# Sample Appeal Letter for SOLIRIS® (eculizumab) injection, for intravenous use in anti-aquaporin-4 (AQP4) antibody-positive Neuromyelitis Optica Spectrum Disorder (NMOSD)

*As part of the appeal process, payers may request additional documentation from the prescribing physician to support coverage of SOLIRIS when coverage has been denied. 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, etc). The letter may be submitted with the denied claim, or in response to a payer's request for additional documentation. The letter should include patient-specific information, address the reason for denial, be on the prescriber's letterhead, be signed by the prescriber, and submitted to a payer to support a claim for SOLIRIS.*

*This sample appeal letter is provided for informational purposes only and is not based upon 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

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**

**Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris and may become rapidly life-threatening or fatal if not recognized and treated early.**

- **Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.**
- **Immunize patients with meningococcal vaccines at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection. (See *Serious Meningococcal Infections* for additional guidance on the management of the risk of meningococcal infection).**
- **Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Monitor patients for early signs of meningococcal infections and evaluate immediately if infection is suspected.**

**Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS, prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747) or at www.solirisrems.com.**

**Please see Important Safety Information on pages 1 and 7 and the Full Prescribing Information for SOLIRIS® (eculizumab), including Boxed WARNING regarding serious 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 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 7 and the Full Prescribing Information for SOLIRIS® (eculizumab), including Boxed WARNING regarding serious meningococcal infections.**

# 1 DISEASE SUMMARY MAY INCLUDE THE FOLLOWING:

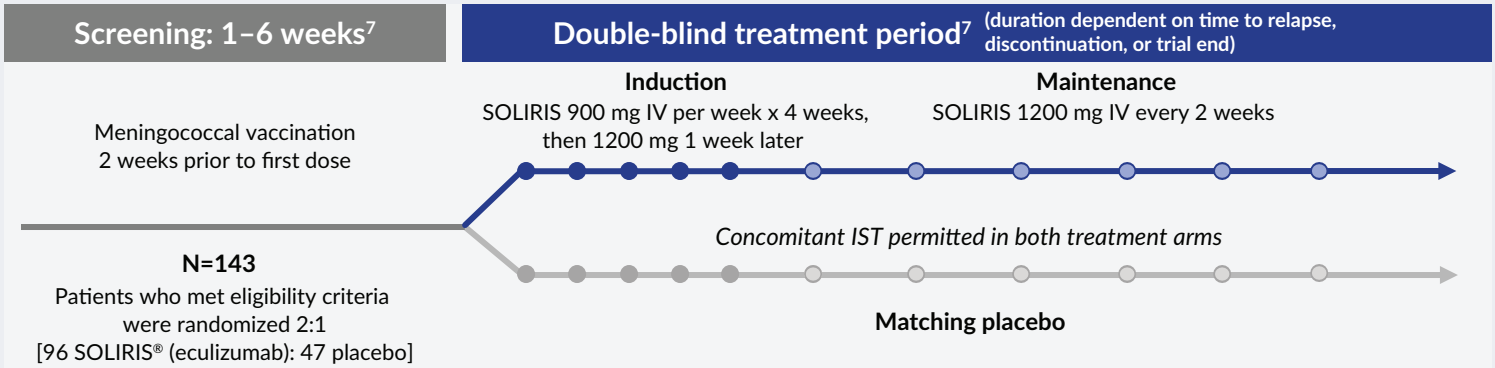
- [Name of patient] is a[n] [age]-year-old [male/female] born [MM-DD-YEAR] who requires treatment with SOLIRIS after being diagnosed with anti-AQP4 antibody-positive NMOSD on [date of diagnosis MM-DD-YEAR];
- Clinical, imaging, and antibody findings including serology results confirming anti-AQP4 antibody 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 7 and the Full Prescribing Information for SOLIRIS® (eculizumab), including Boxed WARNING regarding serious 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.

**References**


1. Jarius S, et al. *J Neuroinflamm*. 2012;9:14.
2. Wingerchuk DM, et al. *Neurology*. 1999;53(5):1107-1114.
3. Kitley J, et al. *Brain*. 2012;135:1834–1849.
4. Mealy MA, et al. *Arch Neurol*. 2012;69(9):1176-1180.
5. Flanagan EP, et al. *Ann Neurol*. 2016;79(5):775-783.
6. Dutra BG, et al. *RadioGraphics*. 2018;38(1):169-193.
7. Data on file. Alexion Pharmaceuticals, Inc.; Boston, MA.
8. Pittock SJ, et al. *N Engl J Med*. 2019;381(7):614-625.
9. SOLIRIS. Prescribing information. Alexion Pharmaceuticals, Inc.; 2020.
10. Olie KH, et al. *Am J Kidney Dis*. 2005;45(1):e12-e15.
11. Berner R, et al. *Pediatr Nephrol*. 2002;17(3):190-192.
12. Brodsky RA, et al. *Haematologica*. 2020;106(1):230-237. doi:10.3324/haematol.2019.236877.
13. Ueda T, et al. *J Nippon Med Sch*. 2013;80(2):155-159.
14. Chaplin DD. *J Allergy Clin Immunol*. 2010;125(2 suppl 2):S3-S23.
15. National Multiple Sclerosis Society. MS treatment guidelines during coronavirus. Accessed January 4, 2021. https://www.nationalmssociety.org/coronavirus-covid-19-information/multiple-sclerosis-and-coronavirus/ms-treatment-guidelines-during-coronavirus

## SELECT IMPORTANT SAFETY INFORMATION (continued)

### Contraindications

- Patients with unresolved serious *Neisseria meningitidis* infection
- Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection

### Warnings and Precautions

**Serious Meningococcal Infections**

**Risk and Prevention**

The use of Soliris increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis).

Vaccinate or revaccinate for meningococcal disease according to the most current ACIP recommendations for patients with complement deficiencies. Immunize patients without a history of meningococcal vaccination at least 2 weeks prior to receiving the first dose of Soliris. If Soliris must be initiated immediately in an unvaccinated patient, administer meningococcal vaccine(s) as soon as possible and provide 2 weeks of antibacterial drug prophylaxis. Discontinue Soliris in patients who are undergoing treatment for serious meningococcal infections.

**REMS**

Prescribers must counsel patients about the risk of meningococcal infection, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccine(s).

**Other Infections**

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

Patients may have increased susceptibility to infections, especially with encapsulated bacteria. Additionally, *Aspergillus* infections have occurred in immunocompromised and neutropenic patients. Use caution when administering Soliris to patients with any systemic infection.

**Infusion-Related Reactions**

Administration of Soliris may result in infusion-related reactions, including anaphylaxis or other hypersensitivity reactions. 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 Anti-AQP4 positive-NMOSD placebo-controlled trial (≥10%) are: upper respiratory infection, nasopharyngitis, diarrhea, back pain, dizziness, influenza, arthralgia, pharyngitis, and contusion.