EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Antisense oligonucleotide targeted to the *SMN2* gene for the treatment of 5q spinal muscular atrophy

On 2 April 2012, orphan designation (EU/3/12/976) was granted by the European Commission to Isis USA Ltd, United Kingdom, for antisense oligonucleotide targeted to the *SMN2* gene 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), 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 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 less than 0.4 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of fewer than 20,000 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).

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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?

The SMN protein is made by two genes, the *SMN1* and *SMN2* genes. Most patients with 5q spinal muscular atrophy lack the *SMN1* gene but have the *SMN2* gene, which mostly produces a 'short' SMN protein which cannot work properly.

This medicine is an 'anti-sense oligonucleotide' medicine. It is expected to make the *SMN2* gene produce adequate levels of the SMN protein of normal length, thereby increasing the survival of motor neurons. It is expected to do so by blocking the cutting ('splicing') of the molecule produced from the *SMN2* gene that serves as the 'template' for the SMN protein. This is expected to lead to an increased production of the normal-length SMN protein.

This medicine is expected to be given by injection into the fluid surrounding the spinal cord and brain.

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 the medicinal product in experimental models was ongoing.

At the time of submission, no clinical trials with the medicinal product in patients with 5q spinal muscular atrophy had been started.

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 February 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.

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	Antisense oligonucleotide targeted to the *SMN2* gene	Treatment of 5q spinal muscular atrophy
Bulgarian	Антисенс олигонуклеотид насочен към *SMN2* гена	Лечение на 5q спинална мускулна атрофия
Czech	Antisense oligonukleotid pro *SMN2* gen	Léčba 5q spinální muskulární atrofie
Danish	Antisense-oligonukleotid rettet mod *SMN2*-genet	Behandling af 5q spinal muskelatrofi
Dutch	Antisense oligonucleotide gericht op het *SMN2*-gen	Behandeling van 5q spinale spieratrofie
Estonian	Antisense oligonukleotiid *SMN2* geenile.	5q spinaalse lihasatroofia ravi
Finnish	*SMN2*-geenin antisense oligonukleotidi	Selkärangan 5q lihassurkastuman hoito
French	Oligonucléotide antisens dirigé contre le gène *SMN2*	Traitement de l'amyotrophie spinale 5q
German	Antisense-Oligonukleotid gegen das *SMN2*-Gen	Behandlung der 5q spinalen Muskelatrophie
Greek	Αντινοηματικό ολιγονουκλεοτίδιο που στοχεύει το γονίδιο *SMN2*	Θεραπεία της νωτιαίας μυϊκής ατροφίας (5q)
Hungarian	az SMN2 génhez targetált antiszensz oligonukleotid	5q spinális izomatrophia kezelése
Italian	Oligonucleotide antisenso mirato al gene *SMN2*	Trattamento dell'atrofia muscolare spinale 5q
Latvian	Antisense oligonukleotīds mērķēts uz *SMN2* gēnu	5q spinālas muskuļu atrofijas ārstēšana
Lithuanian	Priešprasmis oligonukleotidas, nukreiptas į *SMN2* geną	Spinalinės raumenų atrofijos gydymas, esant 5q delecijoms
Maltese	Antisense oligonucleotide immirata għall-ġene *SMN2*	Kura tal-atrofija muskolari spinali 5q
Polish	Oligonukleotyd antysensowny, który ma wpływ na gen *SMN2*	Leczenie rdzeniowego zaniku mięśni 5q
Portuguese	Oligonucleótido anti-senso direcionado contra o gene *SMN2*	Tratamento da atrofia muscular espinal 5q
Romanian	Oligonucleotid antisens dirijat împotriva genei *SMN2*	Tratamentul amiotrofiei spinale 5q
Slovak	Antisense oligonukleotid cielený na gén *SMN2*	Liečba 5q spinálnej svalovej atrofie
Slovenian	Protismerni oligonukleotid, ki deluje na *SMN2* gen	Zdravljenje 5q spinalne mišične atrofije
Spanish	Oligonucleótido antisentido dirigido contra el gen *SMN2*	Tratamiento de la atrofia muscular espinal 5q
Swedish	Antisense-oligonukleotid riktad mot *SMN*-	Behandling av 5q spinal muskelatrofi

[1] At the time of designation

Language	Active ingredient	Indication
	2-genen	
Norwegian	Antisense-oligonukleotid rettet mot genet SMN2	Behandling av 5q spinal muskelatrofi
Icelandic	Antisense ólígónúkleótíð sem beinist að SMN2 geni	Meðferð við 5q mænuvöðvarýrnunar