Sample Letter of Medical Necessity for SOLIRIS® (eculizumab)

for Paroxysmal Nocturnal Hemoglobinuria (PNH)

INDICATION

SOLIRIS is indicated for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.[1]

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 7-8 and 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

Introduction

Payers may request a letter of medical necessity to support coverage of SOLIRIS. 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 SOLIRIS.

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 SOLIRIS or that any payment received will cover providers' costs.

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Please see Important Safety Information on pages 1 and 7-8 and 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]
[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 SOLIRIS® (eculizumab)
[Request for Expedited Review Due to Medical Emergency]
Insured: [Name]; Policy Number: [Policy Number]; Group Number: [Group 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 SOLIRIS® (eculizumab). SOLIRIS is indicated for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.

Patient History and Diagnosis
[Name of patient] is a[n] [age]-year-old [male/female] born [MM-DD-YEAR] who requires treatment with SOLIRIS after being diagnosed with PNH on [date of diagnosis MM-DD-YEAR].

1 **Medical History (Including Clinical Signs, Symptoms, and Laboratory Results)** (reference page 5 for examples)
[Summary of the rationale for treatment with SOLIRIS for this patient. Provide relevant PNH clinical signs and symptoms and describe the severity of the disease of your patient's current presentation and disease progression in your medical opinion. Include a description of the patient's PNH symptoms, diagnosis, laboratory values, as well as specific clinical presentations and relevant patient-specific clinical scenarios demonstrating serious medical need as well as the specifics of previous treatments and historical management of PNH.]

IF POLICY REQUIRES STEP THERAPY (OPTIONAL)
Your policy requires a step edit through [pegcetacoplan, iptacopan, crovalimab, eculizumab-aagh, or eculizumab-aeeb]. In my medical opinion, [pegcetacoplan, iptacopan, crovalimab, eculizumab-aagh, or eculizumab-aeeb] is not an appropriate step for my patient based on the following relevant criteria [insert reason(s) why pegcetacoplan, iptacopan, crovalimab, eculizumab-aagh, or eculizumab-aeeb may not be appropriate for your patient. Refer to the list of potential considerations from the Sample Appeal Letter for SOLIRIS (US/SOL-P/0104) pages 6 to 11].

In my medical opinion, SOLIRIS is the most appropriate treatment for [name of patient]'s PNH based on the clinical efficacy and safety data.

Treatment Plan
For patients 18 years of age and older with PNH, the recommended dosing regimen with SOLIRIS consists of 600 mg weekly for the first 4 weeks, followed by 900 mg for the fifth dose 1 week later, and then 900 mg every 2 weeks thereafter.

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

Summary

Based on the above, I am confident that you will agree that SOLIRIS is indicated and medically necessary for this patient. For your convenience, I am enclosing [list enclosures such as supporting clinical documentation, Prescribing Information, Food and Drug Administration (FDA) approval letter for SOLIRIS in PNH, copy of patient's insurance card, 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 Identification Number]
[Physician's Practice Name]
[Physician's Phone Number]
[Physician's Fax Number]
[Physician's Email]

Enclosures
[Supporting clinical documentation, Prescribing Information, FDA approval letter for SOLIRIS in PNH, copy of patient's insurance card, etc]

1 Medical History (Including Clinical Signs, Symptoms, and Laboratory Results)

Indicated or Appropriate Patient Population

- ☐ Patients 18 years of age and older with PNH[1]
- ☐ Documented diagnosis of PNH, confirmed by high-sensitivity flow cytometry evaluation of red blood cells (RBCs) and white blood cells (WBCs), with granulocyte or monocyte clone size of ≥5%[2]

Clinical Manifestations to help describe the patient's current clinical presentation[a]

Laboratory Results

- Clone Size: clinical, imaging, and antibody findings including high-sensitivity flow cytometry confirming PNH with a granulocyte or monocyte clone size ≥5%[2-4]
- Lactate Dehydrogenase (LDH): LDH level ≥1.5 times the upper limit of normal[2-5]
- Transfusion History: history of packed RBC transfusions, including both the number of infusions as well as the units transfused[2,3]
- Kidney Function: serum creatinine (SCr) level, glomerular filtration rate (GFR)[3]
- Hematology: hemoglobin, haptoglobin, reticulocyte count, platelets, bilirubin levels, Coombs negativity[3,4]

Signs and Symptoms

- Signs and Symptoms of Intravascular Hemolysis: fatigue, hemoglobinuria, abdominal pain, dyspnea, anemia, history of major adverse vascular events (including thrombosis, chest pain), dysphagia, erectile dysfunction[2-4,6]
- Acute Hemolytic Crisis: onset or recurrence of signs and symptoms of hemolysis[7,8]
- Signs and Symptoms of Thrombosis: atypical thrombotic event, neurologic symptoms, abdominal pain, swelling of the extremities, elevated D-dimer, and presence of clot as confirmed with imaging[3,4,9]
- Signs and Symptoms of Hemolytic Anemia: onset of signs and symptoms of hemolytic anemia (eg, fatigue), along with relevant laboratory values (eg, hemoglobin <10 g/dL, Coombs negativity, LDH, bilirubin levels, haptoglobin, reticulocyte count)[2,10,11]

[a] This list is not all-inclusive of PNH clinical signs, symptoms, and laboratory findings.

Patient Treatment History including names of previous treatments; dosage, frequency, duration, and dates; and the respective clinical responses/impact, if any, on patient symptoms.

Patient Treatment Burden outlining why a SOLIRIS dosing regimen is suited for this patient. Include any relevant information about the patient's ability to perform or adhere to self-injection due to physical or cognitive impairment.

- ☐ Additional documentation of your clinical rationale to initiate SOLIRIS for this patient, such as clinical presentation, recent medical history, or visits related to PNH, etc

Contraindication, if any, or intolerance to other agents indicated to treat PNH (eg, pegcetacoplan, iptacopan, crovalimab, eculizumab-aagh, or eculizumab-aeeb).

- ☐ The patient has hypersensitivity to any of the excipients of pegcetacoplan[12]
- ☐ The patient has hypersensitivity to any of the excipients of iptacopan[13]
- ☐ The patient has hypersensitivity to any of the excipients of crovalimab[14]
- ☐ The patient has hypersensitivity to any of the excipients of eculizumab-aagh[15]
- ☐ The patient has hypersensitivity to any of the excipients of eculizumab-aeeb[16]

1 Medical History (Including Clinical Signs, Symptoms, and Laboratory Results) (cont'd)

Vaccination Documentation

- ☐ Documentation indicating the patient does not have an active meningococcal infection[1]
- ☐ Meningococcal vaccinations: Provide documentation of initial series and/or most recent boosters for meningococcal vaccinations at least 2 weeks prior to the first proposed treatment with SOLIRIS.[1] If vaccinations are pending approval of therapy, please include a scheduled date for the patient to receive the vaccinations
- ☐ If urgent treatment was indicated, include a record of receiving the meningococcal vaccine as soon as possible, along with 2 weeks of antibacterial drug prophylaxis per SOLIRIS Prescribing Information[1]

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 SOLIRIS® (eculizumab).

Online: https://alexionaccessnavigator.com

SELECT IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab) (cont'd)

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.

SELECT IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab) (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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. Children treated with SOLIRIS may be at increased risk of developing serious infections due to *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib). Administer vaccinations for the prevention of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) infections according to ACIP recommendations. Patients receiving SOLIRIS are at increased risk for infections due to these organisms, even if they develop antibodies following vaccination.

Monitoring Disease Manifestations After SOLIRIS Discontinuation

Monitor patients after discontinuing SOLIRIS for at least 8 weeks to detect hemolysis.

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 PNH randomized trial (≥10% overall and greater than placebo) were: headache, nasopharyngitis, back pain, and nausea.

DRUG INTERACTIONS

Plasmapheresis, Plasma Exchange, or Fresh Frozen Plasma Infusion

Concomitant use of SOLIRIS with plasma exchange (PE), plasmapheresis (PP) or fresh frozen plasma infusion (PE/PI) treatment can reduce serum eculizumab concentrations and requires a supplemental dose of SOLIRIS.

Neonatal Fc Receptor Blockers

Concomitant use of SOLIRIS with neonatal Fc receptor (FcRn) blockers may lower systemic exposures and reduce effectiveness of SOLIRIS. Closely monitor for reduced effectiveness of SOLIRIS.

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

References: 1. SOLIRIS. Prescribing Information. Alexion Pharmaceuticals, Inc. **2.** Lee JW, Sicre de Fontbrune F, Wong Lee Lee L, et al. Ravulizumab (ALXN1210) vs eculizumab in adult patients with PNH naive to complement inhibitors: the 301 study. *Blood*. 2019:133(6):530-539. **3.** Sahin F, Akay OM, Ayer M, et al. Pesg PNH diagnosis, follow-up and treatment guidelines. *Am J Blood Res*. 2016;6(2):19-27. **4.** Brodsky RA. Treatment and prognosis of paroxysmal nocturnal hemoglobinuria. UpToDate. Updated November 6, 2024. Accessed November 18, 2024. https://www.uptodate.com/contents/treatment-and-prognosis-of-paroxysmal-nocturnal-hemoglobinuria/print?search=Paroxysmal **5.** Jang JH, Kim JS, Yoon SS, et al. Predictive factors of mortality in population of patients with paroxysmal nocturnal hemoglobinuria (PNH): results from a Korean PNH registry. *J Korean Med Sci*. 2016;31(2):214-221. **6.** Schrezenmeier H, Muus P, Socié G, et al. Baseline characteristics and disease burden in patients in the International Paroxysmal Nocturnal Hemoglobinuria Registry. *Haematologica*. 2014;99(5):922-929. **7.** Risitano AM, Rotoli B. Paroxysmal nocturnal hemoglobinuria: pathophysiology, natural history and treatment options in the era of biological agents. *Biologics*. 2008;2(2):205-222. **8.** Parker CJ. *Wintrobe's Clinical Hematology*. 13th ed. Wolters Kluwer; 2014:785-808. **9.** Besa EC. Paroxysmal nocturnal hemoglobinuria (PNH). Medscape. Updated June 25, 2024. Accessed November 18, 2024. https://emedicine.medscape.com/article/207468-overview **10.** Risitano AM, Rotoli B. Paroxysmal nocturnal hemoglobinuria: pathophysiology, natural history and treatment options in the era of biological agents. *Biologics*. 2008;2(2):205-222. **11.** Tefferi A. Anemia in adults: a contemporary approach to diagnosis. *Mayo Clin Proc*. 2003;78(10):1274-1280. **12.** EMPAVELI. Prescribing Information. Apellis Pharmaceuticals, Inc. **13.** FABHALTA. Prescribing Information. Novartis AG. **14.** PIASKY. Prescribing Information. Genentech, Inc. **15.** EPYSQLI. Prescribing Information. Samsung Bioepis Co., Ltd. **16.** BKEMV. Prescribing Information. Amgen Inc.

ALEXION® AstraZeneca Rare Disease