A Compendium of Generalized Myasthenia Gravis (gMG) References for SOLIRIS® (eculizumab)

When completing a prior authorization (PA), precertification, reauthorization, or appeal request for SOLIRIS in the treatment of adults with anti-acetylcholine receptor (AChR) antibody-positive gMG, insurers may require documentation including clinical notes and impressions, lab results, and other relevant information. The selection of references below, including the SOLIRIS prescribing information and published literature, may be helpful when completing the request to your patient's insurance company.

Some of the literature listed below may include content that is not included in the FDA approved US Full Prescribing Information for SOLIRIS. Please refer to the Indication and Important Safety Information for SOLIRIS on page 3, including **Boxed WARNING regarding serious meningococcal infections**, and the accompanying US Full Prescribing Information.

This compendium is not inclusive of all US and global data and literature for SOLIRIS for anti-AChR antibody-positive gMG. Alexion does not warrant, promise, guarantee, or make any statement that the use or citation of any literature listed below will result in coverage or payment for SOLIRIS.

Abstracts for the references cited below are available online. Most of the publications permit access and download of the articles for personal use; some publications require that the article be purchased in order to gain access.

For ease of use, each reference is categorized by topic, as follows:

Advisory Committee on Immunization Practices (ACIP) Meningococcal Vaccination Recommendations

Freedman M, Kroger A, Hunter P, Ault KA; Advisory Committee on Immunization Practices. Recommended Adult Immunization Schedule, United States, 2020. *Ann Intern Med*. 172(5):337-347

Mbaeyi SA, Bozio CH, Duffy J, et al. MMWR Recomm Rep 2020;69(No. RR-9):1–41. DOI:http://dx.doi.org/10.15585/mmwr.rr6909a1. Meningococcal vaccination: recommendations of the Advisory Committee on Immunization Practices, United States, 2020

Assessment Tools

Clinical Research Standards

Jaretzki A III, Barohn RJ, Ernstoff RM, et al. Myasthenia gravis: recommendations for clinical research standards. Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America. *Neurology*. 2000;55(1):16-23

Myasthenia Gravis Activities of Daily Living (MG-ADL) Profile [Reported by Patient]

Muppidi S, Wolfe GI, Conaway M, Burns TM; MG Composite and MG-QOL15 Study Group. MG-ADL: still a relevant outcome measure. *Muscle Nerve*. 2011;44(5):727-731

Wolfe GI, Herbelin L, Nations SP, et al. Myasthenia gravis activities of daily living profile. *Neurology*. 1999;52:1487-1489

Myasthenia Gravis Composite (MGC) Scale [Reported by Patient and Physician]

Benatar M, Sanders DB, Burns TM, et al; Task Force on MG Study Design of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America. Recommendations for myasthenia gravis clinical trials. *Muscle Nerve*. 2012;45(6):909-917

Burns TM, Conaway MR, Sanders DB; MG Composite and MG-QOL15 Study Group. The MG composite: a valid and reliable outcome measure for myasthenia gravis. *Neurology*. 2010;74(18):1434-1440

Sadjadi R, Conaway M, Cutter G, et al; MG Composite MG-QOL15 Study Group. Psychometric evaluation of the myasthenia gravis composite using Rasch analysis. *Muscle Nerve*. 2012;45(6):820-825

Assessment Tools *(continued)*

Myasthenia Gravis Quality of Life 15 (MG-QoL15r) [Reported by Patient]

Burns TM, Grouse CK, Conway MR, Sanders DB; MG composite and MG qol-15 study group. Construct and concurrent validation of the MG-QOL15 in the practice setting. *Muscle Nerve*. 2010;41(2):219-226

Burns TM, Grouse CK, Wolfe GI, Conway MR, Sanders DB; MG composite and MG qol-15 study group. The MG-QOL15 for following health-related quality of life of patients with myasthenia gravis. *Muscle Nerve*. 2011;43 (1):14-18

Burns TM, Sadjadi R, Utsugisawa K, et al. International clinimetric evaluation of the MG-QOL15, resulting in slight revision and subsequent validation of the MG-QOL15r. *Muscle Nerve*. 2016;54(6):1015-1022

Quantitative Myasthenia Gravis (QMG) Test [Reported by Physician]

Barohn RJ, McIntire D, Herbelin L, et al. Reliability testing of the quantitative myasthenia gravis score. *Ann NY Acad Sci*. 1998;841:769-772

Burden of Disease

Boscoe AN, Xin H, L'Italien GJ, Harris LA, Cutter GR. Impact of refractory myasthenia gravis on health-related quality of life. *J Clin Neuromuscul Dis*. 2019;20(4):173-181

Schneider-Gold C, Hagenacker T, Melzer N, Ruck T. Understanding the burden of refractory myasthenia gravis. *Ther Adv Neurol Disord*. 2019;12:1-16

Pathophysiology

Conti-Fine BM, Milani M, Kaminski HJ. Myasthenia gravis: past, present, and future. *J Clin Invest*. 2006;116(11):2843-2854

Melzer N, Ruck T, Fuhr P, et al. Clinical features, pathogenesis, and treatment of myasthenia gravis: a supplement to the Guidelines of the German Neurological Society. *J Neurol*. 2016;263(8):1473-1494

Howard JF Jr. Myasthenia gravis: the role of complement at the neuromuscular junction. *Ann N Y Acad Sci*. 2018;1412(1):113-128

SOLIRIS Prescribing Information and Publications in gMG

SOLIRIS [prescribing information]. Boston, MA: Alexion Pharmaceuticals, Inc; 2020

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, randomized, double-blind, placebo-controlled, multicentre study. *Lancet Neurol*. 2017;16(12):976-986

Mantegazza R, O'Brien FL, Yountz M, Howard JF; REGAIN study group. Consistent improvement with eculizumab across muscle groups in myasthenia gravis. *Ann Clin Trans Neurol*. 2020;7(8):1327-1339

Muppidi S, Utsugisawa K, Benatar M, et al. Long-term safety and efficacy of eculizumab in generalized myasthenia gravis. *Muscle Nerve*. 2019;60(1):14-24

U.S. Food and Drug Administration, Department of Health and Human Services. SOLIRIS sBLA 125166/S-422 approval letter, October 23, 2017. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2017/125166Orig1s422ltr.pdf

Please see p. 3 for Important Safety Information for SOLIRIS, including Boxed WARNING regarding serious meningococcal infections.

INDICATION & IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab) [injection for intravenous use, 300 mg/30 mL]

Generalized Myasthenia Gravis (gMG)
Soliris is indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris and may become rapidly life-threatening or fatal if not recognized and treated early.

- Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.
- Immunize patients with meningococcal vaccines at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection. (See *Serious Meningococcal Infections* for additional guidance on the management of the risk of meningococcal infection).

Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Monitor patients for early signs of meningococcal infections and evaluate immediately if infection is suspected.

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS, prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747) or at www.solirisrems.com.

Contraindications
- Patients with unresolved serious *Neisseria meningitidis* infection
- Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection

Warnings and Precautions

Serious Meningococcal Infections

Risk and Prevention
The use of Soliris increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis). Vaccinate or revaccinate for meningococcal disease according to the most current ACIP recommendations for patients with complement deficiencies. Immunize patients without a history of meningococcal vaccination at least 2 weeks prior to receiving the first dose of Soliris. If Soliris must be initiated immediately in an unvaccinated patient, administer meningococcal vaccine(s) as soon as possible and provide 2 weeks of antibacterial drug prophylaxis. Discontinue Soliris in patients who are undergoing treatment for serious meningococcal infections.

REMS
Prescribers must counsel patients about the risk of meningococcal infection, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccine(s).

Other Infections
Serious infections with *Neisseria* species (other than *N. meningitidis*), including disseminated gonococcal infections, have been reported. Patients may have increased susceptibility to infections, especially with encapsulated bacteria. Additionally, *Aspergillus* infections have occurred in immunocompromised and neutropenic patients. Use caution when administering Soliris to patients with any systemic infection.

Infusion-Related Reactions
Administration of Soliris may result in infusion-related reactions, including anaphylaxis or other hypersensitivity reactions. Interrupt Soliris infusion and institute appropriate supportive measures if signs of cardiovascular instability or respiratory compromise occur.

Adverse Reactions
The most frequently reported adverse reaction in the gMG placebo-controlled clinical trial (≥10%) is: musculoskeletal pain.

Please see full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious meningococcal infections.

ALEXION®

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