A COMPENDIUM OF GENERALIZED MYASTHENIA GRAVIS (gMG) REFERENCES FOR ULTOMIRIS® (ravulizumab-cwvz)

When completing a prior authorization (PA), precertification, reauthorization, or appeal request for ULTOMIRIS 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 ULTOMIRIS 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 ULTOMIRIS. Please refer to the Indication and Important Safety Information for ULTOMIRIS on pages 5–6, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections, and the accompanying US Full Prescribing Information.

This compendium is not inclusive of all US and global data and literature for ULTOMIRIS 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 ULTOMIRIS.

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

Murthy N, Wodi AP, Bernstein H, Ault KA; Advisory Committee on Immunization Practices. Recommended Adult Immunization Schedule, United States, 2022. *Ann Intern Med*. 2022;175(3):432-443.

Mbaeyi SA, Bozio CH, Duffy J, et al. Meningococcal vaccination: recommendations of the Advisory Committee on Immunization Practices, United States, 2020. *MMWR Recomm Rep*. 2020;69(9):1-41.

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(7):1487-1489.

FDA, US Food and Drug Administration.

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Assessment Tools *(continued)*

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 M, 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.

Myasthenia Gravis Quality of Life 15 (MG-QOL15) [Reported by Patient]

Burns TM, Grouse CK, Conaway MR, Sanders DB; MG Composite and MG-QOL15 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, Conaway MR, Sanders DB; MG Composite and MG-QOL15 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;12:1756286419832242.

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.

Denial Due to Required Step Therapy

Alhaidar MK, Abumurad S, Soliven B, Rezania K. Current treatment of myasthenia gravis. *J Clin Med.* 2022;11(6):1597.

Bril V, Drużdż A, Grosskreutz J, et al. 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.

Efgartigimod alfa-fcab. Prescribing information. argenx BV.

Please see pages 5–6 for Important Safety Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

Denial Due to Required Step Therapy *(continued)*

Efgartigimod alfa and hyaluronidase-qvfc. Prescribing information. argenx BV.

Howard JF Jr, Bresch S, Genge A, et al. 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.

Howard JF Jr, Bril V, Vu T, et al. 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.

Mahic M, Bozorg A, Rudnik J, Zaremba P, Scowcroft A. Treatment patterns in myasthenia gravis: a United States health claims analysis. *Muscle Nerve*. 2023;67(4):297-305.

Rozanolixizumab. Prescribing information. UCB, Inc.

Zilucoplan. Prescribing information. UCB, Inc.

Denial Due to Absence of Thymectomy for Non-Thymomatous Patients Who Are 50 Years of Age or Younger

Vu T, Meisel A, Mantegazza R, et al; CHAMPION MG Study Group. Terminal complement inhibitor ravulizumab in generalized myasthenia gravis. *NEJM Evid*. 2022;1(5):1-12.

Wolfe GI, Kaminski HJ, Aban IB, et al; MGTX Study Group. Randomized trial of thymectomy in myasthenia gravis. *N Engl J Med*. 2016;375(6):511-522.

Narayanaswami P, Sanders DB, Wolfe GI, et al. International consensus guidance for management of myasthenia gravis: 2020 update. *Neurology*. 2021;96(3):114-122.

ULTOMIRIS Prescribing Information and Publications in gMG

ULTOMIRIS. Prescribing information. Alexion Pharmaceuticals, Inc.

Vu T, Meisel A, Mantegazza R, et al; CHAMPION MG Study Group. Terminal complement inhibitor ravulizumab in generalized myasthenia gravis. *NEJM Evid*. 2022;1(5):1-12.

Meisel A, Annane D, Vu T, et al. 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.

Peffault de Latour R, Brodsky RA, Ortiz S, et al. Pharmacokinetic and pharmacodynamic effects of ravulizumab and eculizumab on complement component 5 in adults with paroxysmal nocturnal haemoglobinuria: results of two phase 3 randomised, multicentre studies. *Br J Haematol.* 2020;191(3):476-485.

U.S. Food and Drug Administration, Department of Health and Human Services. ULTOMIRIS sBLA 761108/S-23 approval letter, April 27, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/761108Orig1s023ltr.pdf

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KEY RESOURCES AVAILABLE TO YOU

- Connect with an FRM—Alexion Field Reimbursement Managers (FRMs) provide education and support to HCP offices to facilitate patient access to their prescribed Alexion medications
- The ULTOMIRIS gMG Sample Letter of Medical Necessity resource provides a template for responding to a request for letter of medical necessity from a patient's insurance
- The ULTOMIRIS gMG Sample Appeal Letter resource provides a template to appeal a rejection from a patient's insurance

For additional access resources, please visit:

Explore Alexion Access Navigator

ALEXION ACCESS NAVIGATOR

Alexion Access Navigator is a dedicated resource website for US Healthcare Professionals and their offices that contains downloadable access and reimbursement materials for ULTOMIRIS® (ravulizumab-cwvz).

Online: https://alexionaccessnavigator.com

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INDICATION AND IMPORTANT SAFETY INFORMATION FOR ULTOMIRIS® (ravulizumab-cwvz)

INDICATION

ULTOMIRIS is indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

ULTOMIRIS, 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 ULTOMIRIS, unless the risks of delaying ULTOMIRIS 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 ULTOMIRIS 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, ULTOMIRIS 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

- Initiation in patients with unresolved serious *Neisseria meningitidis* infection.

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

ULTOMIRIS, 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 ULTOMIRIS therapy. 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 ULTOMIRIS therapy is indicated in a patient who is not up to date with meningococcal vaccines according to ACIP recommendations, provide 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 ULTOMIRIS. The benefits and risks of treatment with ULTOMIRIS, 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 they occur. Promptly treat known infections. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection depending on the risks of interrupting treatment in the disease being treated.

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IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

ULTOMIRIS and SOLIRIS REMS

Due to the risk of serious meningococcal infections, ULTOMIRIS 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 the 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 ULTOMIRIS. 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 ULTOMIRIS. Patients must receive counseling about the need to receive meningococcal vaccines and to take antibiotics as directed, signs and symptoms of meningococcal infection, and be instructed to carry the Patient Safety Card at all times during and for 8 months following ULTOMIRIS treatment.

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

Other Infections

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

ULTOMIRIS blocks terminal complement activation; therefore, patients may have increased susceptibility to infections, especially with encapsulated bacteria, such as infections caused by *Neisseria meningitidis* but also *Streptococcus pneumoniae*, *Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*. Patients receiving ULTOMIRIS are at increased risk for infections due to these organisms, even if they develop antibodies following vaccination.

Thromboembolic Event Management

The effect of withdrawal of anticoagulant therapy during treatment with ULTOMIRIS has not been established. Treatment should not alter anticoagulant management.

Infusion-Related Reactions

Intravenous administration may result in systemic infusion-related reactions, including anaphylaxis and hypersensitivity reactions. In clinical trials, infusion-related reactions occurred in approximately 1 to 7% of patients treated with ULTOMIRIS. These events included lower back pain, drop in blood pressure, limb discomfort, drug hypersensitivity (allergic reaction), dysgeusia (bad taste), and drowsiness. These reactions did not require discontinuation of ULTOMIRIS. If signs of cardiovascular instability or respiratory compromise occur, interrupt ULTOMIRIS infusion and institute appropriate supportive measures.

ADVERSE REACTIONS

Most common adverse reactions in adult patients with gMG (incidence ≥10%) were diarrhea and upper respiratory tract infection. Serious adverse reactions were reported in 20 (23%) of patients treated with ULTOMIRIS and in 14 (16%) patients receiving placebo. The most frequent serious adverse reactions were infections reported in at least 8 (9%) patients treated with ULTOMIRIS and in 4 (4%) patients treated with placebo. Of these infections, one fatal case of COVID-19 pneumonia was identified in a patient treated with ULTOMIRIS and one case of infection led to discontinuation of ULTOMIRIS.

DRUG INTERACTIONS

Plasma Exchange, Plasmapheresis, and Intravenous Immunoglobulins

Concomitant use of ULTOMIRIS with plasma exchange (PE), plasmapheresis (PP), or intravenous immunoglobulin (IVIg) treatment can reduce serum ravulizumab concentrations and requires a supplemental dose of ULTOMIRIS.

Neonatal Fc Receptor Blockers

Concomitant use of ULTOMIRIS with neonatal Fc receptor (FcRn) blockers (e.g., efgartigimod) may lower systemic exposures and reduce effectiveness of ULTOMIRIS. Closely monitor for reduced effectiveness of ULTOMIRIS.

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 ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

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