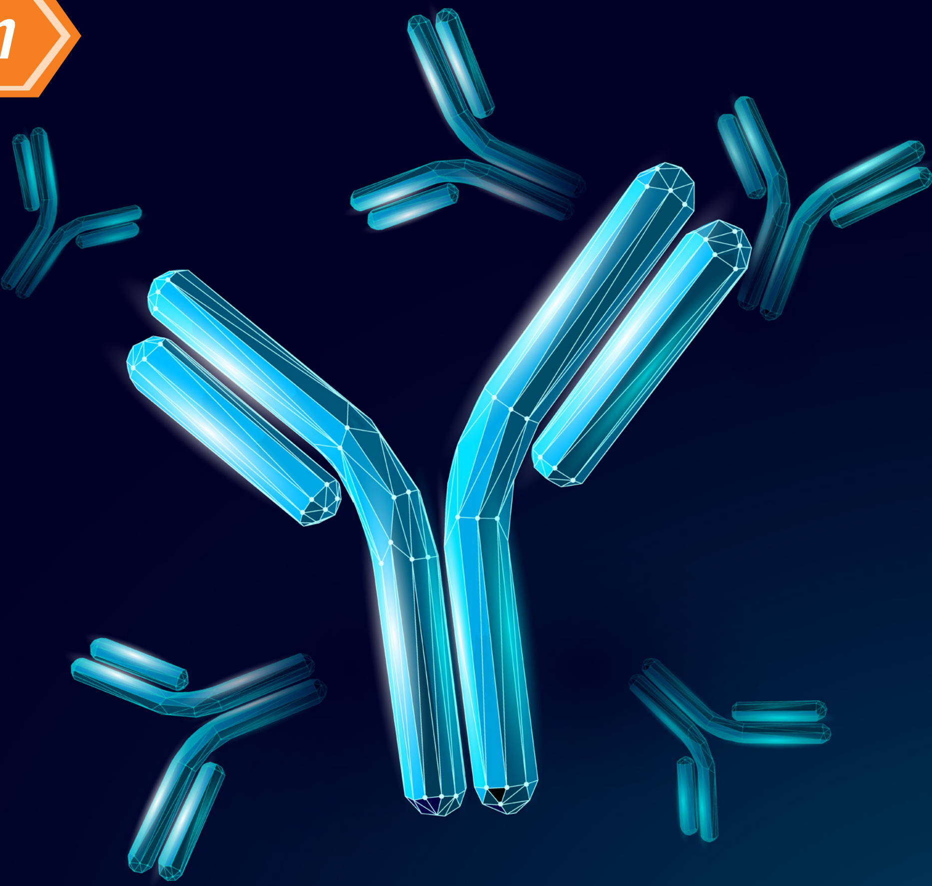
Continuing Education



PHARMACIST & TECHNICIAN CE:

Emerging Therapies for the Treatment of Myasthenia Gravis

by Kirsten Gasser, PharmD

Myasthenia gravis (MG) is an autoimmune disease that affects neuromuscular transmission and is characterized by muscle weakness. This is caused by autoantibodies targeting neuromuscular junction proteins, including the acetylcholine receptor, muscle-specific kinase receptor, and low-density lipoprotein receptor-related protein 4. The disease may initially present with ocular symptoms but often progresses to generalized weakness affecting skeletal, bulbar, or respiratory muscles. MG can be characterized by both symptom presentation and the autoantibody target, identified through serologic testing. The types of MG can predict the severity of the disease and influence treatment decisions.

CE FOR **PHARMACISTS & TECHNICIANS**

Learning Objectives

- Describe the epidemiology and pathophysiology of myasthenia gravis, including key autoantibodies.
- Recognize medications that can exacerbate myasthenia gravis symptoms.
- Define appropriate first-line pharmacologic treatments based on patients' disease defining factors.
- Identify different advantages and disadvantages of the monoclonal antibodies FDA approved for myasthenia gravis.

In recent years, treatment strategies have expanded to include newly approved monoclonal antibodies for MG. These therapies provide additional treatment options for refractory disease; however, cost is a major barrier to access. MG is associated with high healthcare costs, with the highest predictors of increased costs being immunoglobulin and monoclonal antibody utilization.[1] Pharmacists can play a vital role in the management of MG by recognizing medications that have the potential to exacerbate symptoms and identifying appropriate pharmacologic treatment regimens. This article reviews the epidemiology, pathophysiology, and treatment guidelines for MG. Additionally, it will include an overview of the most recent Food and Drug Administration (FDA)-approved therapies for the chronic management of MG. With new treatments emerging, ongoing clinical trials, a rising incidence of the disease, and guidelines that have not yet been updated to reflect recent therapeutic approvals, this overview aims to assist in the selection of treatment regimens and clarify how newer medications fit into the overall management of the disease.

Epidemiology

The worldwide prevalence of MG has been increasing over the years, with the prevalence of MG in the United States approximately 37 per 100,000 people in 2021.[2] Increased life expectancy, along with advancements in diagnosis and treatment, likely contribute to the rising prevalence. It is still not well understood whether MG is considered a hereditary condition. However, a study found the familial rate of MG to be higher than expected for a sporadic disease.[3] The age of onset can range from childhood to late adulthood. The disease more commonly presents in women before the age of 40, with early-onset MG exhibiting a female-to-male ratio of 3:1.[4] In contrast, onset in men is more frequent after the age of 50, with a male-to-female ratio of 3:2. Additionally, onset before the age of 18 occurs in about 10% of cases. It has also been found that MG is more prevalent in patients with African ancestry. A study found that African Americans tended to have earlier disease presentation and more often have a higher percentage of muscle-specific kinase receptor seropositivity.[5]

Pathophysiology

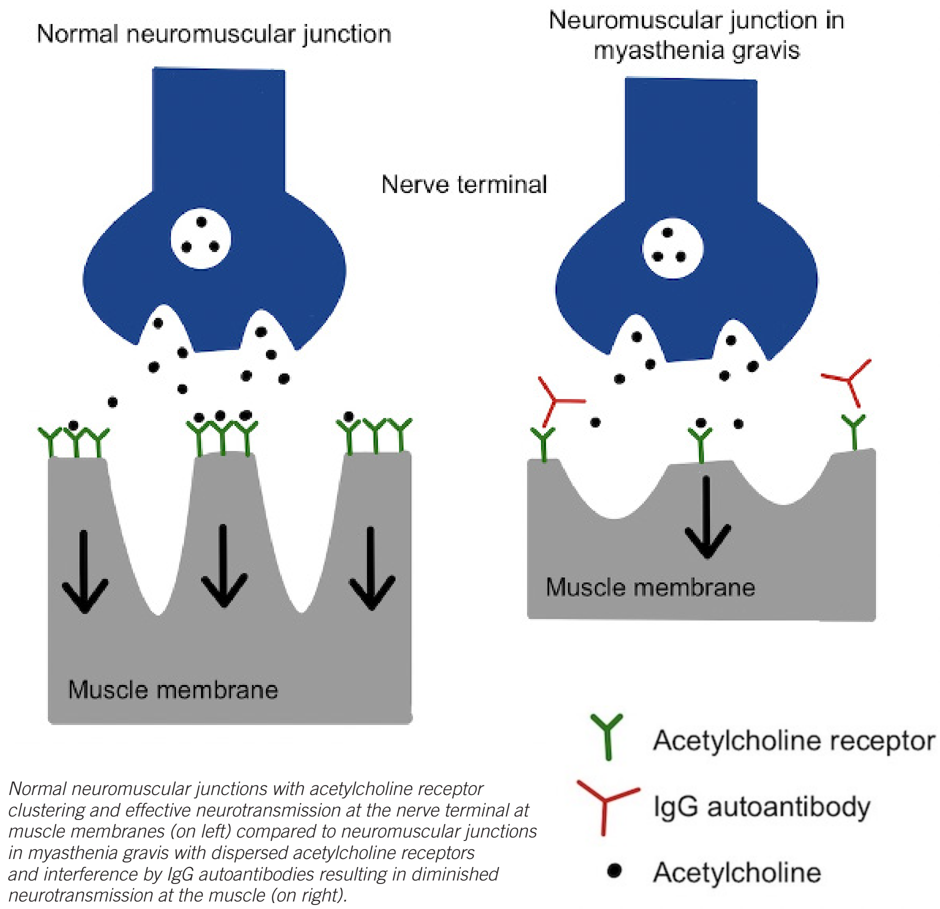
MG can be characterized by the patient's clinical presentation. Ocular MG is defined as symptoms limited to the ocular muscles, including ptosis and diplopia, which is most commonly seen at the time of disease onset. However, the majority of patients with ocular MG will progress to generalized MG within two years.[6] Generalized MG can involve a combination of ocular, skeletal, bulbar, and respiratory muscles. Skeletal muscle weakness often presents as a fatigable weakness from exertion that may fluctuate throughout the day and commonly affect the neck muscles and proximal limbs. Bulbar weakness includes facial expression or oropharyngeal muscles leading to dysarthria and dysphagia. Patients may experience symptom exacerbations that can progress to a myasthenic crisis, a life-threatening emergency characterized by respiratory compromise requiring intubation or noninvasive ventilation. This crisis may be precipitated by triggers such as concurrent infections, surgical procedures, or exacerbating medications.[7] Myasthenic crises may require prolonged intubation and lead to tracheostomy and percutaneous endoscopic gastrostomy tube placement.

Myasthenia gravis is a class II hypersensitivity reaction with immunoglobulin G (IgG) autoantibodies targeting neuromuscular junction proteins.[4] These proteins include the acetylcholine receptor (AChR), the muscle-specific kinase receptor (MuSK), and the low-density lipoprotein receptor-related protein 4 (LRP4).[8] AChR autoantibodies are the most common and are seen in 85% of patients with generalized MG and 50% of patients with ocular MG.[8] MuSK autoantibodies are the second most prevalent with up to 10% of patients being seropositive.[9] There is also a small percentage of patients who present as seronegative with negative assays for AChR, MuSK, and LRP4 antibodies. Of note, with the lower incidence of LRP4 seropositive and seronegative disease, there are limited studies pertaining to these patients and their management.

In the setting of normal muscular function, acetylcholine acts as a neurotransmitter and is released from the motor neuron to bind to acetylcholine receptors on muscle fibers, as shown on the left side of Figure 1. This binding then leads to depolarization and initiation of action potentials resulting in muscle contraction. AChR antibodies interrupt the receptor by binding, blocking, or modulating its activity. LRP4 is a postsynaptic receptor that when activated leads to the phosphorylation and activation of MuSK. Activated MuSK promotes clustering of acetylcholine receptors at the postsynaptic membrane. Both MuSK and LRP4 antibodies disrupt this pathway and result in acetylcholine receptors being more dispersed.[4] As shown on the right side of Figure 1, these autoantibodies disrupt neuromuscular function and prevent normal activation and contraction of muscles, resulting in weakness.

Additionally, MG is also closely associated with thymic abnormalities including thymomas and thymic hyperplasia. Approximately 30% of patients with a thymoma will develop MG and 15% of patients with AChR antibody-positive MG have thymomas.[10] Patients with thymoma-associated MG usually have a more severe presentation of the disease and worse clinical outcomes. The normal function of the thymus is to support T cell development by facilitating their selection, ensuring the maturation of functional T lymphocytes while eliminating self-reactive ones. Thymic abnormalities may be linked

FIGURE 1. Comparison of Normal Neuromuscular Junctions and Neuromuscular Junctions in Myasthenia Gravis



Normal neuromuscular junctions with acetylcholine receptor clustering and effective neurotransmission at the nerve terminal at muscle membranes (on left) compared to neuromuscular junctions in myasthenia gravis with dispersed acetylcholine receptors and interference by IgG autoantibodies resulting in diminished neurotransmission at the muscle (on right).

to MG due to regulation impairment leading to autoreactive T cells.[4]

Diagnosis

In patients presenting with signs and symptoms of myasthenia gravis, serologic autoantibody testing and neuroelectrophysiological testing can be used for diagnostic confirmation.[11] It is recommended to start with AChR serologic testing due to the higher incidence rate, followed by MuSK and LRP4 testing if the patient is AChR seronegative. Neuroelectrophysiological testing is especially useful in patients that are seronegative to all autoantibodies. These tests include repetitive nerve stimulation and single-fiber electromyography. Myasthenia gravis patients may have progressively weaker muscle response to repetitive nerve stimulation. However, the sensitivity of repetitive nerve stimulation is low in ocular MG. Single-fiber electromyography is the most sensitive test for MG diagnosis and measures the neuromuscular jitter. Neuromuscular jitter is the difference in response time to action potentials between two muscle fibers of the same motor unit. Neuromuscular jitters are increased in MG patients due to neuromuscular transmission defects.

Standard of Care Treatment for Myasthenia Gravis

The goal of treatment is to improve patients' physical function and quality of life while minimizing exacerbations. The treatment goal defined by the international guidelines is Minimal Manifestation Status (MMS) or better, meaning that the patient has no symptoms or limitations from their disease, but may have some weakness on examination.[12] Additionally, the goal is no more than grade 1 Common Terminology Criteria for Adverse Events (CTCAE) medication side effects, meaning they have no side effects or mild symptoms not requiring intervention. Recognizing and managing medication side effects to allow patients to reach this goal is another area where pharmacists can make an impact on patients' treatment.

Ocular Myasthenia Gravis

For patients who present with initial ocular MG, anticholinesterase inhibitors, including pyridostigmine or neostigmine, are first-line agents.[13] By inhibiting the breakdown of acetylcholine, acetylcholinesterase inhibitors increase the amount of acetylcholine available for neurotransmission to counteract the decrease or impairment of receptors in MG. For patients who do not respond to initial treatment, immunosuppressants are second line. For immunosuppression, it is recommended to start with corticosteroids and use steroid-sparing agents if corticosteroids are ineffective, contraindicated, or not tolerated. Nonsteroidal immunosuppressive agents that can be used for MG include azathioprine, cyclosporine, mycophenolate mofetil, and tacrolimus.

Generalized Myasthenia Gravis

For patients who present with or progress to generalized symptoms, anticholinesterase inhibitors should be part of the initial treatment in most patients excluding MuSK antibody seropositive patients.[12] Corticosteroids or immunosuppressive therapy should be used in all patients who have not met treatment goals after trialing an anticholinesterase inhibitor. The evidence surrounding the efficacy of oral methotrexate is uncertain, but it can be used if patients do not tolerate or benefit from other steroid-sparing agents.[13] Other treatment options for refractory disease include chronic intravenous immunoglobulin, chronic plasmapheresis, or cyclophosphamide. Intravenous immunoglobulin works by neutralizing or clearing autoantibodies and modulating immune responses. Plasmapheresis works by directly removing autoantibodies from circulation.

AChR Seropositive

Additional guidance for AChR seropositive patients with generalized MG includes the consideration of eculizumab, a complement C5 inhibitor, for severe refractory disease.[13] Rituximab is a monoclonal antibody CD20 inhibitor that leads to B cell depletion, which has shown benefit in a variety of autoimmune diseases, including MuSK myasthenia gravis. Efficacy in AChR MG is uncertain, but rituximab may be trialed if other immunosuppressive treatment options fail.

MuSK Seropositive

These patients have a limited response to pyridostigmine, and immunosuppressive therapy is considered first-line treatment.[12] Due to efficacy seen in trials, rituximab should be considered as an early treatment option if patients do not respond to initial immunotherapy.[13] Intravenous immunoglobulin seems to be less effective in MuSK MG; plasmapheresis is preferred if needed.

Thymoma

Patients with thymoma-associated myasthenia gravis should undergo thymectomy to remove the tumor, with rare exceptions.[13] Thymectomy may be beneficial in other select patients in the absence of thymoma. These patients include both AChR seropositive and seronegative individuals who do not respond to immunosuppressive therapy due to the association with thymic abnormalities that may not be detectable on imaging. Thymectomies may improve disease control, reduce immunotherapy requirements, and reduce exacerbations. However, patients who undergo thymectomy may have an increased risk of cancer and all-cause mortality.[14] Myasthenia gravis patients are also at a higher risk of surgical complications due to their prolonged and unpredictable response to nondepolarizing neuromuscular blockers, which increases their risk of post-operative myasthenic crisis.[15] Current evidence does not support an indication for thymectomy in patients with MuSK or LRP4 antibodies, due to their low association with thymic abnormalities.

Myasthenic Crisis

The main treatment options for myasthenic crises are plasmapheresis and intravenous immunoglobulin.[12] These therapies should be used in combination with immunosuppressive therapy to avoid rebound of antibody levels.

Medications That Can Exacerbate Myasthenia Gravis

Certain medications may exacerbate or cause myasthenia gravis, and are listed in Table 1. Depending on the association and severity, recommendations are provided from the treatment guidelines to avoid use or use with caution in patients with MG. The decision to use these medications in patients should be a shared clinical decision taking into account the disease severity, disease stability, and history of exacerbations. In patients presenting with new-onset MG, pharmacists can help identify potential offending agents by considering the medication's known association with MG and the duration of therapy.

TABLE 1. Medications That May Cause or Exacerbate Myasthenia Gravis[13,15]

Medication	*Associated Risk*	*Recommendations*
Aminoglycosides	May exacerbate MG by impairing neuromuscular transmission	Use with caution if no alternative treatment available
Beta-blockers	May worsen MG with unclear mechanism	Use with caution
Botulinum toxin	Associated with exacerbation of MG due to reduction of acetylcholine release	Avoid use
Chloroquine/ hydroxychloroquine	May cause de novo MG or exacerbate existing disease	Use only if necessary
Corticosteroids	Often used for management of MG, but can cause transient worsening within the first two weeks of use	Monitor carefully with initiation
D-Penicillamine	Strongly associated with causing MG through altered immune response	Avoid use
Fluoroquinolones	Black box warning for exacerbating MG by impairing neuromuscular transmission	Use with caution if no alternative treatment available
Immune checkpoint inhibitors	May cause de novo MG or exacerbate existing disease due to altered immune response	Use with caution
Macrolides	May exacerbate MG by impairing neuromuscular transmission	Use with caution if no alternative treatment available
Magnesium	May exacerbate MG by blocking acetylcholine release; increased risk with intravenous administration	Use only if necessary
Procainamide	May exacerbate MG by impairing neuromuscular transmission	Use with caution
Quinine	May cause de novo MG or exacerbate existing disease	Use only if necessary
Statins	May rarely cause or exacerbate MG	Monitor carefully with initiation
Live-attenuated vaccines	Do not cause or worsen MG, but should not be administered while on immunosuppressive therapy	Avoid use

MG: myasthenia gravis

Monoclonal Antibodies FDA Approved for Myasthenia Gravis

Eculizumab (Soliris™; Alexion Pharmaceuticals, Inc.)

Eculizumab binds to complement protein C5, inhibiting its cleavage into C5a and C5b and preventing the formation of the terminal complement complex C5b-9, thereby reducing its deposition at the neuromuscular junction.[16] In 2017, eculizumab was the first monoclonal antibody approved by the FDA for use in AChR+ generalized MG. The phase 3 clinical trial's primary outcome was the change in Myasthenia Gravis-Specific Activities of Daily Living (MG-ADL) score from baseline to week 26. The MG-ADL tool assesses a patient's ability to talk, chew, swallow, and perform other daily functions. The scale ranges from 0 to 24, with a score of 0 indicating no impairment in daily living. The study did not find a significant difference between eculizumab and placebo (rank-based treatment difference -11.7, 95% CI -24.3 to 0.96; p=0.0698).[17] However, the authors contribute the lack of statistical significance in their primary outcome to their worst-rank analytical approach. The study did find statistically significant differences in secondary endpoints, such as changes from baseline with similar scoring tools, including the Quantitative Myasthenia Gravis scale and the 15-item Myasthenia Gravis Quality of Life score. Additionally, in their open-label extension, they found the MG exacerbation rate was reduced by 75% compared to the year prior to study enrollment (pre-study, 102.4 exacerbations per 100 patient-years; open-label study, 25.4 exacerbations per 100 patient-years; $p < 0.0001$).[18] Additionally, the efficacy and safety were studied in adolescents, leading to eculizumab being the only monoclonal antibody currently approved for pediatric use in patients 6 years of age and older with AChR+ generalized MG.[19]

Eculizumab is given as fixed-dose intravenous infusions, with maintenance doses administered every two weeks after the initial loading period.[17] However, pediatric dosing is dependent on weight. Eculizumab and other complement inhibitors are restricted by a Risk Evaluation and Mitigation Strategies (REMS) program due to the risk of serious meningococcal infections. Patients need to receive both meningococcal vaccines at least two weeks prior to the first dose. If it is necessary to start treatment urgently in an unvaccinated patient, both meningococcal vaccines should be given as soon as possible, and the patient should take 2 weeks of antibacterial drug prophylaxis. Other adverse effects include increased risk of infection, infusion-related reactions, and musculoskeletal pain.

Eculizumab was the only monoclonal antibody approved early enough to be included in the most recent international treatment guidelines for MG.[13] They provided the recommendation that eculizumab should be considered in the treatment of severe, refractory, AChR+ generalized MG. This statement is also supported by Japanese and German guidelines for MG treatment.[20,21] They acknowledged that its role in treatment may evolve with further studies, but at the time recommended trialing other immunosuppressive agents first.

Ravulizumab (Ultomiris™; Alexion Pharmaceuticals, Inc.)

Similarly to eculizumab, ravulizumab inhibits the complement cascade by preventing the formation of terminal complement complex C5b9.[22] It was FDA approved in 2022 for AChR+ generalized MG. A phase 3 clinical trial was conducted with an open-label extension and found that with treatment, the mean change in MG-ADL score from baseline to week 60 was -4.0 (95% CI: -4.8, -3.1; $p < 0.0001$).[23]

Ravulizumab is given intravenously using weight-based dosing, with a loading dose followed by maintenance dosing every 8 weeks, starting 2 weeks post-load.[22] Potential adverse effects include increased risk of infection, infusion-related reactions, headache, and gastrointestinal upset. Ravulizumab is not included in the international treatment guideline updates, but it may have a similar place in therapy to eculizumab due to their shared mechanism of action. This is supported by the German guidelines, which suggest that the use of ravulizumab can be considered in severe, refractory, AChR+ generalized MG.[21]

Zilucoplan (Zilbrysq™; UCB, Inc.)

Zilucoplan is also a humanized monoclonal antibody that binds to complement protein C5 in order to terminate the complement cascade.[24] Zilucoplan was FDA approved in 2023 for AChR+ generalized myasthenia gravis.[25] In the phase 3 clinical trial, the primary efficacy endpoint was the change in MG-ADL score from baseline after 12 weeks of treatment. They found a statistically significant difference when comparing change in MG-ADL score in the treatment group to the placebo group (-4.39 vs -2.30, $p<0.001$).

Zilucoplan is administered as a weight-based, daily subcutaneous injection that patients can self-administer.[25] Possible adverse effects include increased risk of infection, pancreatitis, and pancreatic cysts. Like other complement inhibitors, zilucoplan may be considered for treatment of severe, refractory, AChR+ generalized MG, but there are currently no treatment guidelines to support this.

Efgartigimod alfa (Vyvgart™; Argenx BV)

Myasthenia gravis is an IgG-mediated disease, and the neonatal Fc receptor (FcRn) recycles IgG to extend its half life and prolong the availability of IgG autoantibodies.[26] As previously mentioned, the benefits of removing autoantibodies in MG patients has been proven with plasmapheresis therapy. Efgartigimod is a human IgG1 antibody Fc-fragment, which is a ligand of FcRn. Efgartigimod has been created to have a higher affinity to FcRn than endogenous IgG, which reduces IgG recycling and increases degradation of autoantibodies involved in myasthenia gravis.

Efgartigimod was FDA approved for AChR+ generalized MG in 2021.[27] In the phase 3 clinical trial, the primary efficacy endpoint was the change in MG-ADL scores from baseline after one treatment cycle.[26] Patients were considered an MG-ADL responder if they had a 2-point or greater reduction in MG-ADL score. There was a statistically significant difference in the percentage of MG-ADL responders with 67.7% in the treatment group compared to 29.7% in the placebo group ($p<0.0001$).

Intravenous efgartigimod is a weight-based, once-weekly dose, administered

TABLE 2. Comparison of Monoclonal Antibodies FDA Approved for Myasthenia Gravis

Monoclonal Antibodies	MOA/Target	Dosing Frequency	Route of Administration	Self Administration	REMS Program	FDA Approval: Generalized Myasthenia Gravis			
						AChR+	MuSK+	LRP4+ or sero-negative	Pediatric use
Eculizumab	Complement protein C5	Every 2 weeks	Intravenous		✓	✓			✓
Ravulizumab	Complement protein C5	Every 8 weeks	Intravenous		✓	✓			
Zilucoplan	Complement protein C5	Daily	Subcutaneous	✓	✓	✓			
Efgartigimod alfa	IgG binding region of FcRn	Treatment cycle: once weekly for 4 weeks	Intravenous			✓			
Efgartigimod alfa and hyaluronidase	IgG binding region of FcRn	Treatment cycle: once weekly for 4 weeks	Subcutaneous			✓			
Rozanolixizumab	IgG binding region of FcRn	Treatment cycle: once weekly for 6 weeks	Subcutaneous			✓	✓		

AChR: acetylcholine receptor, FcRn: neonatal Fc receptor, FDA: Food and Drug Administration, IgG: immunoglobulin G, LRP4: lipoprotein receptor-related protein 4, MOA: mechanism of action, MuSK: muscle-specific kinase receptor, REMS: Risk Evaluation and Mitigation Strategies for 4 weeks.[27] Additional treatment cycles can be given, but initiation of subsequent treatment should begin no sooner than 50 days from the start of the previous treatment cycle. The decision to give subsequent cycles should be determined by a clinical evaluation with possible decision factors including response to therapy, duration of response, and side effects. Possible adverse effects include increased risk of infection, hypersensitivity reactions, and infusion-related reactions.

Efgartigimod has a novel mechanism of action and its place in therapy is not outlined in the international guidelines due to its recent FDA approval. The German guidelines suggest that efgartigimod can be considered in severe, refractory, AChR+ generalized MG.[21] While similar to recommendations for complement inhibitors, this provides an additional option with a different mechanism of action for refractory patients.

Efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo™; Argenx BV)

Efgartigimod alfa was combined with hyaluronidase to create a subcutaneous formulation and was FDA approved for use in AChR+ generalized MG in 2023.[28] This formulation has fixed dosing at the same dosing frequency as the intravenous formulation. Despite being subcutaneous, it still needs to be administered by a healthcare professional. The efficacy was evaluated in a phase 3 randomized noninferiority study. Efgartigimod with hyaluronidase was proven to be non-inferior to intravenous efgartigimod in the primary endpoint of percentage change from baseline in IgG level at week 4 (–66.4% vs –62.2%).[29] Additionally, side effects were comparable between the formulations with the added potential for injection site reactions when given subcutaneously.

Rozanolixizumab (Rystiggo™; UCB, Inc.)

Rozanolixizumab is a humanized IgG4 monoclonal antibody that targets the IgG binding region of FcRn.[30] Similarly to efgartigimod, this mechanism reversibly inhibits IgG recycling to increase degradation. Rozanolixizumab was FDA approved in 2023 for generalized MG in patients who are either AChR or MuSK antibody positive. In the phase 3 clinical trial, the primary efficacy endpoint was the change in MG-ADL score from baseline to day 43 of treatment. They found a statistically significant difference of -3.4 in the treatment group compared to -0.8 in the placebo group ($p<0.001$).[31]

Rozanolixizumab is a weight-based, weekly subcutaneous injection, administered for 6 weeks by a healthcare professional.[30] Additional treatment cycles may be administered based on clinical evaluation and no sooner than 63 days from the start of the previous treatment cycle. Possible adverse effects include increased risk of infection, hypersensitivity reactions, administration site reactions, and aseptic meningitis. Similarly to efgartigimod, rozanolixizumab's place in therapy is not clearly defined. However, rozanolixizumab may be considered for treatment of refractory AChR or MuSK seropositive generalized MG.

Overview

Table 2 provides an overview of the current monoclonal antibodies that are FDA approved for the treatment of generalized MG, highlighting the differences that may affect treatment access or preference. In comparison to monoclonal antibodies, all conventional treatment options for MG, with the exception of pyridostigmine, are used off-label. Additionally, the standard of care immunosuppressive agents are much less targeted than newer therapies. However, monoclonal antibodies face several barriers to utilization, including insurance coverage and cost; requiring administration by a healthcare professional, with the exception of zilucoplan; the REMS program for complement inhibitors; and complex dosing frequencies with FcRn antagonists' treatment cycles.

Conclusion

Myasthenia gravis is an autoimmune disorder in which autoantibodies impair neuromuscular function, leading to fatigable muscle weakness. Treatment guidance of MG can be variable based on the patient's symptoms and serologic testing. In addition to traditional treatment options, there have been significant advancements with recently approved therapies. These novel medications have shown promising efficacy in clinical trials with improvement in patient-centered outcomes. Despite their unclear place in therapy, these medications may serve as additional treatment options for refractory patients until further guidance is determined. In particular, of the newer agents, rozanolixizumab is the only one FDA approved for MuSK seropositive patients. Eculizumab is also the only agent FDA approved for use in pediatric patients with AChR seropositive myasthenia gravis. Additionally, certain therapies provide more convenience for patients, with extended dosing intervals or self-administration. Pharmacists can play an important role in the identification of the advantages and disadvantages of these therapies in order to individualize and optimize patient care. Pharmacists can also recognize and manage side effects, as well as identify medications that may exacerbate patients' symptoms. There are still areas that warrant further investigation that could impact treatment in the future, including long-term outcomes of newer therapies and treatment of LRP4+, seronegative, and pediatric patients. Additionally, direct comparison trials of monoclonal antibodies and comparisons to standard of care treatments are still needed.

At the time this article was written Kirsten Gasser was a PGY-1 Pharmacy Resident at SSM Health St. Mary's Hospital in Madison, WI. Kirsten Gasser is now a Pharmacy Clinical Specialist at Boston Medical Center in Boston, MA.

Corresponding Author:

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

Kirsten Gasser - gasserkirsten@gmail.com

Acknowledgements: Catherine Ackeret, PharmD, BCPS; Hannah Hendricks, PharmD

Disclosure: The author declares no real or potential conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria.

References

1. Zhdanava M, Pesa J, Boonmak P, et al. Predictors of high healthcare cost among patients with generalized myasthenia gravis: a combined machine learning and regression approach from a US payer perspective. *Appl Health Econ Health Policy*. 2024;22(5):735-747. doi: 10.1007/s40258-024-00897-x
2. Rodrigues E, Umeh E, Uday A, Navaratnarajah N, Moy K. Incidence and prevalence of myasthenia gravis in the United

States: a claims-based analysis. *Muscle Nerve.* 2024;69(2):166-171. doi: 10.1002/mus.28006
3. Green JD, Barohn RJ, Bartoccion E, et al. Epidemiological evidence for a hereditary contribution to myasthenia gravis: a retrospective cohort study of patients from North America. *BMJ Open*. 2020;10(9):e037909. doi: 10.1136/bmjopen-2020-037909
4. Dresser L, Wlodarski R, Rezania K, Soliven B. Myasthenia gravis: epidemiology, pathophysiology and clinical manifestations. *J Clin Med*. 2021;10(11):2235. doi: 10.3390/jcm10112235
5. Oh SJ, Morgan MB, Lu L, et al. Racial differences in myasthenia gravis in Alabama. *Muscle Nerve*. 2009;39(3):328-332. doi: 10.1002/mus.21191
6. Bever CT Jr, Aquino AV, Penn AS, Lovelace RE, Rowland LP. Prognosis of ocular myasthenia. *Ann Neurol.* 1983;14(5):516-519. doi: 10.1002/ana.410140504
7. Wendell LC, Levine JM. Myasthenic crisis. *Neurohospitalist*. 2011;1(1):16-22. doi: 10.1177/1941875210382918
8. Vinciguerra C, Bevilacqua L, Lupica A, et al. Diagnosis and management of seronegative myasthenia gravis: lights and shadows. *Brain Sci*. 2023;13(9):1286. doi: 10.3390/brainsci13091286
9. Gilhus NE. Myasthenia gravis. *N Engl J Med.* 2016;375(26):2570-2581. doi: 10.1056/NEJMra1602678
10. Álvarez-Velasco R, Gutiérrez-Gutiérrez G, Trujillo JC, et al. Clinical characteristics and outcomes of thymoma-associated myasthenia gravis. *Eur J Neurol.* 2021;28(6):2083-2091. doi: 10.1111/ene.14820
11. Mantegazza R, Cavalcante P. Diagnosis and treatment of myasthenia gravis. *Curr Opin Rheumatol.* 2019;31(6):623-633. doi: 10.1097/BOR.0000000000000647
12. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: executive summary. *Neurology.* 2016;87(4):419-25. doi: 10.1212/WNL.0000000000002790
13. Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of myasthenia gravis: 2020 update. *Neurology.* 2021;96(3):114-122. doi: 10.1212/WNL.0000000000011124
14. Kooshesh KA, Foy BH, Sykes DB, Gustafsson K, Scadden DT. Health consequences of thymus removal in adults. *N Engl J Med.* 2023;389(5):406-417. doi: 10.1056/NEJMoa2302892
15. Sheikh S, Alvi U, Soliven B, Rezania K. Drugs that induce or cause deterioration of myasthenia gravis: an update. *J Clin Med.* 2021;10(7):1537. doi: 10.3390/jcm10071537
16. Howard JF Jr, Utsugisawa K, Benatar M, et al; REGAIN Study Group. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalised myasthenia gravis (REGAIN): a phase 3, randomised, double-blind, placebo-controlled, multicentre study. *Lancet Neurol.* 2017;16(12):976-986. doi: 10.1016/S1474-4422(17)30369-1
17. Alexion Pharmaceuticals, Inc. Soliris (eculizumab) [package insert]. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125166s448,761108s038lbl.pdf. Revised February 2025. Accessed April 24, 2025.
18. Muppidi S, Utsugisawa K, Benatar M, et al; Regain Study Group. Long-term safety and efficacy of eculizumab in generalized myasthenia gravis. *Muscle Nerve.* 2019;60(1):14-24. doi: 10.1002/mus.26447
19. Brandsema JF, Ginsberg M, Hoshino H, et al; MG 303 Study Group. Eculizumab in adolescent patients with refractory generalized myasthenia gravis: a phase 3, open-label, multicenter study. *Pediatr Neurol.* 2024;156:198-207. doi: 10.1016/j.pediatrneurol.2024.04.020
20. Murai H, Utsugisawa K, Motomura M, Imai T, Uzawa A, Suzuki S. The Japanese clinical guidelines 2022 for myasthenia gravis and Lambert–Eaton myasthenic syndrome. *Clin Exp Neuroimmunol.* 2023;14(1):19–27. doi: 10.1111/cen3.12739
21. Wiendl H, Abicht A, Chan A, et al. Guideline for the management of myasthenic syndromes. *Ther Adv Neurol Disord.* 2023;16:1-31. doi: 10.1177/17562864231213240
22. Alexion Pharmaceuticals, Inc. Ultomiris (ravulizumab-cwvz) [package insert]. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761108s037lbl.pdf. Revised September 2024. Accessed April 23, 2025.
23. Meisel A, Annane D, Vu T, et al; CHAMPION MG Study Group. Long-term efficacy and safety of ravulizumab in adults with anti-acetylcholine receptor antibody-positive generalized myasthenia gravis: results from the phase 3 CHAMPION MG open-label extension. *J Neurol.* 2023;270(8):3862-3875. doi: 10.1007/s00415-023-11699-x
24. Howard JF Jr, Bresch S, Genge S, et al; RAISE Study Team. Safety and efficacy of zilucoplan in patients with generalised myasthenia gravis (RAISE): a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet Neurol.* 2023;22(5):395-406. doi: 10.1016/S1474-4422(23)00080-7
25. UCB, Inc. Zilbrysq (zilucoplan) [package insert]. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/216834s008s009lbl.pdf. Revised February 2025. Accessed April 23, 2025.
26. Howard JF Jr, Bril V, Vu T, et al; ADAPT Investigator Study Group. Safety, efficacy, and tolerability of efgartigimod in patients with generalised myasthenia gravis (ADAPT): a multicentre, randomised, placebo-controlled, phase 3 trial. *Lancet Neurol.* 2021;20(7):526-536. doi: 10.1016/S1474-4422(21)00159-9
27. Argenx BV. Vyvgart (efgartigimod alfa-fcab) [package insert]. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761195s004,761304s003lbl.pdf. Revised August 2024. Accessed April 22, 2025.
28. Argenx BV. Vyvgart hytrulo (efgartigimod alfa and hyaluronidase-qvfc) [package insert]. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761304s005%2cs006lbl.pdf. Revised June 2024. Accessed April 23, 2025.
29. Howard JF Jr, Vu T, Li G, et al; ADAPT-SC and ADAPT-SC+ Study Groups. Subcutaneous efgartigimod PH20 in generalized myasthenia gravis: a phase 3 randomized noninferiority study (ADAPT-SC) and interim analyses of a long-term open-label extension study (ADAPT-SC+). *Neurotherapeutics.* 2024;21(5):e00378. doi: 10.1016/j.neurot.2024.e00378
30. UCB, Inc. Rystiggo (rozanolixizumab-noli) [package insert]. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761286s001lbl.pdf. Revised June 2024. Accessed April 23, 2025.
31. Bril V, Drużdż A, Grosskreutz J, et al; MG0003 study team. Safety and efficacy of rozanolixizumab in patients with generalised myasthenia gravis (MycarinG): a randomised, double-blind, placebo-controlled, adaptive phase 3 study. *Lancet Neurol*. 2023;22(5):383-394. doi: 10.1016/S1474-4422(23)00077-7

Assessment Questions

1. **True or False:** It is more common for myasthenia gravis to present after the age of 50 in men.
   a. True
   b. False

2. Which of the following autoantibodies is most commonly associated with myasthenia gravis?
   a. LRP4
   b. AChR
   c. MuSK
   d. FcRn

3. Which of the following is NOT associated with exacerbating myasthenia gravis?
   a. Metoprolol
   b. Ciprofloxacin
   c. Azithromycin
   d. Lisinopril

4. Which of the following medications may cause myasthenia gravis?
   a. Magnesium
   b. Hydroxychloroquine
   c. Botulinum toxin
   d. Vancomycin

5. What is the first line treatment for patients with ocular myasthenia gravis?
   a. Prednisone
   b. Rituximab
   c. Pyridostigmine
   d. Ravulizumab

6. What would be the most appropriate treatment for a patient with MuSK seropositivity experiencing a myasthenic crisis?
   a. Intravenous immunoglobulin
   b. Prednisone
   c. Plasmapheresis
   d. Pyridostigmine

7. Which of the following therapies increases degradation of IgG autoantibodies by binding to the neonatal Fc receptor?
   a. Efgartigimod
   b. Zilucoplan
   c. Eculizumab
   d. Rituximab

8. **True or False:** Rozanolixizumab is a self-administered subcutaneous injection.
   a. True
   b. False

9. Which of the following is FDA approved for the use in pediatric patients with myasthenia gravis?
   a. Zilucoplan
   b. Efgartigimod
   c. Rozanolixizumab
   d. Eculizumab

CE FOR **PHARMACISTS & TECHNICIANS**

Continuing Education Credit Information

The Pharmacy Society of Wisconsin is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. Continuing education credit can be earned by completing the self assessment questions. Questions may be completed online. Participants receiving a score of 70% or better will be granted 1 hour (0.1 CEU) credit through CPE Monitor. Accurate birth date (MMDD) and CPE Monitor ID must be provided in order to receive this credit as required by ACPE. This CE offering is offered free-of-charge to all PSW members. Nonmembers are charged $25.

September/October 2025
Emerging Therapies for the Treatment of Myasthenia Gravis

ACPE Universal Activity Number:
0175-0000-25-079-H01-P,T

Target Audience: Pharmacists
Activity Type: Knowledge-based
Release Date: September 1, 2025
(No longer valid for CE credit after September 1, 2028)

Submit Your CE Online
www.pswi.org/Education/Journal-CE