SAMPLE LETTER OF MEDICAL NECESSITY FOR ULTOMIRIS® (ravulizumab-cwvz) INJECTION

In Adult Patients Who Have Anti-Acetylcholine Receptor (AChR) Antibody-Positive Generalized Myasthenia Gravis (gMG)

Payers may request a letter of medical necessity to support coverage of ULTOMIRIS. The letter should explain why the drug is medically necessary for the specific patient and may include supporting documentation (eg, medical records, peer-reviewed literature, Prescribing Information, clinical treatment history, etc). The letter may be submitted as part of a prior authorization (PA) request, with the claim form, or in response to a payer's request for additional documentation. The letter should include patient-specific information, be on your letterhead, be signed by the prescriber, and be submitted to a payer to support a PA request or claim for ULTOMIRIS.

This sample letter of medical necessity is provided for informational purposes only and is not based on legal advice or official guidance from payers. It is not intended to increase or maximize reimbursement by any payer. Alexion does not warrant, promise, guarantee, or make any statement that the use of this information will result in coverage or payment for ULTOMIRIS or that any payment received will cover providers' costs.

INDICATION

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

SELECT 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)*].

Please see Important Safety Information on pages 5 to 7 and the full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

ULTOMIRIS®
(ravulizumab-cwvz)
injection for intravenous use
300 mg/3 mL vial

US/ULT-g/0060 V4 04/2024

[John Doe, MD]
[Address]
[City, State ZIP Code]
[(888) 555-5555]

[Date]
[Contact Name], [Title] [Name of Health Insurance Plan or PBM]
[Address]
[City, State ZIP Code]

Letter of Medical Necessity for ULTOMIRIS® (ravulizumab-cwvz)
[Request for Expedited Review Due to Medical Urgency]
Insured: [Name]; Policy Number: [Number]; Group Number: [Number]
Date(s) of service: [Date(s)]

Dear [Contact Name],

I am writing on behalf of my patient, [First Name] [Last Name], to request that [name of health insurance company] approve coverage and appropriate reimbursement associated with [Mr/Ms/Mrs/other title] [Last Name]'s treatment with ULTOMIRIS. ULTOMIRIS is indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.

Patient Medical Overview
[Name of patient] is a[n] [age]-year-old [gender] born [MM-DD-YYYY] who requires treatment with ULTOMIRIS after being diagnosed with anti-AChR antibody-positive gMG on [date of diagnosis MM-DD-YYYY].

Medical History (Including Clinical Signs, Symptoms, and Laboratory Results) [see page 3 for reference]
[Provide relevant gMG clinical signs and symptoms and describe the severity of disease of your patient's current presentation and disease progression (eg, patient's medical history of myasthenic crises) based on your medical opinion. Include specific clinical presentations, relevant patient-specific clinical scenarios demonstrating serious medical need, and previous treatments for gMG.]

If Policy Requires Step Therapy/Trial or Failure of Recommended Therapy
Your policy requires a step edit through [recommended therapy per clinical policy]. In my medical opinion, [recommended therapy per clinical policy] is not an appropriate step for my patient. [Include rationale for ineligibility or failure of step therapies. If multiple steps are required, include reasons for each gMG treatment (ie, immunosuppressive therapies). Discuss rationale for using ULTOMIRIS. Include your professional opinion of your patient's likely prognosis or disease progression without treatment. Please see "Treatment Rationale to Support Appeal" in sample appeal letter for ULTOMIRIS® resource.]

For C5 Inhibitor-Treated Patients Transitioning to ULTOMIRIS (if relevant) [see page 4 for reference]
[Provide treatment rationale for transitioning your patient from an existing C5 therapy to ULTOMIRIS.]

In my medical opinion, ULTOMIRIS is the most appropriate treatment for [name of patient]'s anti-AChR antibody-positive gMG based on the clinical efficacy and safety data.

Treatment Plan
For adult patients with anti-AChR antibody-positive gMG, the recommended dosing regimen with ULTOMIRIS includes a weight-based loading dose. Maintenance dosing starts 2 weeks after the initial loading dose and then occurs once every 8 weeks.

Patients 40 to <60 kg 2,400 mg loading dose; 3,000 mg maintenance dose (every 8 weeks)
Patients 60 to <100 kg 2,700 mg loading dose; 3,300 mg maintenance dose (every 8 weeks)
Patients ≥100 kg 3,000 mg loading dose; 3,600 mg maintenance dose (every 8 weeks)

Summary
Based on the above facts, I am confident you will agree that ULTOMIRIS, a complement inhibitor, is indicated and medically necessary for this patient. For your convenience, I am enclosing [list enclosures such as supporting clinical documentation, Prescribing Information, FDA approval letter for ULTOMIRIS in gMG, etc].

If you have any further questions, please feel free to call me at [provider's telephone number] to discuss. Thank you in advance for your immediate attention to this request.

Sincerely,

[Provider's Name]
[Provider's Identification Number]
[Provider's Practice Name]
[Provider's Phone Number]
[Provider's Fax Number]
[Provider's Email]

Enclosures
[Supporting clinical documentation, ULTOMIRIS Full Prescribing Information, FDA press release for ULTOMIRIS in gMG, etc]

MEDICAL HISTORY (INCLUDING CLINICAL SIGNS, SYMPTOMS, AND LABORATORY RESULTS)

- ☐ Evidence of a positive serological test for **anti-AChR antibodies** (include laboratory results and date) and any other context you consider relevant to the laboratory result
- ☐ Status based on the **Myasthenia Gravis Foundation of America (MGFA) Clinical Classification** Class I to V (MGFA Class II-IV assessed in CHAMPION-MG clinical trial population)[1]
- ☐ Score on the **Myasthenia Gravis-Activities of Daily Living (MG-ADL)** scale 0–24; MG-ADL total score of ≥6 assessed in CHAMPION-MG clinical trial population,[1] including case notes and other clinical impressions. If patient or caregiver has tracked changes in their MG-ADL total score, include the score history from baseline through therapy changes; payers may require the MG-ADL total scores for initial approval and reauthorizations of treatment
- ☐ Previous experience (including any variability in performance), if any, with receiving ULTOMIRIS, including any changes in the **Quantitative Myasthenia Gravis (QMG)** total score (scale 0–39)
- ☐ **Previous treatment** on corticosteroids, immunosuppressants (eg, azathioprine, tacrolimus, mycophenolate mofetil, cyclosporine, methotrexate, cyclophosphamide, etc), intravenous immune globulin, chronic plasmapheresis, plasma exchange, eculizumab, efgartigimod alfa-fcab, efgartigimod alfa and hyaluronidase-qvfc, rozanolixizumab, and/or zilucoplan (such as name of treatments, dosage, frequency, duration including dates, reasons for failures/intolerances, serious adverse reactions, adherence issues, and impact, if any, on patient's symptoms)
- ☐ Current use of medications for comorbid conditions that may impact treatment of gMG[2,3]
- ☐ **Contraindications or allergies,** if any, to any agents used in the treatment of gMG
- ☐ **History of complications, exacerbations, or myasthenic crises** leading to emergency room visits, hospital admissions, and/or intensive care unit stays
- ☐ Record of receiving the **meningococcal vaccines** at least 2 weeks prior to the first proposed treatment with ULTOMIRIS
- ☐ **Clinical signs and symptoms, including severity,** to help describe the patient's current clinical presentation[4,]*:
  - ○ Ocular muscle weakness: Ptosis and diplopia, or sometimes blurry vision
  - ○ Axial muscle weakness: Neck flexor or extensor weakness
  - ○ Oropharyngeal muscle weakness: Chewing difficulties, dysarthria, dysphagia, facial muscles frequently involving eyelid closure, drooling
  - ○ Limb muscle weakness: Proximal limb weakness, with arms more affected than legs
  - ○ Respiratory muscle weakness: Orthopnea, tachypnea, exertional dyspnea-poor inspiratory sniff, cough

*List is not all inclusive of gMG clinical signs and symptoms.

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TREATMENT RATIONALE FOR TRANSITIONING C5 INHIBITOR–TREATED PATIENTS TO ULTOMIRIS

- ☐ The patient had a previous diagnosis of anti-AChR antibody-positive gMG that met requirements for initiating eculizumab, was clinically stable on eculizumab, and has had a beneficial response as evidenced by [change from baseline in MG-ADL total score, change from baseline in QMG total score][1]
- ☐ ULTOMIRIS was engineered through the modification of eculizumab to result in an extended half-life[5,6]
  - ○ Switching to ULTOMIRIS reduces maintenance dosing frequency to 6 to 7 infusions per year, from 26 infusions per year with eculizumab[1]
  - ○ The annualized cost of treatment is expected to be reduced by ~26% to 39% with ULTOMIRIS compared with eculizumab based on wholesale acquisition cost (WAC)[1,7,8]
- ☐ ULTOMIRIS has the same mechanism of action as eculizumab
- ☐ The patient will not receive ULTOMIRIS concomitantly with other complement inhibitors (eg, eculizumab) or Fc receptor blockers (eg, efgartigimod alfa-fcab, efgartigimod alfa and hyaluronidase-qvfc, and rozanolixizumab)

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 Appeal Letter resource provides a template to appeal a rejection from a patient's insurance
- ☐ The Reauthorization Guide is a resource that provides education and support about the reauthorization process, including health plan requirements and timing implications
- ☐ The ULTOMIRIS Full Prescribing Information provides details and directions on how to prescribe ULTOMIRIS and pertinent efficacy and safety data
- ☐ The FDA Approval Letter provides information on the response from the FDA in reference to the supplemental biologics license application filed for ULTOMIRIS

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

HCP, healthcare provider.

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INDICATION & IMPORTANT SAFETY INFORMATION

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IMPORTANT SAFETY INFORMATION

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- **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*.

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IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

Serious Meningococcal Infections (continued)

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.

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.

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IMPORTANT SAFETY INFORMATION (CONTINUED)

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.

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References: 1. ULTOMIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. **2.** Basoff D, et al. Poster presented at: the Annual Meeting of the Academy of Managed Care Pharmacy (AMCP) 2023; May 21-24, 2023; San Antonio, TX, USA. **3.** Drugs.com. Drug Interaction Checker. Accessed October 12, 2023. https://www.drugs.com/interaction/list/ **4.** Meriggioli MN, Sanders DB. *Lancet Neurol*. 2009;8(5):475-490. **5.** Peffault de Latour R, et al. *Br J Haematol*. 2020;191(3):476-485. **6.** Sheridan D, et al. *PLoS One*. 2018;13(4):e0195909. **7.** SOLIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. **8.** IBM Micromedex. RED BOOK. Accessed August 21, 2023. https://www.micromedexsolutions.com

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