlorobenzylo)piperydyno-4-ylometoksy]chinazolino-2,4-diaminy	Leczenie rdzeniowego zaniku mięśni 5q
Portuguese	Dihidrocloreto de 5-[1-(2,6 diclorobenzil)piperidina-4-il-metoxil]quinazolina 2,4-diamina	Tratamento da atrofia muscular espinal 5q
Romanian	Diclorhidrat de 5-[1-(2,6-diclorobenzil)piperidin-4-il-metoxi]quinazolin-2,4-diamină	Tratamentul amiotrofiei spinale 5q
Slovak	5-[1-(2,6-dichlorobenzyl)piperidín-4-ylmetoxy]chinazolín-2,4-diamín dihydrochlorid	Liečba 5q spinálnej svalovej atrofie
Slovenian	5-[1-(2,6-diklorobenzil)piperidin-4-ilmetoksi]kinazolin-2,4-diamin dihidroklorid	Zdravljenje 5q spinalne mišične atrofije
Spanish	Diclorhidrato de 5-[1-(2,6-diclorobencil)piperidina-4-ilmetoxi]quinazolina-2,4-diamina	Tratamiento de la atrofia muscular espinal 5q
Swedish	5-[1-(2,6-diklorobensyl)piperidin-4-ylmetoxi]kinazolin-2,4-diamindihydroklorid	Behandling av 5q spinal muskelatrofi
Norwegian	5-[1-(2,6-diklorbenzyl)piperidin-4-ylmetoksy]kinazolin-2,4-diamindihydroklorid	Behandling av 5q spinal muskelatrofi
Icelandic	5-[1-(2,6-díklórbensýl) píperidín-4-ýlmetoxý] kvínasólín 2,4 díamín tvívetnisklóríð	Meðferð við 5q mænuvöðvarýrnunar