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Public summary of opinion on orphan designation

Risdiplam for the treatment of spinal muscular atrophy

On 26 February 2019, orphan designation (EU/3/19/2145) was granted by the European Commission to Roche Registration GmbH, Germany, for risdiplam for the treatment of spinal muscular atrophy.

What is spinal muscular atrophy?

Spinal muscular atrophy is an inherited disease usually diagnosed in the first year of life 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.

Spinal muscular atrophy is a long-term debilitating and life-threatening disease because it causes breathing problems and muscle wasting that worsens over time.

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

At the time of designation, spinal muscular atrophy affected approximately 0.4 in 10,000 people in the European Union (EU). This was equivalent to a total of 21,000 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, the medicine Spinraza (nusinersen) was authorised for the treatment of spinal muscular atrophy. Spinraza is given by injection into the spine. Patients also 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 muscle function, and ventilators to help with breathing.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with spinal muscular atrophy. Early data indicate that the medicine may improve

*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 28), Norway, Iceland and Liechtenstein. This represents a population of 518,400,000 (Eurostat 2019).

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patients' survival and muscle strength compared with results seen with the authorised treatment; additionally, since the medicine is to be given by mouth, it may be usable in a broader population. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

The SMN protein can be made by two genes, *SMN1* and *SMN2*. Patients with spinal muscular atrophy lack a working *SMN1* gene but have the *SMN2* gene, which mostly produces a short SMN protein that does not work as well as a full-length protein.

Risdiplam is a small molecule that enables the *SMN2* gene to produce a full length protein, which is able to work normally. This is expected to increase survival of motor neurons and reduce symptoms of the disease.

What is the stage of development of this medicine?

The effects of risdiplam have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with risdiplam in patients with spinal muscular atrophy were ongoing.

At the time of submission, risdiplam was not authorised anywhere in the EU for spinal muscular atrophy. Orphan designation of risdiplam had been granted in the United States and Switzerland for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 24 January 2019 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:

Contact details of the current sponsor for this orphan designation can be found on the EMA website.

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	Risdiplam	Treatment of spinal muscular atrophy
Bulgarian	Рисдиплам	Лечение на спинална мускулна атрофия
Croatian	Risdiplam	Liječenje spinalne mišićne atrofije
Czech	Risdiplam	Léčba spinální muskulární atrofie
Danish	Risdiplam	Behandling af spinal muskelatrofi
Dutch	Risdiplam	Behandeling van spinale spieratrofie
Estonian	Risdiplaam	Spinaalse lihasatroofia ravi
Finnish	Risdiplaami	Spinaalisen lihasatrofian hoito
French	Risdiplam	Traitement de l'amyotrophie spinale
German	Risdiplam	Behandlung der spinalen Muskelatrophie
Greek	Ρισδιπλάμη	Θεραπεία της νωτιαίας μυϊκής ατροφίας
Hungarian	Risdiplam	Spinális izomatrophia kezelése
Italian	Risdiplam	Trattamento dell'atrofia muscolare spinale
Latvian	Risdiplāms	Spinālās muskuļu atrofijas ārstēšana
Lithuanian	Risdiplamas	Spinalinės raumenų atrofijos gydymas
Maltese	Risdiplam	Kura tal-atrofija muskolari tas-sinsla
Polish	Rysdiplam	Leczenie rdzeniowego zaniku mięśni
Portuguese	Risdiplam	Tratamento da atrofia muscular espinal
Romanian	Risdiplam	Tratamentul amiotrofiei spinale
Slovak	Risdiplam	Liečba spinálnej svalovej atrofie
Slovenian	Risdiplam	Zdravljenje spinalne mišične atrofije
Spanish	Risdiplam	Tratamiento de la atrofia muscular espinal
Swedish	Risdiplam	Behandling av spinal muskelatrofi
Norwegian	Risdiplam	Behandling av spinal muskelatrofi
Icelandic	Risdiplam	Meðferð við mænuvöðvarýrnun

[1] At the time of designation