Sample Letter of Medical Necessity for SOLIRIS® (eculizumab)

for Paroxysmal Nocturnal Hemoglobinuria (PNH)

INDICATION

Paroxysmal Nocturnal Hemoglobinuria (PNH)

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

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, including Boxed WARNING regarding serious 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.

[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 or iptacopan]. In my medical opinion, [pegcetacoplan or iptacopan] is not an appropriate step for my patient based on the following relevant criteria [insert reason(s) why pegcetacoplan or iptacopan 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]

[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 and iptacopan).

- ☐ The patient has hypersensitivity to any of the excipients of pegcetacoplan[10]
- ☐ The patient has hypersensitivity to any of the excipients of iptacopan[11]

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]

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 27, 2023. Accessed January 3, 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 December 7, 2023. Accessed January 3, 2024. https://emedicine.medscape.com/article/207468-overview **10.** EMPAVELI. Prescribing information. Apellis Pharmaceuticals, Inc. **11.** FABHALTA. Prescribing information. Novartis AG.

Please see Important Safety Information on pages 1 and 7 and the full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious meningococcal infections.

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

SELECT IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab) (cont.)

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.

Monitoring Disease Manifestations After Soliris Discontinuation

Treatment Discontinuation for PNH

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. 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) are: headache, nasopharyngitis, back pain, and nausea.

Please see Important Safety Information on pages 1 and 7 and the full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious meningococcal infections.

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ALEXION®
AstraZeneca Rare Disease