Sample Letter of Appeal for VOYDEYA™ (danicopan)

for Extravascular Hemolysis (EVH) in Adult Patients With Paroxysmal Nocturnal Hemoglobinuria (PNH)

INDICATION & SELECT IMPORTANT SAFETY INFORMATION FOR VOYDEYA

INDICATION

VOYDEYA is indicated as an add-on therapy to ravulizumab or eculizumab for the treatment of extravascular hemolysis (EVH) in adults with paroxysmal nocturnal hemoglobinuria (PNH).

Limitation of Use:
VOYDEYA has not been shown to be effective as monotherapy and should only be prescribed as an add-on to ravulizumab or eculizumab.

SELECT IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFECTIONS CAUSED BY ENCAPSULATED BACTERIA

VOYDEYA, a complement inhibitor, increases the risk of serious infections, especially those caused by encapsulated bacteria, such as *Neisseria meningitidis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae* type B [*see Warnings and Precautions (5.1)*]. Life-threatening and fatal infections with encapsulated bacteria 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 encapsulated bacteria specifically, *Neisseria meningitidis* and *Streptococcus pneumoniae* at least 2 weeks prior to the first dose of VOYDEYA, unless the risks of delaying therapy with VOYDEYA outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated 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 encapsulated bacteria.**
- **Patients receiving VOYDEYA are at increased risk for invasive disease caused by encapsulated bacteria, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious infections and evaluate immediately if infection is suspected.**

Because of the risk of serious infections caused by encapsulated bacteria, VOYDEYA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the VOYDEYA REMS [*see Warnings and Precautions (5.2)*].

Please see pages 1, 12-13 for Important Safety Information, including Boxed WARNING regarding serious and life-threatening or fatal infections and accompanying full Prescribing Information for VOYDEYA (danicopan), pages 14-15 for Important Safety Information, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections and accompanying full Prescribing Information for ULTOMIRIS, and pages 16-17 for Important Safety Information, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections and accompanying full Prescribing Information for SOLIRIS.

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Introduction

~10% to 20% of patients treated with ULTOMIRIS® (ravulizumab-cwvz) or SOLIRIS® (eculizumab) may experience EVH.[1-3] Patients with EVH may experience persistent signs and symptoms of anemia with or without the need for blood transfusion.[1,3-5]

When a payer (health plan or pharmacy benefit manager [PBM]) denies a request for VOYDEYA™ (danicopan) prescribed as an add-on therapy to ULTOMIRIS or SOLIRIS for the treatment of EVH in adult patients with PNH, your patient has the right to appeal the decision.[1] If your patient wishes to appeal, you and your staff may assist by submitting an appeal letter and supporting documentation. VOYDEYA has not been shown to be effective as monotherapy and should only be prescribed as an add-on to ULTOMIRIS or SOLIRIS.[1]

As part of the appeals process, payers may request additional clinical documentation from you to support coverage of VOYDEYA. You may submit a letter in response to the denial letter or a payer's request for additional documentation. Your letter should explain why VOYDEYA is medically necessary for the specific patient and include supporting 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 Alexion. 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 of VOYDEYA.

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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 or electronic submission process, 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 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 and any payer-specific guidelines.

In cases of medical urgency, you or your patient may request an expedited review and can expect to receive a decision within 72 hours. For more information, please visit the payer's website or 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 you with ways to resolve it in a timely manner.

- **If the denial is due to inaccurate or incomplete information,** carefully review the prior authorization (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 or clinical reason for the denial,** ensure that your appeal letter includes specific and relevant medical information to support VOYDEYA™ (danicopan) use according to the payer's criteria. Your letter should clearly explain why you believe VOYDEYA 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, laboratory results, etc

For more information on the overall appeals process, please refer to the VOYDEYA Access Guide.

Alexion's dedicated Field Reimbursement Managers (FRMs) can work with you. In the event of a PA or reauthorization 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 appeals and resubmission processes, peer-to-peer review, appeals process, and associated timelines
- Review of the redacted denial letter to provide specific guidance on next steps and best practices

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[John Doe, MD/DO/NP/PA]
[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]

Re: [First/Second]-Level Appeal for Coverage Denial of VOYDEYA™ (danicopan)
[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 VOYDEYA™ (danicopan) as an add-on therapy to [ULTOMIRIS® (ravulizumab-cwvz) or SOLIRIS® (eculizumab)] for the treatment of extravascular hemolysis (EVH) in adult patients with paroxysmal nocturnal hemoglobinuria (PNH). In the letter referenced above, you stated that the reason for denial was [insert reason for denial: eg, a requirement of a history of trial/failure of, contraindication, or intolerance to pegcetacoplan or iptacopan therapy, lack of transfusion history, omission of necessary laboratory results (hemoglobin level, absolute reticulocyte count, absolute neutrophil count, platelet count), or signs and symptoms of EVH]. 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 will need to address every denial reason stated in the denial letter from the insurance plan. Provide a clear rationale and explain why you disagree with the denial reason. Refer to "Treatment Rationale to Support Appeal" on pages 6-9.

If applicable, describe your patient's treatment goals and your rationale as to why a step therapy through pegcetacoplan or iptacopan is not optimal for meeting these goals. Clearly explain why you have concerns regarding the requirement that your patient must have a history of trial/failure of, contraindication, or intolerance to pegcetacoplan or iptacopan. Refer to "Treatment Rationale to Support Appeal" on pages 6-9].

In my medical opinion, VOYDEYA as an add-on therapy to [ULTOMIRIS or SOLIRIS] is 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," "Optional Medical History," and "Attachments and Supporting Documentation" on pages 6-11; provide any laboratory results if applicable].

2

SUMMARY AND OPTIONAL MEDICAL HISTORY

[After addressing each stated reason for denial, you may wish to summarize your appeal and restate your patient's relevant medical history and laboratory results.]

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

SAMPLE ONLY
Please copy onto your letterhead.

As stated in my initial authorization request, [Name of patient] is currently stable on [ULTOMIRIS or SOLIRIS] and appropriate for treatment [or continued treatment] with VOYDEYA due to [Name of patient] experiencing EVH. This treatment regimen of VOYDEYA with ULTOMIRIS or SOLIRIS may help with the symptoms of EVH and the potentially devastating consequences of intravascular hemolysis (IVH).

Based on my assessment of their current clinical symptoms and laboratory results, they require [insert recommendation for addressing patient's current therapeutic needs (eg, effective EVH control shown by: improvement in hemoglobin levels, reduced need for or avoidance of red blood cell transfusions, reduced number of red blood cells transfused, improvement in fatigue, improvement in reticulocyte counts, improvement in platelet counts, improvement in absolute neutrophil counts, and improvement in other symptoms of hemolysis such as abdominal pain)] for which VOYDEYA treatment is medically necessary.

[Note: Payer policies may require physician attestation regarding the discussion of alternative treatment options and shared decision-making of a PNH with EVH treatment plan with patients previously or currently treated with VOYDEYA. To fulfill these requirements for continued use of VOYDEYA, the following text must be included in the appeal.]

I have counseled the patient on alternative chronic treatment options for PNH with EVH. My patient is involved in the decision-making process regarding their PNH therapy plan. Collectively, we have determined that VOYDEYA is the most clinically appropriate treatment choice for managing their EVH at this time.

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

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 [healthcare provider's phone number] to discuss.

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

Sincerely,

[Healthcare Provider's Name], [MD/DO/NP/PA]
[National Provider Identifier]
[Healthcare Provider's Practice Name]
[Healthcare Provider's Phone Number]
[Healthcare Provider's Fax Number]
[Healthcare Provider's Email]

Enclosures
[At the bottom of your letter, list the items you have enclosed. Be sure to include every article that you referenced or any new documentation.]

1 Treatment Rationale to Support Appeal

In your appeal letter, you may choose to include some of the reasons below for justification. Be sure to attach the supporting references and any additional documentation in your reply.

- **Denial due to indication:** VOYDEYA™ (danicopan) is indicated as an add-on therapy to ULTOMIRIS® (ravulizumab-cwvz) or SOLIRIS® (eculizumab) for the treatment of extravascular hemolysis (EVH) in adults with paroxysmal nocturnal hemoglobinuria (PNH).[1]
- **Denial due to vaccinations against serious infections caused by encapsulated bacteria:** Provide documentation of initial series and/or most recent booster(s) for vaccinations against serious infections caused by encapsulated bacteria, including *Neisseria meningitidis* (serogroups A, C, W, Y, and B), *Streptococcus pneumoniae*, and *Haemophilus influenzae* type B. Provide documentation of initial series and/or more recent boosters for vaccinations against *Neisseria meningitidis* (serogroups A, C, W, Y, and B) and *Streptococcus pneumoniae* at least 2 weeks prior to initiation of VOYDEYA.[1] If vaccinations are pending approval of therapy, please include a scheduled date for the patient to receive vaccinations.
- **Denial due to lack of transfusion history:** Patients did not need to have transfusion histories to be included in the phase 3 trial for VOYDEYA.[1] Therefore, my patient is still eligible for treatment with VOYDEYA as [he is/she is/they are] experiencing EVH.
- **Denial due to patient not meeting thrombotic risk:** Thrombotic risk has been associated with intravascular hemolysis (IVH), but not EVH.[6-8] Therefore, my patient, who is experiencing EVH, does not need to experience thrombosis in order to receive treatment with VOYDEYA for EVH.
- **Denial due to lack of patient treatment history with SOLIRIS or ULTOMIRIS:** Provide documentation of treatment history with a stable dose of [ULTOMIRIS or SOLIRIS].
- **Denial due to omission of necessary laboratory results:** Provide any appropriate or confirmatory laboratory values [evidence of anemia with decreased hemoglobin level, elevated absolute reticulocyte count, decreased platelet count, elevated absolute neutrophil count, increased alanine aminotransferase (ALT), and/or increased aspartate aminotransferase (AST)].[1,2,9,10]
- **Denial due to omission of clinical signs and symptoms of EVH:** Fatigue, transfusion burden, anemia, hematological indicators, and other symptoms of hemolysis including abdominal pain.[11-15]
- **Denial due to step therapy:** Please see the sections below for supporting statements against the use of step therapy through pegcetacoplan or iptacopan:

Click here to see denial due to required use of pegcetacoplan

Click here to see denial due to required use of iptacopan

1 Treatment Rationale to Support Appeal (cont.)

- **Denial due to required use of pegcetacoplan:** In my medical opinion, pegcetacoplan is not an appropriate step or alternative option for my patient based on the following relevant clinical criteria [below is a list of potential considerations why pegcetacoplan may not be appropriate for your patient given their case or specific clinical presentation. One or more of these reasons may apply to your patient's individual case].
  - **Health risk in performing or adhering to self-injection due to physical and/or cognitive impairment:** In my opinion [Name of patient] is unlikely to be able to perform the steps necessary to regularly self-administer pegcetacoplan given [insert complicating factors that may contribute to nonadherence to pegcetacoplan (physical and mental impairments, reduced functional capacity, lack of psychosocial or caregiver support, and/or patient lifestyle)]. Pegcetacoplan administration requires patients to self-administer twice weekly subcutaneous infusions via an infusion pump or an on body injector.[16] Given this route of administration, I do not believe that [Name of patient] can successfully adhere to this treatment regimen.
  - **Patient is currently stable on ULTOMIRIS® (ravulizumab-cwvz) or SOLIRIS® (eculizumab):** My primary concern when treating a patient with paroxysmal nocturnal hemoglobinuria is control of IVH which leads to the most devastating effects of the disease leading to morbidity and early mortality.[6,7] ULTOMIRIS and SOLIRIS are the standard of care for controlling IVH, and as such I am not comfortable transitioning my patient off of [ULTOMIRIS or SOLIRIS] but stress the need to provide relief of signs and symptoms of EVH.[17-20] VOYDEYA™ (danicopan) met all the primary and secondary endpoints in the phase 3 trial.[1,21] My patient meets the inclusion criteria of that trial.
  - **Patient has or has a history of breakthrough hemolysis (BTH) and/or major adverse vascular events (MAVEs):** Based on my experience and what I have heard from colleagues, therapy with pegcetacoplan resulted in a relatively high rate of BTH events. Therefore, I am not comfortable with switching my patient to pegcetacoplan especially since my patient's BTH is currently well-controlled with [ULTOMIRIS or SOLIRIS]. In my medical opinion, pegcetacoplan is not an appropriate step or alternative treatment option for my patient.[22]

PEGASUS Study Design – Select Patient Inclusion Criteria

In my medical opinion, pegcetacoplan is not an appropriate step for my patient as they would not have been included in the PEGASUS phase 3 clinical trial based on the following select relevant study inclusion criteria.[23,24] [List specific reason(s) based on provided select "PEGASUS Study – Select Patient Inclusion Criteria" below]

- Patients with hemoglobin level <10.5 g/dL despite treatment with stable doses of eculizumab for ≥3 months prior to screening[23,24]
- Patients were required to have reticulocytes >1.0 × upper limit of normal (ULN), platelets >50 × 10^9/L, and neutrophils >0.5 × 10^9/L[23,24]
- Participants were also required to have a body mass index <35.0 kg/m^2 [23,24]

PRINCE Study Design – Select Patient Inclusion Criteria

In my medical opinion, pegcetacoplan is not an appropriate step for my patient as they would not have been included in the PRINCE phase 3 clinical trial based on the following select relevant study inclusion criteria.[25] [List specific reason(s) based on provided select "PRINCE Study – Select Patient Inclusion Criteria" below]

- Hemoglobin level below the lower limit of normal (LLN) (male: <13.6 g/dL and female: <12.0 g/dL)[25]
- Ferritin levels ≥LLN (≥13 ng/mL) or total iron binding capacity ≤ULN (≤155 µg/dL)[25]
- A body mass index ≤35 kg/m^2, platelets >50,000/mm^3, and absolute neutrophil count >500/mm^3 [25]
- PNH diagnosis confirmed by high-sensitivity flow cytometry (granulocyte or monocyte clone >10%)[25]

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1 Treatment Rationale to Support Appeal (cont.)

- **Denial due to required use of iptacopan:** In my medical opinion, iptacopan is not an appropriate step or alternative treatment option for my patient based on the following relevant clinical criteria [below is a list of potential considerations why iptacopan may not be appropriate for your patient given their case or specific clinical presentation. One or more of these reasons may apply to your patient's individual case].
  - **Patient has or has a history of BTH and/or MAVEs:** Of the patients treated with iptacopan in the APPLY-PNH trial 48-week data, ~5% (n=3/62) experienced MAVEs and ~10% (n=6/62) had BTH.[26] In my medical opinion, iptacopan is not an appropriate step or alternative treatment option for [Name of patient] as they currently have evidence of BTH due to new or worsening [fatigue, hemoglobinuria, abdominal pain, dyspnea, anemia (hemoglobin <10 g/dL), MAVEs including thrombosis, dysphagia, or erectile dysfunction][27-29] [and/or a past medical history of BTH].
  - **Patient has thrombocytopenia and/or a history of thrombocytopenia:** In the APPLY-PNH clinical trial for iptacopan, 6% (4/62) of the patients in the iptacopan group vs 0% in the anti-C5 [SOLIRIS® (eculizumab) and ULTOMIRIS® (ravulizumab-cwvz)] group had thrombocytopenia.[30] In my medical opinion, iptacopan is not an appropriate step for [Name of patient] as they currently have laboratory evidence of thrombocytopenia with a platelet count of [insert platelet count] [and/or a past medical history of thrombocytopenia].
  - **Patient is taking a CYP2C8 inducer and/or a CYP2C8 inhibitor:** CYP2C8 inducers (eg, rifampin) may decrease iptacopan exposure, which may result in loss of or reduced efficacy of iptacopan. In my medical opinion, iptacopan is not an appropriate step for [Name of patient] as they are currently on a CYP2C8 inducer, [Name of CYP2C8 inducer], and will require additional monitoring for loss of efficacy of iptacopan. Further, if the loss of efficacy of iptacopan becomes evident, the patient may have to go through dose adjustments and/or discontinuation of [Name of CYP2C8 inducer] on which they are currently stable.[30]

    Strong CYP2C8 inhibitors (eg, gemfibrozil) may increase iptacopan exposure, which may result in an increased risk for adverse reactions with iptacopan. Therefore, coadministration of iptacopan with CYP2C8 inhibitors is not recommended. In my medical opinion, iptacopan is not an appropriate step for [Name of patient] as they are currently on a strong CYP2C8 inhibitor, [Name of strong CYP2C8 inhibitor], putting them at risk for increased adverse reactions of iptacopan such as hyperlipidemia.[30]
  - **Patient is currently stable on ULTOMIRIS or SOLIRIS:** My primary concern when treating a patient with paroxysmal nocturnal hemoglobinuria is control of IVH which leads to the most devastating effects of the disease leading to morbidity and early mortality.[6,7] ULTOMIRIS and SOLIRIS are the standard of care for controlling IVH, and as such I am not comfortable transitioning my patient off of [ULTOMIRIS or SOLIRIS] but stress the need to provide relief of signs and symptoms of EVH.[17-20] VOYDEYA™ (danicopan) met all the primary and secondary endpoints in the phase 3 trial.[1,21] My patient meets the inclusion criteria of that trial.
  - **Iptacopan lacks real-world evidence:** Iptacopan was recently approved in 2023 and lacks real-world evidence.[31] ULTOMIRIS has 6 years of approved use while SOLIRIS has 17 years of approved use, and they both demonstrated established safety and efficacy for patients with PNH.[18,19] ULTOMIRIS and SOLIRIS demonstrate improvement in MAVEs, including thrombosis, which is associated with mortality in patients with PNH.[25,26,32,33] Adding on VOYDEYA to [ULTOMIRIS or SOLIRIS] enables my patient to remain on this critical backbone therapy while providing the ability to improve EVH. In my medical opinion, iptacopan is not an appropriate step or alternative treatment option for my patient.

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1 Treatment Rationale to Support Appeal (cont.)

APPLY-PNH Study Design – Select Patient Inclusion Criteria

In my medical opinion, iptacopan is not an appropriate step for my patient as they would not have been included in the APPLY-PNH phase 3 clinical trial based on the following select relevant study inclusion criteria.[34] [List specific reason(s) based on provided select "APPLY-PNH Study – Select Patient Inclusion Criteria" below]

- Mean hemoglobin level <10 g/dL[34]
- Diagnosis of PNH confirmed by high-sensitivity flow cytometry with the clone size ≥10%[34]

APPOINT-PNH Study Design – Select Patient Inclusion Criteria

In my medical opinion, iptacopan is not an appropriate step for my patient as they would not have been included in the APPOINT-PNH phase 3 clinical trial based on the following select relevant study inclusion criteria.[35] [List specific reason(s) based on provided select "APPOINT-PNH Study – Select Patient Inclusion Criteria" below]

- Mean hemoglobin level <10 g/dL[35]
- Diagnosis of PNH confirmed by high-sensitivity flow cytometry with the clone size ≥10%[35]

Rationale for Reauthorization for Patients Currently Receiving VOYDEYA™ (danicopan)

Health plans often require a PA for patients receiving specialty medications and orphan drugs treating rare diseases. In many cases, after a patient has received a PA, the patient will need a reauthorization (sometimes known as a renewal authorization) after a specified time period. Obtaining a reauthorization for your patient is often required to confirm that the drug continues to be medically necessary and that the patient has responded to therapy.

- **Denial due to new documentation not previously required:**
  The reauthorization requirements for [Name of patient] have changed since they were initially authorized for treatment with VOYDEYA. [List of additional documentation that is now required] [is/are] now required to obtain reapproval for VOYDEYA. I am requesting a medical exception to continue [Name of patient]'s current treatment based on the original authorization criteria because they have had a demonstrated clinical improvement as evidenced by [insert demonstrated clinical response rationale and/or documentation].

- **Denial due to specific reauthorization clinical improvement criteria:**
  In my medical opinion, [Name of patient] is currently responding positively to treatment with VOYDEYA as evidenced by [list specific measures such as: improvement in hemoglobin levels, reduced need for or avoidance of red blood cell transfusions, reduced number of red blood cell units transfused, improvement in fatigue, improvement in reticulocyte counts].[11,21] Although [Name of patient] may partially meet [list specific denial reason/specified laboratory result or clinical measure] reauthorization criteria, I believe VOYDEYA is still the optimal therapy for reaching this patient's treatment goals of [controlling EVH, preventing red blood cell transfusions].[11,21]

- **Denial due to change in policy-required step edit:**
  [Name of patient] was diagnosed with PNH on [date], was diagnosed with EVH on [date], and has received VOYDEYA treatment since [date of first oral administration]. [Name of patient] received authorization for VOYDEYA based on initial PA criteria. [He is/She is/They are] currently responding positively to treatment with VOYDEYA as demonstrated by [improvement in hemoglobin levels, reduced need for or avoidance of red blood cell transfusions, reduced number of red blood cell units transfused, improvement in fatigue, improvement in reticulocyte counts].[11,21] [He is/She is/They are] currently stable on this treatment regimen, and it would be clinically inappropriate to require them to stop treatment with VOYDEYA or switch to another therapy given the risk of [hemolysis, hematologic instability].[12,13,15,36]

2 Optional Medical History

You may find it helpful to include a brief impactful medical history in your patient's appeal letter with only the most clinically significant facts repeated, such as:

- Laboratory results confirming a diagnosis of EVH
  - Hemoglobin level ≤9.5 g/dL
  - Absolute reticulocyte count ≥120 x 10^9/L
  - Platelet count ≥30,000/µL
  - Absolute neutrophil count ≥500/µL
- Clinical signs and symptoms of EVH
  - Fatigue
  - Transfusion burden
  - Anemia
  - Hematological indicators
  - Other symptoms of hemolysis including abdominal pain
- Clinical rationale for initiating VOYDEYA™ (danicopan) in this patient
  - History of transfusions
  - Impact of PNH on patient's level of physical function
  - Health risk in performing self-injection due to physical and/or cognitive impairment (ie, physical and mental impairments, reduced functional capacity, and lack of psychosocial or caregiver support)

3 Attachments and Supporting Documentation

In the appeal, you only need to include the original appeal letter and new supporting documentation. If you referred to any specific articles or obtained any photographs or attestations, be sure to attach them to the appeal.

Additional resources that may be used in submitting your letter of appeal may include the VOYDEYA Prescribing Information, the original denial letter, the VOYDEYA Letter of Medical Necessity, and the VOYDEYA Access Guide.

IMPORTANT SAFETY INFORMATION for VOYDEYA™ (danicopan) (cont.)

CONTRAINDICATIONS

Initiation in patients with unresolved serious infection caused by encapsulated bacteria, including *Neisseria meningitidis*, *Streptococcus pneumoniae*, or *Haemophilus influenzae* type B.

WARNINGS AND PRECAUTIONS

Serious Infections Caused by Encapsulated Bacteria
VOYDEYA, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by encapsulated bacteria, including *Neisseria meningitidis* (caused by any serogroup, including non-groupable strains), *Streptococcus pneumoniae*, and *Haemophilus influenzae* type B. Life-threatening and fatal infections with encapsulated bacteria have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors.

Complete, update, or revaccinate patients in accordance with ACIP recommendations considering the duration of VOYDEYA therapy. 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 VOYDEYA therapy is indicated in a patient who is not up to date with vaccines against encapsulated bacteria according to ACIP recommendations, provide antibacterial drug prophylaxis and administer these 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 VOYDEYA. The benefits and risks of treatment with VOYDEYA, 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 encapsulated bacteria.

Vaccination does not eliminate the risk of serious encapsulated bacterial infections, despite development of antibodies following vaccination. Closely monitor patients for early signs and symptoms of serious infection and evaluate patients immediately if an infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if they occur. Promptly treat known infections. Serious infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of VOYDEYA in patients who are undergoing treatment for serious infections.

VOYDEYA REMS
Due to the risk of serious infections caused by encapsulated bacteria, VOYDEYA is available only through a restricted program called VOYDEYA REMS. Per the REMS requirements:

Prescribers must enroll in the REMS, counsel patients about the risk of serious infections caused by encapsulated bacteria, provide patients with the REMS educational materials, assess patient vaccination status for vaccines against encapsulated bacteria, and vaccinate if needed according to current ACIP recommendations 2 weeks prior to the first dose of VOYDEYA. Antibacterial drug prophylaxis must be prescribed if treatment must be started urgently and the patient is not up to date with vaccines against encapsulated bacteria according to current ACIP recommendations at least 2 weeks prior to the first dose of VOYDEYA.

Pharmacies that dispense VOYDEYA must be certified in the VOYDEYA REMS and must verify prescribers are certified.

Patients must receive counseling from the prescriber about the need to receive vaccinations against encapsulated bacteria per ACIP recommendations, to take antibiotics as directed, the early signs and symptoms of serious infection, and be instructed to carry the Patient Safety Card at all times during and for 1 week following the last dose of VOYDEYA.

Further information is available at www.voydeyarems.com or 1-888-765-4747.

Hepatic Enzyme Increases
Hepatic enzyme elevations have been observed in patients treated with VOYDEYA. A total of 14% of patients receiving VOYDEYA had elevations in serum alanine aminotransferase (ALT). ALT elevations >3× the upper limit of normal (ULN) and ≤5× ULN occurred in 9% of VOYDEYA-treated patients, and ALT elevations >5× ULN and ≤10× ULN occurred in 5% of VOYDEYA-treated patients.

Assess liver enzyme test results prior to the initiation of VOYDEYA and periodically during treatment. Consider treatment interruption or discontinuation if elevations are clinically significant or if the patient becomes symptomatic. VOYDEYA has not been studied in patients with severe hepatic impairment.

Monitoring of PNH Manifestations After VOYDEYA Discontinuation
After discontinuing treatment with VOYDEYA, closely monitor patients for at least 2 weeks after the last dose for signs and symptoms of hemolysis. If discontinuation of VOYDEYA is necessary, continue background treatment with ravulizumab or eculizumab or consider alternative therapy if necessary. The signs and symptoms of hemolysis may include sudden decrease in hemoglobin or fatigue.

If hemolysis occurs after discontinuation of VOYDEYA, consider restarting treatment with VOYDEYA, if appropriate.

Hyperlipidemia
VOYDEYA increases total cholesterol and LDL-cholesterol. Of the 50 VOYDEYA-treated patients who had a normal total cholesterol level at baseline, 30% developed Grade 1 hypercholesterolemia. Of the 6 VOYDEYA-treated patients who had Grade 1 hypercholesterolemia at baseline, 1 patient experienced increased total cholesterol that worsened to Grade 2. Of the 54 VOYDEYA-treated patients who had LDL-cholesterol ≤130 mg/dL at baseline, 13% developed LDL-cholesterol >130-160 mg/dL, and 9% developed LDL-cholesterol >160-190 mg/dL.

IMPORTANT SAFETY INFORMATION for VOYDEYA™ (danicopan) (cont.)

WARNINGS AND PRECAUTIONS (cont.)

Hyperlipidemia (cont.)
Some patients required cholesterol-lowering medications. Monitor serum lipid parameters periodically during treatment with VOYDEYA and initiate cholesterol-lowering medication, if indicated.

ADVERSE REACTIONS

The most common adverse reaction reported in ≥10% of patients treated with VOYDEYA was headache. Serious adverse reactions were reported in 5% of patients who received VOYDEYA and included pancreatitis, cholecystitis, and increased blood bilirubin. No specific serious adverse reaction was reported in more than 1 patient treated with VOYDEYA. Adverse reactions reported in ≥5% of patients treated with VOYDEYA and greater than placebo in the randomized, controlled period included vomiting, pyrexia, increased alanine aminotransferase, hypertension, and pain in the extremities. Clinically relevant adverse reactions in <5% of patients included increased serum triglycerides.

DRUG INTERACTIONS

BCRP Substrates
Danicopan is a Breast Cancer Resistance Protein (BCRP) inhibitor. Concomitant use of VOYDEYA with a BCRP substrate increases the plasma concentrations of the BCRP substrate, which may increase the risk for adverse reactions associated with the BCRP substrate. If used together, monitor patients more frequently for adverse reactions associated with the BCRP substrate and consider dose reduction of the BCRP substrate according to its prescribing information.

Rosuvastatin
Danicopan significantly increased rosuvastatin exposure. The dose of rosuvastatin should not exceed 10mg once daily when concomitantly used with VOYDEYA.

P-glycoprotein Substrates
Danicopan is an inhibitor of P-glycoprotein (P-gp). Concomitant administration of VOYDEYA with P-gp substrates may increase the plasma concentrations of the P-gp substrates. Dose adjustment might be necessary for P-gp substrates where minimal concentration changes may lead to serious adverse reactions.

USE IN SPECIFIC POPULATIONS

Pregnancy
There are no available data on VOYDEYA use in pregnant individuals to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. There are risks to the mother and fetus associated with untreated PNH in pregnancy. The use of VOYDEYA in pregnant women or women planning to become pregnant may be considered following an assessment of the risks and benefits.

Lactation
There are no data on the presence of VOYDEYA in human milk, the effects on the breastfed child, or the effect on milk production. VOYDEYA is present in animal milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk.

Because of the potential for serious adverse reactions in the breastfed child, including serious infections with encapsulated bacteria and liver enzyme increases, advise patients not to breastfeed during treatment with VOYDEYA and for 3 days after the last dose.

Hepatic Impairment
No dose adjustment is required in patients with mild to moderate hepatic impairment. Studies have not been conducted in patients with severe hepatic impairment, therefore, avoid use of VOYDEYA in this patient population.

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 VOYDEYA (danicopan), including Boxed WARNING regarding serious and life-threatening or fatal infections.

INDICATION & IMPORTANT SAFETY INFORMATION for ULTOMIRIS® (ravulizumab-cwvz)

INDICATION

ULTOMIRIS is indicated for the treatment of adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH).

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

ULTOMIRIS, 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 ULTOMIRIS, unless the risks of delaying ULTOMIRIS 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 ULTOMIRIS 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, ULTOMIRIS 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

- Initiation in patients with unresolved serious *Neisseria meningitidis* infection.

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

ULTOMIRIS, 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 ULTOMIRIS therapy. 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 ULTOMIRIS therapy is indicated in a patient who is not up to date with meningococcal vaccines according to ACIP recommendations, provide 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 ULTOMIRIS. The benefits and risks of treatment with ULTOMIRIS, 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 they occur. Promptly treat known infections. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of ULTOMIRIS 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, ULTOMIRIS 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 the 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 ULTOMIRIS. 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 ULTOMIRIS. Patients must receive counseling about the need to receive meningococcal vaccines and to take antibiotics as directed, signs and symptoms of meningococcal infection, and be instructed to carry the Patient Safety Card at all times during and for 8 months following ULTOMIRIS treatment.

Further information is available at www.UltSolREMS.com or 1-888-765-4747.

IMPORTANT SAFETY INFORMATION for ULTOMIRIS® (ravulizumab-cwvz) (cont.)

WARNINGS AND PRECAUTIONS (cont.)

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

ULTOMIRIS blocks terminal complement activation; therefore, patients may have increased susceptibility to infections, especially with encapsulated bacteria, such as infections caused by *Neisseria meningitidis* but also *Streptococcus pneumoniae*, *Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*. Children treated with ULTOMIRIS 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 ULTOMIRIS are at increased risk for infections due to these organisms, even if they develop antibodies following vaccination.

Monitoring Disease Manifestations after ULTOMIRIS Discontinuation
After discontinuing treatment with ULTOMIRIS, closely monitor for signs and symptoms of hemolysis, identified by elevated LDH along with sudden decrease in PNH clone size or hemoglobin, or re-appearance of symptoms such as fatigue, hemoglobinuria, abdominal pain, shortness of breath (dyspnea), major adverse vascular event (including thrombosis), dysphagia, or erectile dysfunction. Monitor any patient who discontinues ULTOMIRIS for at least 16 weeks to detect hemolysis and other reactions. If signs and symptoms of hemolysis occur after discontinuation, including elevated LDH, consider restarting treatment with ULTOMIRIS.

Thromboembolic Event Management
The effect of withdrawal of anticoagulant therapy during treatment with ULTOMIRIS has not been established. Treatment should not alter anticoagulant management.

Infusion-Related Reactions
Administration of ULTOMIRIS may result in systemic infusion-related reactions, including anaphylaxis and hypersensitivity reactions. In clinical trials, infusion-related reactions occurred in approximately 1 to 7% of patients, including lower back pain, abdominal pain, muscle spasms, drop or elevation in blood pressure, rigors, limb discomfort, drug hypersensitivity (allergic reaction), and dysgeusia (bad taste). These reactions did not require discontinuation of ULTOMIRIS. If signs of cardiovascular instability or respiratory compromise occur, interrupt ULTOMIRIS and institute appropriate supportive measures.

ADVERSE REACTIONS

Adverse reactions reported in ≥10% or more of patients with PNH were upper respiratory tract infection and headache. Serious adverse reactions were reported in 15 (6.8%) patients receiving ULTOMIRIS. The serious adverse reactions in patients treated with ULTOMIRIS included hyperthermia and pyrexia. No serious adverse reaction was reported in more than 1 patient treated with ULTOMIRIS. One fatal case of sepsis was identified in a patient treated with ULTOMIRIS. In clinical studies, clinically relevant adverse reactions in 1% of adult patients include infusion-related reactions.

Adverse reactions reported in ≥10% of pediatric patients treated with ULTOMIRIS who were treatment-naïve vs. Eculizumab-experienced were anemia (20% vs. 25%), abdominal pain (0% vs. 38%), constipation (0% vs. 25%), pyrexia (20% vs. 13%), upper respiratory tract infection (20% vs. 75%), pain in extremity (0% vs. 25%), and headache (20% vs. 25%).

DRUG INTERACTIONS

Plasma Exchange, Plasmapheresis, and Intravenous Immunoglobulins
Concomitant use of ULTOMIRIS with plasma exchange (PE), plasmapheresis (PP), or intravenous immunoglobulin (IVIg) treatment can reduce serum ravulizumab concentrations and requires a supplemental dose of ULTOMIRIS.

Neonatal Fc Receptor Blockers
Concomitant use of ULTOMIRIS with neonatal Fc receptor (FcRn) blockers (e.g., efgartigimod) may lower systemic exposures and reduce effectiveness of ULTOMIRIS. Closely monitor for reduced effectiveness of ULTOMIRIS.

USE IN SPECIFIC POPULATIONS

Pregnancy Exposure Registry
There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ULTOMIRIS during pregnancy. Healthcare providers and patients may call 1-833-793-0563 or go to www.UltomirisPregnancyStudy.com to enroll in or to obtain information about the registry.

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

INDICATION & IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab)

INDICATION

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

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.

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.

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

WARNINGS AND PRECAUTIONS (cont.)

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

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. 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 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