



ULTOMIRIS[®]
(ravulizumab-cwvz)
injection for intravenous use
300 mg/3 mL vial

Sample Letter of Medical Necessity for ULTOMIRIS

for Paroxysmal Nocturnal Hemoglobinuria (PNH)

INDICATION

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

SELECT 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)*].

Please see Important Safety Information on pages [1](#), [8](#), and [9](#) and accompanying full [Prescribing Information](#) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

Introduction

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

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

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Please see Important Safety Information on pages **1**, **8**, and **9** and accompanying full **Prescribing Information** for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.



[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 ULTOMIRIS® (ravulizumab-cwvz)
[Request for Expedited Review Due to Medical Urgency]
Insured: [Name]; Policy Number: [Number]; Group Number: [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 ULTOMIRIS® (ravulizumab-cwvz). ULTOMIRIS is indicated for the treatment of adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH).

Patient History and Diagnosis

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

- 1 **For Complement Inhibitor Treatment-Naïve Patients** (reference page 5 for examples)
[Summary of rationale for treatment with ULTOMIRIS for this patient. Provide relevant PNH clinical signs and symptoms and describe the severity of 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.]
- 2 **For Complement Inhibitor Treatment-Experienced Patients** (reference page 6 for examples)
[Summary of rationale for treatment with ULTOMIRIS for this patient. Provide relevant PNH clinical signs and symptoms and describe the severity of 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 available, include patient's baseline clinical notes/laboratory values and documentation outlining initial prior authorization criteria required for ULTOMIRIS approval.]

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 ULTOMIRIS (US/ULT-P/0313) pages 6 to 13].

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



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

SAMPLE ONLY
Please copy onto your letterhead.

Treatment Plan

For [name of patient], the recommended dosing regimen with ULTOMIRIS for PNH is a loading dose of [insert weight-based loading dose] followed by a maintenance dose of [insert weight-based maintenance dose] every [insert frequency] that starts 2 weeks after the initial loading dose.

Dosing Reference

For patients with PNH, the recommended dosing regimen with ULTOMIRIS includes a weight-based loading dose. Maintenance dosing starts 2 weeks after the initial loading dose and then occurs once every 4 weeks for patients 5 to <20 kg or every 8 weeks for patients \geq 20 kg.

Patients 5 to <10 kg 600 mg loading dose; 300 mg maintenance dose (every 4 weeks)

Patients 10 to <20 kg 600 mg loading dose; 600 mg maintenance dose (every 4 weeks)

Patients 20 to <30 kg 900 mg loading dose; 2,100 mg maintenance dose (every 8 weeks)

Patients 30 to <40 kg 1,200 mg loading dose; 2,700 mg maintenance dose (every 8 weeks)

Patients 40 to <60 kg 2,400 mg loading dose; 3,000 mg maintenance dose (every 8 weeks)

Patients 60 to <100 kg 2,700 mg loading dose; 3,300 mg maintenance dose (every 8 weeks)

Patients \geq 100 kg 3,000 mg loading dose; 3,600 mg maintenance dose (every 8 weeks)

Summary

Based on the above, I am confident you will agree that ULTOMIRIS 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 ULTOMIRIS 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 ULTOMIRIS in PNH, copy of patient's insurance card, etc]

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

1 Complement Inhibitor Treatment-Naïve Patients

Indicated or Appropriate Patient Population

- Adult and pediatric patients one month of age and older with PNH¹
- 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 $\geq 5\%$ 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 $\geq 5\%$ ²⁻⁴
- Lactate Dehydrogenase (LDH): LDH level ≥ 1.5 times the upper limit of normal²⁻⁵
- 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 level (SCr), 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 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.

- The patient is not transfusion-dependent (17.9% of patients in Study 301 had not received packed RBC transfusions in the 1-year prior to study entry)²
- The patient has bone marrow failure (a sub-analysis of patients with bone marrow failure disorders from the ULTOMIRIS Study 301 demonstrated efficacy through 1 year)¹⁰

Patient Treatment Burden outlining why an ULTOMIRIS 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 or any history of non-adherence to oral medications.

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

Please see Important Safety Information on pages 1, 8, and 9 and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.



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 pegcetacoplan¹¹
- The patient has hypersensitivity to any of the excipients of iptacopan¹²

Vaccination Documentation

- Documentation indicating patient does not have active meningococcal infection¹
- 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 ULTOMIRIS.¹ If vaccinations are pending approval of therapy, please include a scheduled date for patient to receive the vaccinations
- If urgent treatment was indicated, include record of receiving the meningococcal vaccine as soon as possible, along with 2 weeks of antibacterial drug prophylaxis per ULTOMIRIS Prescribing Information¹

2 Complement Inhibitor Treatment-Experienced Patients

Indicated or Appropriate Patient Population

- Adult and pediatric patients one month of age and older with PNH¹
- Documented diagnosis of PNH, confirmed by high-sensitivity flow cytometry evaluation of RBCs and WBCs, with granulocyte or monocyte clone size of $\geq 5\%$ ¹³

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 $\geq 5\%$ ^{3,4,13}
- **Lactate Dehydrogenase (LDH):** LDH level ≥ 1.5 times the upper limit of normal^{3-5,13}
- **Transfusion History:** history of packed RBC transfusions, including both the number of infusions as well as the units transfused^{3,13}
- **Kidney Function:** serum creatinine level (SCr), 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^{3,4,6,13}
- **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 List is not all-inclusive of PNH clinical signs, symptoms, and laboratory findings.

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

- The patient was diagnosed with PNH on [insert date of diagnosis] and has been stable on a complement inhibitor therapy
- The patient is not transfusion dependent (12.8% of patients in Study 302 received a packed RBC/whole blood transfusion within 1 year prior to first dose)¹³
- History of failure or intolerance to proximal complement inhibitors (eg, pegcetacoplan and iptacopan)
- Inadequate control of LDH, a measure of intravascular hemolysis, with other approved therapies for PNH¹⁴⁻¹⁷ (in Study 302, there was a decrease of 0.82% in LDH change from baseline with ULTOMIRIS compared with an increase of 8.39% with SOLIRIS® (eculizumab) (difference, 9.21% [95% CI: -0.42%, 18.84%]). ULTOMIRIS demonstrated non-inferiority to SOLIRIS [$P_{inf} < 0.0006$])¹³
- Inadequate control of breakthrough hemolysis (BTH) with other approved therapies for PNH¹⁴⁻¹⁷ (in Study 302, BTH was reported in 0 ULTOMIRIS and 5 [5.1%] SOLIRIS patients, difference, 5.1% [95% CI: -8.89%, 18.99%; $P_{inf} < 0.0004$])¹³

Patient Treatment Burden including rationale for why an ULTOMIRIS dosing regimen is well-suited for this patient. For adult patients, switching to ULTOMIRIS reduces maintenance dosing frequency to 6 to 7 infusions per year.¹ Include any relevant information about the patient's ability to perform or adhere to self-injection due to physical or cognitive impairment or any history of non-adherence to oral medications.

- The patient has a history of non-adherence to oral medications
- The patient has a [physical and/or cognitive impairment] that may affect the patient's ability to perform or adhere to self-injection and lacks psychosocial or caregiver support
- The patient has reduced functional capacity due to their [insert complicating factor] and lacks psychosocial or caregiver support
- The patient's lifestyle is not suited for self-administration of a [twice daily oral dosing regimen or twice weekly subcutaneous injection] as the patient [insert lifestyle factors such as frequent travel for work]

Contraindications, if any, or intolerance to other agents indicated to treat PNH (eg, pegcetacoplan and iptacopan)

- The patient has hypersensitivity to pegcetacoplan or to any of the excipients¹¹
- The patient has hypersensitivity to iptacopan or to any of the excipients¹²



ALEXION ACCESS NAVIGATOR

Alexion Access Navigator is a dedicated resource website for US Healthcare Professionals and their offices that contains downloadable access and reimbursement materials for ULTOMIRIS® (ravulizumab-cwvz).

Online: <https://alexionaccessnavigator.com>

Please see Important Safety Information on pages 1, 8, and 9 and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

SELECT IMPORTANT SAFETY INFORMATION for ULTOMIRIS® (ravulizumab-cwvz) (cont'd)

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.

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.

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SELECT IMPORTANT SAFETY INFORMATION for ULTOMIRIS® (ravulizumab-cwvz) (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.**

References 1. ULTOMIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. 2. Lee JW, Sicre de Fontbrune F, Wong Lee L, et al. Ravulizumab (ALXN1210) vs eculizumab in adult patients with PNH naïve to complement inhibitors: the 301 study. *Blood*. 2019;133(6):530-539. 3. Sahin F, Akay OM, Ayer M, et al. 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 November 30, 2023. <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 May 20, 2021. Accessed November 30, 2023. <https://emedicine.medscape.com/article/207468-overview> 10. Risitano AM, Jang J, Gyeong-Won L. Transfusion requirements in adult patients with paroxysmal nocturnal hemoglobinuria with or without a history of bone marrow disorder receiving ravulizumab and eculizumab: results from a phase 3 non-inferiority study extension. *Blood*. 2020;136(Suppl 1):31-33. 11. EMPAVELI. Prescribing information. Alexion Pharmaceuticals, Inc. 12. FABHALTA. Prescribing information. Novartis AC. 13. Kulasekararaj AG, Hill A, Rottinghaus ST, et al. Ravulizumab (ALXN1210) vs eculizumab in C5-inhibitor-experienced adult patients with PNH: the 302 study. *Blood*. 2019;133(6):540-549. 14. Hillmen P, Szer J, Weitz I, et al. Pegcetacoplan versus eculizumab in paroxysmal nocturnal hemoglobinuria. *N Engl J Med*. 2021;384(11):1028-1037. 15. Apellis and Sobi report positive top-line results at 48 weeks from the phase 3 PEGASUS study of pegcetacoplan in PNH. News release. Apellis; December 2020. 16. Kulasekararaj AG, Gandhi S, Brodsky RA. Pegcetacoplan versus eculizumab in PNH. *N Engl J Med*. 2021;385(18):1724-1725. 17. Ueda Y, Takamori H, Nishimura JI. Pegcetacoplan versus eculizumab in PNH. *N Engl J Med*. 2021;385(18):1723-1724.