Sample Appeal Letter for SOLIRIS® (eculizumab) Injection, for Intravenous Use in Anti-Aquaporin-4 (AQP4) Antibody-Positive Neuromyelitis Optica Spectrum Disorder (NMOSD)

When a payer (health plan or pharmacy benefit manager [PBM]) denies a prior authorization (PA), precertification, or reauthorization request for SOLIRIS prescribed for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive, your patient has the right to appeal the decision. If your patient wishes to appeal, you and your staff may assist by submitting an appeal letter and supporting documentation.

As part of the appeals process, payers may request additional documentation from you to support coverage of SOLIRIS when approval for its use has been denied. Your letter should explain why SOLIRIS is medically necessary for the specific patient and may include supporting documentation. The letter may be submitted in response to the denial letter or to a payer's request for additional documentation. The letter should include patient-specific information, address the reason for denial, be presented on the prescriber's letterhead, and be signed by the prescriber. The provided Sample Appeal Letter gives you a framework for composing an appeal.

This Sample Appeal Letter is provided for informational purposes only and is not 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 SOLIRIS or that any payment received will cover providers' costs.

INDICATION & IMPORTANT SAFETY INFORMATION FOR SOLIRIS

INDICATION

SOLIRIS is indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

SELECT 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)*].

Please see Important Safety Information on pages 1 and 6 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

SOLIRIS® (eculizumab) Injection for Intravenous Use 300 mg/30 mL vial

[John Doe, MD]
[12345 West Main Street]
[City Name, FL 33223]
[(888) 555-5555]

SAMPLE ONLY
Please copy onto your letterhead.

[Date]
[Contact Name] [Title]
[Name of Health Insurance Company]
[Address] [City, State Zip Code]

RE: Insured: [Name]; Policy Number: [Number]; Group Number: [Number]
Date(s) of service: [Date(s) of administration]; Claim number: [Claim number]

Dear [Name of Contact],

I am writing to appeal the coverage determination for my patient [patient name] with anti-aquaporin-4 (AQP4) antibody-positive NMOSD.

- NMOSD relapses are unpredictable and tend to be severe and recurrent.[1-3] Over time, relapses have been shown to be inevitable for the majority of patients with NMOSD[1,2,4];
- Severe disability can result after even a single relapse[5] and up to 76% of patients may not fully recover[1];
- Complement activation is an important cause of anti-AQP4 antibody-positive NMOSD pathophysiology.[6]

[Insert reason for denial and why you disagree.]

This letter provides information about my patient's medical history and treatment rationale.

1 DISEASE SUMMARY (Reference page 3 for examples):
[Provide a brief discussion of patient's symptoms and treatments for anti-AQP4 antibody-positive NMOSD, including any relevant patient-specific clinical scenarios supportive of your treatment selection.]

2 TREATMENT RATIONALE (Reference page 4 for examples):
In my medical opinion, SOLIRIS is the most appropriate treatment for [name of patient]'s anti-AQP4 antibody-positive NMOSD based upon the clinical efficacy and safety data.

[Based on your medical judgment, insert additional treatment rationale to support this appeal.]

Based on the above facts, I am confident you will agree that SOLIRIS is indicated and medically necessary for this patient, and I request that you reverse the coverage determination.

For your convenience, I am enclosing [list enclosures such as a paper copy of original claim form, a copy of the summary of benefits showing the denial, supporting clinical documentation, etc]. If you have any further questions, please feel free to call me at [physician's telephone number] to discuss.

Thank you in advance for your immediate attention to this request.

Sincerely,

[Physician's name], MD
[Physician's practice name] [Phone number]

Please copy language above the line for sample letter.

Please see Important Safety Information on pages 1 and 6 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

1 DISEASE SUMMARY MAY INCLUDE THE FOLLOWING:

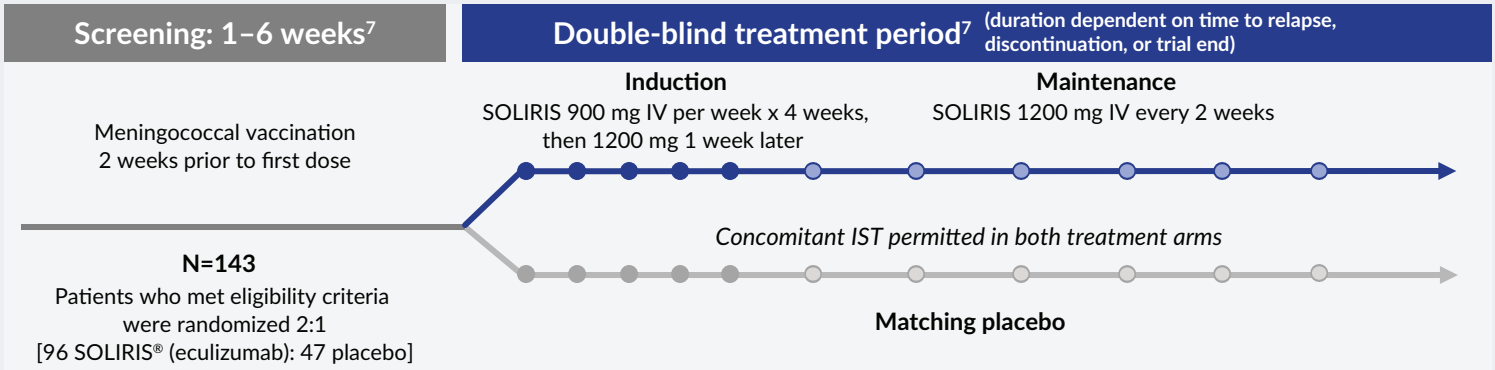
- [Name of patient] is a[n] [age]-year-old [male/female] born [MM-DD-YEAR] who requires treatment with SOLIRIS after being diagnosed with anti-AQP4 antibody-positive NMOSD on [date of diagnosis MM-DD-YEAR];
- Clinical, imaging, and antibody findings including serology results confirming anti-AQP4 antibody status;
- Past medical history including if the patient has experienced optic neuritis, longitudinally extensive transverse myelitis, area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting), acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic clinical syndrome with anti-AQP4 antibody-positive NMOSD–typical diencephalic magnetic resonance imaging lesions, symptomatic cerebral syndrome with anti-AQP4 antibody-positive NMOSD–typical brain lesions and pertinent negative findings for other diagnoses such as multiple sclerosis (MS), sarcoidosis, or neoplasm;
- Detailed relapse history including at least 2 relapses in the year prior to request for initiating SOLIRIS or at least 3 relapses in the past 2 years with at least 1 relapse within the past year prior to request for initiating SOLIRIS;
- Status based on the Expanded Disability Status Scale (EDSS) score (required to be ≤7, consistent with the presence of at least limited ambulation with aid);
- Previous and/or current treatment on intravenous corticosteroids at a dose of ≤20 mg/day or immunosuppressants at a stable dosage, including name of treatments, dosage, frequency, and duration including dates and impact, if any, on patient's symptoms;
- Treatments the patient will NOT be receiving in combination with SOLIRIS including disease-modifying therapies for MS or anti-interleukin-6 therapy;
- Has not received rituximab or mitoxantrone within 3 months or IVIG within 3 weeks prior to initiation;
- Contraindications, if any, to any agents used in treatment of anti-AQP4 antibody-positive NMOSD;
- Disease-related complications leading to emergency treatment, hospital admissions, and/or other interventions;
- Description of how anti-AQP4 antibody-positive NMOSD has impacted the patient's level of function physically, visually, and neurologically;
- Record of receiving the meningococcal vaccine at least 2 weeks prior to the first proposed treatment with SOLIRIS. If the patient was not vaccinated they were provided with two weeks of antibacterial drug prophylaxis;
- Previous experience, if any, with receiving SOLIRIS including submission of medical records demonstrating a positive clinical response from baseline.

Please copy language above the line for sample letter.

2 TREATMENT RATIONALE TO SUPPORT APPEAL

PREVENT (Prevention of Relapses in Neuromyelitis Optica): Phase 3, randomized, double-blind, placebo-controlled, time-to-event study evaluating the efficacy and safety of SOLIRIS in 143 adult patients with anti-AQP4 antibody-positive NMOSD who received SOLIRIS (N=96) or placebo (N=47).

THE FOLLOWING EFFICACY AND SAFETY DATA ARE BASED ON THE TRIAL DESIGN BELOW.



Trial design[7,8]

- **Sample size:** 143 patients
- **Trial completion:** Confirmation of 23rd adjudicated relapse
- **Primary endpoint:** Time to first adjudicated on-trial relapse
  - Estimated number of patients relapse free at 48 weeks
- **Secondary endpoints:** Annualized relapse rate, neurologic function, disease-related disability

- SOLIRIS is a complement inhibitor that is FDA-approved for treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive
- In the SOLIRIS PREVENT study of patients with anti-AQP4 antibody-positive NMOSD, SOLIRIS was superior to placebo based on time to first adjudicated on-trial relapse (primary endpoint). The time to first adjudicated on-trial relapse was significantly longer in SOLIRIS-treated patients compared to patients on placebo (relative risk reduction 94%; Hazard Ratio=0.058; 95% CI: 0.017, 0.197; *P*<0.0001)[9]
- 98% of patients treated with SOLIRIS were relapse free at 48 weeks vs 63% with placebo log-rank *P*-value <0.0001[8,9]
- SOLIRIS has an established safety profile[7,9]
- SOLIRIS has a black box warning regarding serious meningococcal infections. The most frequently reported adverse reactions in the NMOSD placebo-controlled trial (≥10%) are: upper respiratory infection, nasopharyngitis, diarrhea, back pain, dizziness, influenza, arthralgia, pharyngitis, and contusion[9]
- SOLIRIS is a monoclonal antibody that specifically binds to the complement protein C5 with high affinity, thereby inhibiting its cleavage to C5a and C5b and preventing the generation of the terminal complement complex C5b-9. The precise mechanism by which eculizumab exerts its therapeutic effect in NMOSD is unknown but is presumed to involve inhibition of aquaporin-4-antibody–induced terminal complement C5b-9 deposition[9]

Please copy language above the line for sample letter.

Please see Important Safety Information on pages 1 and 6 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

2 TREATMENT RATIONALE TO SUPPORT APPEAL (cont.)

- Potential references and information to support appeal relevant to immune system function and COVID-19 in patients with anti-AQP4 antibody-positive NMOSD:
  - Infection has been shown to amplify complement activity, which could have the potential to exacerbate a patient's underlying condition in a complement-mediated disease[10-13]
  - As part of the immune system, B cells are responsible for protection against viruses and other pathogens.[14] In light of the recent outbreak of the coronavirus (COVID-19), the National Multiple Sclerosis Society's National Medical Advisory Committee published its recommendations regarding B-cell depletion in the treatment of multiple sclerosis (MS). For the MS guidance, please refer to https://www.nationalmssociety.org/coronavirus-covid-19-information/multiple-sclerosis-and-coronavirus/ms-treatment-guidelines-during-coronavirus[15]

Please copy language above the line for sample letter.

IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab)

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.

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. 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 reactions in the NMOSD placebo-controlled trial (≥10%) were: upper respiratory infection, nasopharyngitis, diarrhea, back pain, dizziness, influenza, arthralgia, pharyngitis, and contusion.

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

References

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ALEXION® AstraZeneca Rare Disease