Sample Letter of Medical Necessity for VOYDEYA™ (danicopan)

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

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

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 Important Safety Information on pages 1 and 5-6 and accompanying full Prescribing Information for VOYDEYA (danicopan), including Boxed WARNING regarding serious and life-threatening or fatal infections.

Voydeya™ (danicopan) 50mg·100mg tablets

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

[Date]
[Contact Name] [Title] [Name of Health Insurance Plan or PBM]
[Address]
[City, State, ZIP Code]

Letter of Medical Necessity for VOYDEYA™ (danicopan)
[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 VOYDEYA™ (danicopan). 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).

Patient History and Diagnosis
[Patient's Name], born on [MM-DD-YEAR], is [age] years old, diagnosed with PNH, and currently undergoing treatment with [ravulizumab-cwvz or eculizumab]. As a result of experiencing extravascular hemolysis since [date of diagnosis MM-DD-YEAR], [he/she] now requires treatment with VOYDEYA as an add-on to [ravulizumab-cwvz or eculizumab].

For Complement Inhibitor Treatment–Experienced Patients (Reference medical history examples on page 4)
[Summary of rationale for treatment with VOYDEYA for this patient. Provide relevant PNH with EVH medical history 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 EVH 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 EVH. If available, include patient's baseline clinical notes/laboratory values and documentation outlining initial prior authorization criteria required for VOYDEYA approval.]

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

Treatment Plan
For [name of patient], the recommended dosing regimen with VOYDEYA is a starting dose of 150 mg three times a day administered orally. The dose can be increased to 200 mg three times a day if the patient's hemoglobin (Hgb) level has not increased by greater than 2 g/dL after 4 weeks of therapy, if the patient required a transfusion during the previous 4 weeks, or to achieve an appropriate Hgb response based on clinical judgment. VOYDEYA must not be administered as monotherapy and should be prescribed as an add-on to ravulizumab-cwvz or eculizumab.

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

Summary

Based on the above, I am confident that VOYDEYA is the best treatment 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 VOYDEYA, 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 VOYDEYA, copy of patient's insurance card, etc]

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

Complement Inhibitor Treatment–Experienced Patients

Indicated or Appropriate Patient Population

- Adults with paroxysmal nocturnal hemoglobinuria (PNH) who are experiencing extravascular hemolysis (EVH) and are receiving treatment with ravulizumab or eculizumab[1]
- Documented diagnosis of PNH with EVH confirmed by anemia (hemoglobin [Hgb] ≤9.5 g/dL) with absolute reticulocyte count ≥120 × 10^9/L with or without transfusion support[1-4]

Laboratory Results

- Transfusion history: history of packed red blood cell transfusions, including both the number of infusions as well as the units transfused[1,2,4]
- Hematology: hemoglobin ≤9.5 g/dL, absolute reticulocyte count ≥120 x 10^9/liter, platelet count ≥30,000/microliters (µL), absolute neutrophil counts ≥500/µL[1,2,3,5]
- Hepatic enzyme increases: aspartate aminotransferase (AST) and alanine aminotransferase (ALT)

Signs and Symptoms

- Signs and symptoms of EVH: fatigue, transfusion burden, anemia, hematological indicators, and other symptoms of hemolysis including abdominal pain[4,6-9]

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], was diagnosed with EVH on [insert date of diagnosis], and has failed or not tolerated current treatment with [pegcetacoplan or iptacopan] and would benefit from dual therapy with [ravulizumab-cwvz or eculizumab] and danicopan

Vaccination Documentation

- Documentation indicating patient does not have active serious infections caused by encapsulated bacteria including *Neisseria meningitidis* (serogroups A, C, W, Y, and B), *Streptococcus pneumoniae*, and *Haemophilus influenzae* type B[1]
- 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 at least 2 weeks prior to initiation of VOYDEYA.[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 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, as soon as possible along with antibacterial drug prophylaxis[1]

Contraindication, if any, or intolerance to agents indicated to treat PNH (including proximal complement inhibitors)

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

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.

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

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SELECT IMPORTANT SAFETY INFORMATION (cont.)

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.

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References: 1. VOYDEYA. Prescribing information. Alexion Pharmaceuticals, Inc. **2.** Lee JW, Griffin M, Kim JS, et al. Patients with paroxysmal nocturnal hemoglobinuria and clinically significant extravascular hemolysis on ravulizumab or eculizumab showed hemoglobin response superiority with add-on danicopan vs placebo. Presented at: European Hematology Association Hybrid Congress; June 8-11, 2023; Frankfurt, Germany. Abstract #P771. **3.** Kulasekararaj A, Mellor J, Earl L, et al. Prevalence of clinically significant extravascular hemolysis in stable C5 inhibitor-treated patients with PNH and its association with disease control, quality of life and treatment satisfaction. Presented at: European Hematology Association 2023 Hybrid Congress; June 8-11, 2023; Frankfurt, Germany. Abstract #PB2056. **4.** Data on file. Alexion Pharmaceuticals, Inc.; 2023. **5.** Danicopan as add-on therapy to a C5 inhibitor in paroxysmal nocturnal hemoglobinuria (PNH) participants who have clinically evident extravascular hemolysis (EVH) (ALPHA). ClinicalTrials.gov identifier: NCT04469465. Updated July 24, 2023. Accessed January 11, 2024. https://clinicaltrials.gov/study/NCT04469465 **6.** Dhaliwal G, Cornett PA, Tierney LM Jr. Hemolytic anemia. *Am Fam Physician*. 2004;69(11):2599-2606. **7.** Berentsen S, Hill A, Hill QA, Tvedt THA, Michel M. Novel insights into the treatment of complement-mediated hemolytic anemias. *Ther Adv Hematol*. 2019;10:1-20. **8.** Kulasekararaj AG, Brodsky RA, Hill A. Monitoring of patients with paroxysmal nocturnal hemoglobinuria on a complement inhibitor. *Am J Hematol*. 2021;96(7):E232-E235. **9.** Brodsky RA. Paroxysmal nocturnal hemoglobinuria. *Blood*. 2014;124(18):2804-2811. **10.** EMPAVELI. Prescribing information. Apellis Pharmaceuticals, Inc.; 2021. **11.** FABHALTA. Prescribing information. Novartis AG.

ALEXION®
AstraZeneca Rare Disease