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Public summary of opinion on orphan designation

Recombinant mutated extracellular domain of the human acetylcholine receptor subunit alpha1 for the treatment of myasthenia gravis

On 25 July 2019, orphan designation EU/3/19/2187 was granted by the European Commission to Toleranzia AB, Sweden, for recombinant mutated extracellular domain of the human acetylcholine receptor subunit alpha1 for the treatment of myasthenia gravis.

What is myasthenia gravis?

Myasthenia gravis is a disease that leads to muscle weakness and tiredness. It is an autoimmune disorder in which the immune system (the body's natural defences) attacks and damages targets called acetylcholine receptors on muscle cells. For a muscle to contract, a substance called acetylcholine is released from a nerve and attaches to the acetylcholine receptors on the muscle cells. In myasthenia gravis, because of the damage to these receptors, the muscles cannot contract normally. In most patients, the disease is associated with abnormalities of a gland in the chest called the thymus, which is part of the immune system.

In myasthenia gravis, the muscles involved in swallowing and those around the eyes are commonly affected first, causing difficulty in swallowing and the eyelids to droop. Muscle weakness typically worsens towards the end of the day and after exercise.

Myasthenia gravis is a long-term debilitating disease and may be life-threatening when the muscles involved in breathing are affected.

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

At the time of designation, myasthenia gravis affected approximately 1.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 88,000 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).

*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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What treatments are available?

At the time of designation, several medicines were authorised in the EU for the treatment of myasthenia gravis, including acetylcholine esterase inhibitors (medicines that prevent breakdown of acetylcholine) and medicines that work on the immune system. Surgery to remove the thymus gland (thymectomy) was performed in some patients.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with myasthenia gravis because laboratory studies have shown that it slowed down worsening of the disease. 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 active substance in the medicine is a protein similar to a part of the acetylcholine receptor but, unlike the natural receptor, it is not active. Cells of the immune system (the body's defences) adjust to accept the medicine without attacking it. As a result, it is thought that these cells will also accept the very similar natural acetylcholine receptors. Giving the medicine to patients is therefore expected to stop the immune system from attacking natural acetylcholine receptors and slow down worsening of the disease.

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 medicine in experimental models was ongoing.

No clinical trials with the medicine in patients with myasthenia gravis had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of myasthenia gravis. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 20 June 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 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	Recombinant mutated extracellular domain of the human acetylcholine receptor subunit alpha1	Treatment of myasthenia gravis
Bulgarian	Рекомбинантен мутантен извънклетъчен домен на човешката ацетилхолинова рецепторна субединица α1	Лечение на миастения гравис
Croatian	Rekombinantna mutirana izvanstanična domena podjedinice alfa1 ljudskog receptora acetilkolina	Liječenje miastenije gravis
Czech	Rekombinantní mutovaná extracelulární doména podjednotky α1 lidského acetylcholinového receptoru	Léčba myasthenie gravis
Danish	Rekombinant muteret ekstracellulær domæne af den menneskelige acetylcholinreceptor-subenhed α1	Behandling af myasthenia gravis
Dutch	Recombinant gemuteerd extracellulair domein van de menselijke acetylcholine receptor subeenheid α1	Behandeling van myasthenia gravis
Estonian	Inimese atsetüülkoliini retseptori alaühiku alfa-1 rekombinantne muundatud rakuväline domeen	Myasthenia Gravise ravi
Finnish	Solunulkoinen, mutatoitu, rekombinantti ihmisen asetyylikoliinireseptorin alayksikköön α1 kuuluva domeeni	Myasthenia graviksen hoito
French	Domaine extracellulaire recombinant muté de la sous-unité α1 du récepteur de l'acétylcholine humain	Traitement de la myasthénie grave
German	Rekombinante mutierte extrazelluläre Domäne der Untereinheit α1 des humanen Acetylcholinerezeptors.	Behandlung der Myasthenia Gravis
Greek	Ανασυνδυασμένη μεταλλαγμένη εξωκυττάρια περιοχή της α1 υπομονάδας του ανθρώπινου υποδοχέα ακετυλοχολίνης	Θεραπεία της βαρείας μυασθένειας
Hungarian	Humán acetilkolin receptor α1 alegységének rekombináns mutálódott extracelluláris doménje	Myasthenia gravis kezelése
Italian	Dominio extracellulare mutato ricombinante della subunità α1 del recettore dell'acetilcolina umana	Trattamento della miastenia grave
Latvian	Cilvēka acetilholīna receptora α1 apakšvienības rekombinants, mutēts ārpussūnas domēns	*Myasthenia gravis* ārstēšanai
Lithuanian	Rekombinantinis mutuotas ekstraląstelinis žmogaus acetilcholino receptoriaus subvieneto α1 domenas	Generalizuotos miastenijos gydymas

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	Qasam ekstraċellulari mutat rikombinanti tar-riċettur tal-aċetilkolina umana subunità alfa1	Kura ta' myasthenia gravis
Polish	Zrekombinowana, zmutowana domena zewnątrzkomórkowa ludzkiej podjednostki receptora acetylocholiny α1	Leczenie miastenii gravis
Portuguese	Domínio extracelular mutante recombinante da subunidade α1 do receptor de acetilcolina humana	Tratamento da miastenia gravis
Romanian	Domeniu extracelular mutant recombinant al subunității α1 a receptorului uman pentru acetilcolină	Tratamentul miasteniei gravis
Slovak	Rekombinantná mutovaná extracelulárna doména ľudskej acetylcholínovej receptorovej podjednotky α1	Liečba myasthenie gravis
Slovenian	Rekombinantna mutirana zunajcelična domena človeške acetilholinske receptorske podenote α1	Zdravljenje miastenije gravis
Spanish	Dominio extracellular mutado recombinante de la subunidad α1 del receptor humano de acetilcolina	Tratamiento de la miastenia gravis
Swedish	Rekombinant muterad extracellulär domän av den humana acetylkolinreceptorns subenhet α1	Behandling av myasthenia gravis
Norwegian	Rekombinant mutert ekstracellulært domene av den humane acetylkolinreseptorens subenheten alfa1	Behandling av myasthenia gravis
Icelandic	Raðbrigða stökkbreytt utanfrumuhneppi α1 undireiningar asetýlkólínviðataka manna	Meðferð við vöðvaslensfári