UCB News

UCB receives CHMP positive opinion for rozanolixizumab for treatment of adults with generalized myasthenia gravis in Europe

- The Committee for Medicinal Products for Human Use (CHMP) positive opinion[1] is based on the pivotal Phase 3 MycarinG study in generalized myasthenia gravis (gMG) in adult patients,[2] which demonstrated treatment with rozanolixizumab resulted in statistically significant and clinically meaningful improvements in gMG-specific outcomes compared to placebo,[2] including everyday activities such as breathing, talking, swallowing, and being able to rise from a chair[3]
- If approved by the European Commission, rozanolixizumab will be the first emerging therapy approved in Europe for adults with both anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody-positive gMG, the two most common subtypes of gMG
- The decision follows CHMP positive opinion for UCB's zilucoplan in Europe for the treatment of adult patients with gMG earlier this year, alongside similar U.S. FDA and Japanese MHLW approvals of rozanolixizumab and zilucoplan for the treatment of gMG in adult patients[4,5,6,7]
- UCB is the first and only company to offer a gMG-focused portfolio, providing patients and clinicians the option of two targeted therapies for both anti-AChR and anti-MuSK antibody-positive gMG

Brussels (Belgium) 10 November 2023, 18:00 CET – UCB (Euronext Brussels: UCB), a global biopharmaceutical company, today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a positive opinion recommending granting marketing authorization for rozanolixizumab as an add-on to standard therapy for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.[1]

Rozanolixizumab 140 mg/ml solution for injection is a humanized IgG4 monoclonal antibody that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG.[2] If approved by the European Commission, rozanolixizumab will be the first emerging therapy approved in Europe for adults with both anti-AChR and anti-MuSK antibody-positive gMG, the two most common subtypes of gMG.

In September 2023, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) also issued a positive opinion recommending granting marketing authorization for UCB's zilucoplan in the European Union (EU) as an add-on to standard therapy for the treatment of gMG in adult patients who are anti-AChR antibody-positive[4]. Zilucoplan is a once-daily subcutaneously (SC)-injected, self-administered peptide inhibitor of complement component 5 (C5 inhibitor).[8]

In progressing a portfolio of medicines for the treatment of gMG, with the aim of providing HCPs the option of addressing either complement activation or pathogenic antibodies for appropriate patients, UCB hopes to offer a comprehensive portfolio of targeted therapeutics, embodying a commitment to addressing the gMG community's unmet needs.

"There is a significant need to bring more targeted, well-tolerated, effective treatment options that address the pathophysiology of gMG disease. If approved by the European Commission, UCB will be the first and only company to offer a gMG-focused portfolio with rozanolixizumab and zilucoplan, providing patients and clinicians the option of two targeted therapies. We believe that the inclusion of both anti-muscle-specific tyrosine kinase (MuSK) antibody positive patients and anti-AChR positive patients within the CHMP marketing

authorization recommendation for rozanolixizumab could support clinicians to tailor their prescribing decisions to meet individual needs of their patients.' said Iris Loew-Friedrich, Executive Vice-President and Chief Medical Officer at UCB. *'This latest European gMG regulatory milestone, alongside approvals for both zilucoplan and rozanolixizumab in the U.S. and Japan in recent months, further reinforces the commitment we have made to the gMG community to help transform their experiences, outcomes and expectations. We are truly proud and excited for the future."*

The CHMP opinion for rozanolixizumab is supported by safety and efficacy data from the pivotal Phase 3 MycarinG study (NCT03971422), published in *The Lancet Neurology* in May 2023.[2]**Error! Bookmark not defined.** The primary efficacy endpoint was the comparison of the change from baseline between treatment groups (rozanolixizumab 7mg/kg, rozanolixizumab 10mg/kg) or placebo in the MG-ADL score at Day 43. MG-ADL is a measurement tool that assesses the impact of gMG on daily functions of 8 items that are typically affected in gMG. These include activities such as breathing, talking, swallowing, and being able to rise from a chair.[3] Each item is assessed on a 4-point scale where a score of 0 represents normal function and a score of 3 represents loss of ability to perform that function. A total score ranges from 0 to 24, with the higher scores indicating more impairment. Reductions in MG-ADL score from baseline to Day 43 were greater in the rozanolixizumab 7 mg/kg group (least-squares mean change –3.37 [SE 0.49]) and in the rozanolixizumab 10 mg/kg group (–3.40 [0.49]) than with placebo (–0.78 [0.49]; for 7 mg/kg, least-squares mean difference −2.59 [95% CI −4.09 to −1.25], p<0.001; for 10 mg/kg, −2.62 [−3.99 to −1.16], p<0.001).[2]

Secondary efficacy endpoints included change from baseline to Day 43 in the Myasthenia Gravis Composite (MG-C) and the Quantitative Myasthenia Gravis (QMC) scores. The MG-C is a 10-item instrument that measures the symptoms and signs of MG based on physician examination and patient history. Items are related to ptosis, double vision, eye closure, talking, chewing, swallowing, breathing, neck flexion, shoulder abduction, and hip flexion. Each item is scored on an ordinal scale with four possible categories and weighted. The total score ranges from 0 to 50, with higher scores indicating more severe impairments. The MG-C is composed of items originating from other scales (i.e., QMG, MMT, MG-ADL). A statistically significant difference favoring rozanolixizumab compared to placebo was observed in the MG-C score change from baseline to Day 43 [least squares mean difference] -3.90 (95% CI (−6.63 to −1.25), p<0.001 for rozanolixizumab 7mg/kg; least-squares mean difference −5.53 (95% CI −8.30 to −2.97), p<0.001 for rozanolixizumab 10mg/kg.[2]

The QMG is a 13-item categorical grading system that assesses muscle weakness. Each item is assessed on a 4-point scale where a score of 0 represents no weakness and a score of 3 represents severe weakness. A total possible score ranges from 0 to 39, where higher scores indicate more severe impairment.[9] A statistically significant difference favoring rozanolixizumab compared to placebo was observed in the QMG total score change from baseline to Day 43 [least squares mean difference -3.48 (95% CI (−5.61 to −1.58), p<0.001 for rozanolixizumab 7mg/kg; least-squares mean difference −4.76 (95% CI −6.82 to −2.86), p<0.001 for rozanolixizumab 10mg/kg.[2]

The most common adverse reactions (reported in at least 10% of patients treated with rozanolixizumab) were headache, diarrhea and pyrexia.[1]

gMG is a rare, chronic, heterogeneous, unpredictable autoimmune disease characterized by dysfunction and damage at the neuromuscular junction (NMJ).[10,11,12] gMG has a global prevalence of 100–350 cases per every 1 million people.[11]

"*With the news of the CHMP's positive opinion of rozanolixizumab, we are very proud and excited to potentially provide the gMG community with further treatment options and new hope. Following recent approvals in the U.S. and Japan, it is our commitment to bring widespread access of innovative treatment options to a broader patient population living with myasthenia gravis. And, with our two different medicines for gMG, each with a distinct mechanism of action, UCB offers the community a unique portfolio of treatments that embodies our commitment to addressing the gMG community's unmet needs*." said Jean-Christophe Tellier, CEO, UCB. "*We would like to take this time to extend our gratitude to the patients, care partners and investigators who participated in the MycarinG study, and to our employees and collaborators for their dedication and support to the gMG community*."

This announcement follows approval of rozanolixizumab and zilucoplan by the Japanese Ministry of Health, Labour and Welfare (MHLW) for treatment of gMG in adult patients (only for patients who inadequately respond to steroids or other immunosuppressants), and approval of rozanolixizumab by the U.S. Food and Drug Administration (FDA) for the treatment of gMG in adult patients who are anti-AChR or anti-MuSK antibody positive.[7,5] Orphan designation was granted by the European Commission in 2020 to rozanolixizumab for the treatment of myasthenia gravis and successfully maintained after having received the positive CHMP Opinion.[13]

The CHMP's positive opinion for rozanolixizumab is now being reviewed by the European Commission, which grants centralized marketing authorizations for medicinal products in the EU. Feedback from the European Commission is anticipated during Q1 2024.

About rozanolixizumab
Rozanolixizumab 140 mg/ml solution for injection is a subcutaneously administered, humanized monoclonal antibody that specifically binds, with high affinity, to human neonatal Fc receptor (FcRn). It has been designed to block the interaction of FcRn and Immunoglobulin G (IgG), accelerating the catabolism of antibodies and reducing the concentration of pathogenic IgG autoantibodies.[2]

In June 2023, rozanolixizumab-noli was approved by the FDA, for the treatment of gMG in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody-positive, having been granted Priority Review for its Biologic License Application (BLA).[5]

In September 2023, rozanolixizumab was granted approval by the Japanese Ministry of Health, Labour and Welfare (MHLW) for the treatment of generalized myasthenia gravis (gMG) in adult patients (only for patients who inadequately respond to steroids or other immunosuppressants).[7]

Rozanolixizumab is currently under review by the Center of Drug Evaluation of the China National Medical Products Administration, the Australian Therapeutic Goods Administration (TGA), Health Canada and Switzerland (Swissmedic) for the treatment of adults with gMG. Responses from regulatory agencies to these submissions are expected during H2 2023 and H1 2024.

About zilucoplan
Zilucoplan is a once-daily SC, self-administered peptide inhibitor of complement component 5 (C5 inhibitor). As the only once-daily generalized myasthenia gravis (gMG) target therapy for self-administration by adult patients with anti-acetylcholine receptor (AChR) antibody-positive gMG, zilucoplan inhibits complement-mediated damage to the neuromuscular junction through its targeted mechanism of action.[8]

In October 2023, zilucoplan was approved by the U.S. Food and Drug Administration (FDA) for the treatment of gMG in adult patients who are anti-acetylcholine receptor (AchR) antibody-positive.[6]

In September 2023, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a positive opinion recommending granting marketing authorization for zilucoplan in the European Union (EU) as an add-on to standard therapy for the treatment of gMG in adult patients who are anti-AChR antibody-positive.[4] A final decision on approval in the EU is expected before the end of the year, in line with the EMA's standard review timeline.

Also in September 2023, the Japanese Ministry of Health, Labour and Welfare (MHLW) approved zilucoplan for the treatment of gMG in adult patients (only for patients who inadequately respond to steroids or other immunosuppressants).[7]

Zilucoplan is currently under review by the Australian Therapeutic Goods Administration (TGA) and Health Canada for the treatment of adults with gMG. Responses from regulatory agencies to these submissions are expected during H2 2023 and H1 2024.

Orphan designation was granted by the FDA in 2019 to zilucoplan for the treatment of myasthenia gravis.[14]

About generalized Myasthenia Gravis (gMG)
gMG is a rare autoimmune disease with a global prevalence of 100–350 cases per every 1 million people.[11] People living with gMG can experience a variety of symptoms, including severe muscular weakness that can result in double vision, drooping eyelids, difficulty with swallowing, chewing and talking, as well as life-threatening weakness of the muscles of respiration.[10,15]

In gMG, pathogenic autoantibodies can impair synaptic transmission at the neuromuscular junction (NMJ) by targeting specific proteins on the post-synaptic membrane.[16] This disrupts the ability of the nerves to stimulate the skeletal muscle and results in a weaker contraction. gMG can occur in any race, gender or age.[10,15]

About the MycarinG study[2]
The MycarinG study (NCT03971422) is a multi-center, Phase 3, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of rozanolixizumab in adult patients with gMG, with an open-label extension.

The primary endpoint for the MycarinG study is change in the Myasthenia Gravis-Activities of Daily Living (MG-ADL) score, an eight-item patient-reported scale developed to assess MG symptoms and their effects on daily activities. Additional endpoints include changes in the Myasthenia Gravis composite (MG-C) score, the Quantitative MG (QMG) score, patient-reported outcomes at Day 43 and adverse events (AEs). The majority of patients taking part in the MycarinG study opted to enroll in any future extensions to this clinical trial. As a result, UCB is exploring the potential for further extension studies into this treatment.

For more information about the trial, visit https://clinicaltrials.gov/ct2/show/NCT03971422.

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About UCB
UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With approximately 8,600 people in approximately 40 countries, the company generated revenue of €5.5 billion in 2022. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news.

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