

20 September 2011
EMA/COMP/512027/2011
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

On 30 August 2011, orphan designation (EU/3/11/892) was granted by the European Commission to Repligen Europe Limited, Ireland, for 5-[1-(2,6-dichlorobenzyl)piperidin-4-ylmethoxy]quinazoline-2,4-diamine dihydrochloride for the treatment of 5q spinal muscular atrophy.

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) protein, 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. Muscle weakness is usually more severe in the proximal musculature (the muscles closest to the trunk). The disease is linked to a defect on chromosome 5q and is usually diagnosed in the first year of life.

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

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 is 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

*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 506,300,000 (Eurostat 2011).

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 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 (splicing) messenger RNA (genetic material involved in protein synthesis).

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of 5-[1-(2,6-dichlorobenzyl)piperidin-4-ylmethoxy]quinazoline-2,4-diamine dihydrochloride in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with 5q spinal muscular atrophy had been started.

At the time of submission, this medicine was not authorised anywhere in the EU for 5q spinal muscular atrophy. Orphan designation of this medicine 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 10 June 2011 recommending the granting of this designation.

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 languages¹, 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
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-üülmetsü]kinasoliin-2,4-diamiindihüdrokloriid	5q spinaalse lihasatroofia ravi
Finnish	5-[1-(2,6-diklorobentsyyli)piperidin-4-yylietoksi]kinatsolin-2,4-diamiinidihydrokloridi	Selkärangan 5q lihassurkastuman hoito
French	5-[1-(2,6-dichlorobenzyl)pipéridine-4-ylméthoxy]quinazoline-2,4-diamine dihydrochloride	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] quinazolin-2,4-diamin dicloridrato	Trattamento dell'atrofia muscolare spinale 5q
Latvian	5-[1-(2,6-dihlorbenzil)-piperidīn-4-ilmetoksi]hinazolīn-2,4-diamīna dihidrohlors	5q spinālas muskuļu atrofijas ārstēšana
Lithuanian	5-[1-(2,6-dichlorobenzil)piperidin-4-ilmetoksi]kvinazolino-2,4-diamino dihidrochloridas	Spinalinės raumenų atrofijos gydymas, esant 5q delecijoms

¹ At the time of designation

Language	Active ingredient	Indication
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-dichlorobenzyl)piperidyno-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	5-[1-(2,6-diclorobenzil)piperidin-4-il-metoxi]quinazolin-2,4-diamin dihidroclorid	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] kínasólín 2,4 díamín tvívetnisklóríð	Meðferð við 5q mænuvöðvarýrnunar