Sample Appeal Letter for SOLIRIS® (eculizumab)

In Adult Patients Who Have Anti-Acetylcholine Receptor (AChR) Antibody-Positive Generalized Myasthenia Gravis (gMG)

When a payer (health plan or pharmacy benefit manager [PBM]) denies a prior authorization (PA), pre-certification, or reauthorization request for SOLIRIS prescribed for the treatment of anti-acetylcholine receptor (anti-AChR) antibody-positive generalized myasthenia gravis (gMG), 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

SOLIRIS is indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) 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 6-7 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

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General Tips for Completing an Appeal Letter

Understand the appeals process for the specific payer. It's important to follow the payer's guidelines when submitting an appeal. Payers may have their own appeal request forms, which are usually available on their website. If a form is required, include it with your own letter. Be sure to contact the payer with any questions and to obtain written instructions for their appeals process.

When submitting an appeal, timing is critical. Refer to the denial letter to find the timelines for submitting the appeal, as well as any payer-specific guidelines.

In cases of medical urgency, your patient may request an expedited review and can expect to receive a decision within 72 hours. For more information, please visit HealthCare.gov.

Understand the reason for denial. It's important to read the denial letter carefully to understand the reason(s) provided. You may also call the payer to discuss a denial with them; this may help inform you about ways to resolve it in a timely manner.

- **If the denial is due to inaccurate or incomplete information,** carefully review the PA or reauthorization request that you submitted to identify information that is incorrect or was omitted. Resubmit the PA or reauthorization request when all the required information is accurate and complete.
- **If there is a medical reason for the denial,** ensure that your appeal letter includes specific and relevant medical information to support SOLIRIS use according to the payer's criteria. Your letter should clearly explain why you believe SOLIRIS is the most appropriate option for this patient.

Provide all supporting documentation at the same time and in the requested order, as shown in the individual payer's appeal instructions. This might include:

- The payer's appeal form (if required)
- Your appeal letter
- A copy of the payer's denial letter
- Supporting documentation, such as clinical notes, lab results, etc

Our dedicated Field Reimbursement Managers (FRMs) can work with you
In the event of a PA denial, FRMs can provide you or your office staff with educational support and guidance. FRMs can help with:

- Payer options for PA resubmission, including details about the resubmission process, peer-to-peer review, appeals process, and associated timelines
- Review of the redacted denial letter or Explanation of Benefits (EOB) letter to provide specific guidance on next steps and best practices

[John Doe, MD]
[Address]
[City, State ZIP]
[(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]

Re: [First/Second]-Level Appeal for Coverage Denial of SOLIRIS® (eculizumab)
[Request for Expedited Review Due to Medical Urgency]

Denial Letter Date: [MM/DD/YYYY]
Denial Reference #: [Denial Reference #]

Patient: [Name]
Date of Birth: [MM/DD/YYYY]
Member ID Number: [Insurance ID Number] Group Number: [Insurance Group Number]
Rx Bin: [Rx Bin Number] Rx PCN: [Rx PCN Number] Rx Group: [Rx Group Number]

Dear [Contact Name],

I am writing to appeal the coverage denial for [name of patient]'s treatment with SOLIRIS® (eculizumab) for anti-AChR antibody-positive generalized myasthenia gravis (gMG). In the letter referenced above, you stated that the reason for denial was [insert reason for denial]. This letter provides information about my patient's medical history and my treatment rationale.

1 REASON(S) FOR DENIAL AND TREATMENT RATIONALE

[In the appeal letter, you need to address every denial reason(s) stated in the denial letter from the insurance plan. Clearly explain why the reason(s) stated by the insurance plan as a cause for denial of coverage do not preclude use of SOLIRIS. Refer to "Treatment Rationale to Support Appeal" and "Resources Available to You" on pages 4 and 5, respectively. During the appeal process, it is generally not helpful to provide additional information beyond the specific denial reasons.]

In my medical opinion, SOLIRIS remains the most appropriate treatment for [name of patient]. The stated reason(s) for denial was [insert each denial reason and address each reason point by point, referring to "Treatment Rationale to Support Appeal" and "Resources Available to You" on pages 4 and 5, respectively; provide any laboratory results if applicable].

2 SUMMARY AND OPTIONAL MEDICAL HISTORY

As stated in my initial authorization request, [name of patient] presented with [insert specific clinical presentations and treatments for anti-AChR antibody-positive gMG, including any relevant patient-specific clinical scenarios demonstrating serious medical need. Consider referring to "Treatment Rationale to Support Appeal" on page 4 for a list of potential benefits from SOLIRIS treatment that may be relevant to this specific patient. You may also wish to consult the Common Prior Authorization Criteria for SOLIRIS resource for an abbreviated list of common signs and symptoms of gMG.]

For the above reasons, I request that you reverse the coverage determination.

3

For your additional information, I am enclosing [list enclosures, such as a copy of the denial letter, 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.
[Physician's Name], MD
[Physician's Identification Number]
[Physician's Practice Name]
[Physician's Phone Number]
[Physician's Fax Number]
[Physician's Email]

Enclosures
[At the bottom of your letter, list the items you have enclosed, such as the original denial letter and SOLIRIS Full Prescribing Information. Be sure to include every article that you referenced or any new documentation.]

1 Treatment Rationale to Support Appeal

Below are some common reasons your patient's PA, precertification, or reauthorization request may be denied. In your appeal letter, ensure that each reason for denial is addressed by sharing your medical expertise on why the requirement is satisfied or should not apply in your patient's individual case. Be sure to attach the supporting references and any additional documentation in your reply.

- **Denial due to indication:** SOLIRIS is indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.
- **Denial due to previous failed treatments:** Upon diagnosis with anti-AChR antibody-positive gMG, [Patient Name] was treated with [list treatments and the respective clinical responses here]. My rationale for treatment with SOLIRIS at this time is [include rationale here].
- **Denial due to pyridostigmine:** Pyridostigmine treatment was tried with the following results: [Describe clinical response and/or failure with pyridostigmine treatment]. For [this reason/these reasons], [include rationale for treatment with SOLIRIS].
- **Denial due to required use of Rituximab:**[1] In my medical opinion rituximab is not an appropriate step for my patient due to [his/her] history of [describe relevant medical history which may include the following (not all inclusive):
  - o Heart issues (eg, angina, acute myocardial infarction, heart arrhythmia, etc).] This condition is listed in the rituximab prescribing information as a warning and precaution in Section 5.7 under "Cardiovascular Adverse Reactions."
  - o Renal failure or insufficiencies.] This condition is listed in the rituximab prescribing information as a warning and precaution in Section 5.8 under "Renal Toxicity."
  - o Cytopenias and/or hypogammaglobulinemia.] This condition is listed in the rituximab prescribing information as a warning and precaution in Section 5.6 under "Infections," and Section 6.1 under "Cytopenias and hypogammaglobulinemia."
- **Denial due to required use of efgartigimod:**[2,3] In my medical opinion, efgartigimod is not an appropriate step for my patient as they would have been excluded from the ADAPT phase 3 clinical trial based on the following relevant study exclusion criteria. [List specific reason(s) based on provided select 'ADAPT Study Design – Select Patient Exclusion Criteria' below]

  ADAPT Study Design—Select Patient Exclusion Criteria
  - o Pregnant and lactating women, and those intending to become pregnant during the trial or within 90 days after the last dosing.
  - o Male patients who are sexually active and do not intend to use effective methods of contraception during the trial or within 90 days after the last dosing or male patients who plan to donate sperm during the trial or within 90 days after the last dosing.
  - o Patients with worsening muscle weakness secondary to concurrent infections or medications.
  - o Patients with known seropositivity or who test positive for an active viral infection for HBV (except patients who are seropositive because of HBV vaccination), HCV, or HIV.
- **Denial due to Myasthenia Gravis-Activities of Daily Living (MG-ADL) Score:*** Documentation of current score ≥6 on the MG-ADL scale, including case notes and other clinical impressions. If patient or caregiver has tracked changes in their MG-ADL score, include the score history; payers may require the MG-ADL scores for initial approval and reauthorizations of treatment.

*MG-ADL total score is based on a scale of 0 to 24; MG-ADL score of ≥6 assessed in REGAIN clinical trial population.[4]

Please see Important Safety Information on pages 1 and 6-7 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

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- **Denial due to AChR antibody test:** Evidence of a positive serological test for AChR antibodies (include laboratory results and date), and any other context you consider relevant around this laboratory result.
- **Denial due to meningococcal vaccinations:** Provide documentation of initial series and/or most recent booster(s) for MenACWY and MenB vaccinations.

2 Optional Medical History

- [Name of patient] is a[n] [age]-year-old [male/female] born [MM/DD/YYYY] who requires treatment with SOLIRIS after being diagnosed with anti-AChR antibody-positive gMG on [date of diagnosis MM/DD/YYYY].
- **Current symptoms:**[5] Examples such as profound muscle weakness throughout the body, as demonstrated by slurred speech, impaired swallowing, double vision, upper and lower extremity weakness, disabling fatigue, and/or shortness of breath due to respiratory muscle weakness
  - o It may be helpful to highlight in particular your patient's severity of disease based on your medical opinion and disease progression (eg, history of myasthenic crises, likelihood of impending crises, etc).
- **Myasthenia Gravis Foundation of America (MGFA) Clinical Classification***

  Documentation of status on the MGFA Clinical Classification Class II to V; include patient-specific clinical features/presentations and symptom severity. If classification has been tracked, include past MGFA Clinical Classification statuses.

*MGFA Clinical Classification is based on Class I to V; MGFA Class II-IV assessed in REGAIN clinical trial population.[4]

- Attestation that the patient has tried and failed therapies the plan requires before use of SOLIRIS is permitted, such as 2 immunosuppressants; oral corticosteroids; intravenous immunoglobulin, plasmapheresis, pyridostigmine, and/or rituximab in order to meet the plan's medical policy; pre-certification; or PA criteria.
- Documentation of your clinical rationale to initiate SOLIRIS for this patient, such as contraindications to other therapies, clinical presentation, recent medical history, or visits related to gMG, etc.

3 Resources Available to You

- The *Common Prior Authorization Criteria for SOLIRIS* resource provides you with information about common criteria used by health plans to make PA decisions for SOLIRIS for anti-AChR antibody-positive gMG.
- The *Clinical Reference Library Overview* provides information about specific scientific data and publications that may provide additional evidence for your Appeal Letter.

References: 1. Rituximab Prescribing information. Genentech Inc., 2021. **2.** Howard JF, Jr, et al. *Lancet Neurol*. 2021;20(7):526-536. **3.** An Efficacy and Safety Study of ARGX-113 in Patients With Myasthenia Gravis Who Have Generalized Muscle Weakness (ADAPT). ClinicalTrials.gov identifier: NCT03669588. Updated March 18, 2021. Accessed December 14, 2021. https://clinicaltrials.gov/ct2/show/NCT03669588 **4.** SOLIRIS. Prescribing information. Alexion Pharmaceuticals, Inc.; 2020. **5.** Meriggioli MN, et al. *Lancet Neurol*. 2009;8(5):475-490.

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INDICATION & IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab)

INDICATION

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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)*].

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.

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WARNINGS AND PRECAUTIONS (cont.)

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 reaction in the gMG placebo-controlled clinical trial (≥10%) was: musculoskeletal pain.

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.

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ALEXION®
AstraZeneca Rare Disease