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 pages 3 and 4, including Boxed WARNING regarding serious meningococcal infections**, and the 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 *(cont'd)*

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. Alexion Pharmaceuticals, Inc.

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

INDICATION

SOLIRIS is indicated for the treatment of generalized myasthenia gravis (gMG) in adult and pediatric patients six years of age and older who are anti-acetylcholine receptor (AChR) antibody positive.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

SOLIRIS, a complement inhibitor, increases the risk of serious infections caused by *Neisseria meningitidis* [*see Warnings and Precautions (5.1)*]. Life-threatening and fatal meningococcal infections have occurred in patients treated with complement inhibitors. These infections may become rapidly life-threatening or fatal if not recognized and treated early.

- **Complete or update vaccination for meningococcal bacteria (for serogroups A, C, W, Y, and B) at least 2 weeks prior to the first dose of SOLIRIS, unless the risks of delaying SOLIRIS therapy outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against meningococcal bacteria in patients receiving a complement inhibitor. *See Warnings and Precautions (5.1)* for additional guidance on the management of the risk of serious infections caused by meningococcal bacteria.**
- **Patients receiving SOLIRIS are at increased risk for invasive disease caused by *Neisseria meningitidis*, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious meningococcal infections and evaluate immediately if infection is suspected.**

Because of the risk of serious meningococcal infections, SOLIRIS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called ULTOMIRIS and SOLIRIS REMS [*see Warnings and Precautions (5.2)*].

CONTRAINDICATIONS

- SOLIRIS is contraindicated for initiation in patients with unresolved serious *Neisseria meningitidis* infection.

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

SOLIRIS, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by meningococcal bacteria (septicemia and/or meningitis) in any serogroup, including non-groupable strains. Life-threatening and fatal meningococcal infections have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors.

Revaccinate patients in accordance with ACIP recommendations considering the duration of therapy with SOLIRIS. Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information.

If urgent SOLIRIS therapy is indicated in a patient who is not up to date with meningococcal vaccines according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer meningococcal vaccines as soon as possible. Various durations and regimens of antibacterial drug prophylaxis have been considered, but the optimal durations and drug regimens for prophylaxis and their efficacy have not been studied in unvaccinated or vaccinated patients receiving complement inhibitors, including SOLIRIS. The benefits and risks of treatment with SOLIRIS, as well as those associated with antibacterial drug prophylaxis in unvaccinated or vaccinated patients, must be considered against the known risks for serious infections caused by *Neisseria meningitidis*.

Vaccination does not eliminate the risk of serious meningococcal infections, despite development of antibodies following vaccination.

Closely monitor patients for early signs and symptoms of meningococcal infection and evaluate patients immediately if infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if these signs and symptoms occur. Promptly treat known infections. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of SOLIRIS in patients who are undergoing treatment for serious meningococcal infection, depending on the risks of interrupting treatment in the disease being treated.

ULTOMIRIS and SOLIRIS REMS

Due to the risk of serious meningococcal infections, SOLIRIS is available only through a restricted program called ULTOMIRIS and SOLIRIS REMS.

Prescribers must enroll in the REMS, counsel patients about the risk of serious meningococcal infection, provide patients with REMS educational materials, assess patient vaccination status for meningococcal vaccines (against serogroups A, C, W, Y, and B) and vaccinate if needed according to current ACIP recommendations two weeks prior to the first dose of SOLIRIS. Antibacterial drug prophylaxis must be prescribed if treatment must be started urgently and the patient is not up to date with both meningococcal vaccines according to current ACIP recommendations at least two weeks prior to the first dose of SOLIRIS. Patients must receive counseling about the need to receive meningococcal vaccines and to take antibiotics as directed, the signs and symptoms of meningococcal infection, and be instructed to carry the Patient Safety Card with them at all times during and for 3 months following SOLIRIS treatment.

Further information is available at www.UltSolREMS.com or 1-888-765-4747.

Please see additional Important Safety Information on page 4 and full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Other Infections

Serious infections with *Neisseria* species (other than *Neisseria meningitidis*), including disseminated gonococcal infections, have been reported.

SOLIRIS blocks terminal complement activation; therefore, patients may have increased susceptibility to infections, especially with encapsulated bacteria, such as infections with *Neisseria meningitidis* but also *Streptococcus pneumoniae*, *Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*. Additionally, *Aspergillus* infections have occurred in immunocompromised and neutropenic patients. Children treated with SOLIRIS may be at increased risk of developing serious infections due to *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib). Administer vaccinations for the prevention of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) infections according to ACIP recommendations. Patients receiving SOLIRIS are at increased risk for infections due to these organisms, even if they develop antibodies following vaccination.

Thrombosis Prevention and Management
The effect of withdrawal of anticoagulant therapy during SOLIRIS treatment has not been established. Therefore, treatment with SOLIRIS should not alter anticoagulant management.

Infusion-Related Reactions
Administration of SOLIRIS may result in infusion-related reactions, including anaphylaxis or other hypersensitivity reactions. In clinical trials, no patients experienced an infusion-related reaction which required discontinuation of SOLIRIS. 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 adult gMG placebo-controlled clinical trial (≥10%) was: musculoskeletal pain.

DRUG INTERACTIONS

Plasmapheresis, Plasma Exchange, Fresh Frozen Plasma Infusion, or IVIg
Concomitant use of SOLIRIS with plasma exchange (PE), plasmapheresis (PP), fresh frozen plasma infusion (PE/PI), or in patients with gMG on concomitant IVIg treatment can reduce serum eculizumab concentrations and requires a supplemental dose of SOLIRIS.

Neonatal Fc Receptor Blockers
Concomitant use of SOLIRIS with neonatal Fc receptor (FcRn) blockers may lower systemic exposures and reduce effectiveness of SOLIRIS. Closely monitor for reduced effectiveness of SOLIRIS.

To report SUSPECTED ADVERSE REACTIONS contact Alexion Pharmaceuticals, Inc. at 1-844-259-6783 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

ALEXION®
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US/SOL-g/0275 V5 04/2025