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

In Anti-Aquaporin-4 (AQP4) Antibody-Positive Neuromyelitis Optica Spectrum Disorder (NMOSD) in Adults

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 neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin 4 (AQP4) 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, 6, and 7 and the full Prescribing Information for ULTOMIRIS® (ravulizumab-cwvz), 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-N/0029 V1 03/2024

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

SAMPLE ONLY
PLEASE COPY ONTO YOUR LETTERHEAD.

[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 anti-aquaporin-4 (AQP4) antibody-positive neuromyelitis optica spectrum disorder (NMOSD).

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-AQP4 antibody-positive NMOSD on [date of diagnosis MM-DD-YYYY].

Medical History (including Clinical Signs, Symptoms, and Laboratory Results) [see page 3 for reference]

[Provide relevant NMOSD 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 relapses) based on your medical opinion. Include specific clinical presentations, relevant patient-specific clinical scenarios demonstrating serious medical need, and previous treatments for NMOSD.]

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-AQP4 antibody-positive NMOSD based on the clinical efficacy and safety data.

Treatment Plan

For adult patients with anti-AQP4 antibody-positive NMOSD, the recommended dosing regimen with ULTOMIRIS consists of a single weight-based IV loading dose of ULTOMIRIS on Day 1, followed by regular weight-based maintenance dosing beginning on Day 15 and once every 8 weeks thereafter.

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 NMOSD, 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, Prescribing Information, FDA press release for ULTOMIRIS in NMOSD, etc.]

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

- ☐ Clinical, imaging, and laboratory findings including serology confirming **anti-AQP4 antibody status**, at least one core clinical characteristic, and exclusion of alternative diagnoses[1]
- ☐ Detailed **history of relapse(s)**
- ☐ Status based on the **Expanded Disability Status Scale (EDSS)** (0-10; note, required to be ≤7)
- ☐ List names of **previous and/or current treatments** including dosage, frequency, duration including dates, and impact, if any, on patient's symptoms
- ☐ **Contraindications**, if any, to any agents used in treatment of anti-AQP4 antibody-positive NMOSD
- ☐ **Additional documentation** of your clinical rationale to initiate ULTOMIRIS for this patient, such as clinical presentation, disease-related complications, recent medical history, or visits related to anti-AQP4 antibody-positive NMOSD, etc
- ☐ Description of how anti-AQP4 antibody-positive NMOSD has impacted the patient's **level of function** physically, visually, and neurologically
- ☐ **Meningococcal vaccinations:** Provide documentation of initial series and/or most recent booster(s) for MenACWY and MenB vaccinations at least 2 weeks prior to the first proposed treatment with ULTOMIRIS or antibiotics for prophylaxis of meningococcal infection until at least 2 weeks after meningococcal vaccinations[2]
- ☐ **Previous experience**, if any, with receiving ULTOMIRIS
- ☐ **Clinical signs and symptoms** to help describe the patient's current clinical presentation[3-5,*]
  - ○ Respiratory dysfunction or failure
  - ○ Loss of bowel/bladder function
  - ○ Sensory and motor disability
  - ○ Severe weakness and impaired mobility
  - ○ Paralysis (paraparesis to paraplegia)
  - ○ Optic neuritis leading to pain in eye and loss of visual acuity

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

Please Note: Healthcare insurance provider policies may not be in place during the first several months following FDA approval. It is important to submit the letter of medical necessity to insurance providers along with the FDA letter, clinical study details, and ULTOMIRIS Prescribing Information.

Please see Important Safety Information on pages 5, 6, and 7 and the full Prescribing Information for ULTOMIRIS® (ravulizumab-cwvz), including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

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300 mg/3 mL vial

TREATMENT RATIONALE FOR TRANSITIONING C5 INHIBITOR-TREATED PATIENTS TO ULTOMIRIS

- ☐ The patient had a previous diagnosis of NMOSD that met requirements for initiating eculizumab, was clinically stable on eculizumab, and has had a beneficial response (ie, decrease in frequency of relapses)
- ☐ ULTOMIRIS was engineered through the modification of eculizumab to result in an extended half-life[6,7]
  - The annualized cost of treatment is expected to be reduced by approximately 26% to 39% with ULTOMIRIS compared with eculizumab based on wholesale acquisition cost (WAC)[2,8,9]
  - Switching to ULTOMIRIS reduces maintenance dosing frequency to 6 to 7 infusions per year[2]
- ☐ The patient will not receive ULTOMIRIS concomitantly with other biologics for the treatment of NMOSD (eg, eculizumab, inebilizumab, satralizumab, rituximab, tocilizumab)
- ☐ ULTOMIRIS is an established complement protein C5 inhibitor with more than 3 years of postmarketing experience including more than 600 patients studied across multiple indications in phase 3 randomized controlled trials[2]

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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IMPORTANT SAFETY INFORMATION

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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

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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INDICATION AND IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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 NMOSD (incidence >10%) were COVID-19, headache, back pain, arthralgia, and urinary tract infection. Serious adverse reactions were reported in 8 (13.8%) patients with NMOSD receiving ULTOMIRIS.

INDICATION AND IMPORTANT SAFETY INFORMATION (CONT'D)

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 accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

References: 1. Wingerchuk DM, et al. *Neurology*. 2015;85(2):177-189. **2.** ULTOMIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. **3.** Wingerchuk DM, et al. *Lancet Neurol.* 2007;6(9):805-815. **4.** Hinson SR, et al. *Handb Clin Neurol.* 2016;133:377-403. **5.** Jarius S, Wildemann B. *J Neuroinflammation*. 2013;10:8. **6.** Peffault de Latour R, et al. *Br J Haematol.* 2020;191(3):476-485. **7.** Sheridan D, et al. *PLoS One.* 2018;13(4):e0195909. **8.** SOLIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. **9.** IBM Micromedex. RED BOOK. Accessed March 22, 2024. https://www.micromedexsolutions.com

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AstraZeneca Rare Disease