Only ULTOMIRIS has demonstrated targeted terminal complement inhibition to reduce the risk of life-threatening vascular events for more than 5 years.[1-4]

96% (n=233/244) of patients **did not experience major adverse vascular events[†] through 5+ years[1]**

86% (n=209/243) of patients **did not experience breakthrough IVH[‡] through the 5-year extension period[1]**

Normalized LDH[4] | **Minimized transfusions[4]** | **Stabilized hemoglobin[4]** | **Controlled fatigue[2,3,5]**

*Based on US market share data.

[†]ULTOMIRIS was evaluated in 2 phase 3, randomized, open-label, active-controlled, noninferiority, multicenter studies evaluating the efficacy and safety of ULTOMIRIS with eculizumab in patients with PNH who were complement inhibitor-naïve and had active hemolysis (Study 301) and in clinically stable adult patients with PNH who had received eculizumab treatment for ≥6 months and had LDH levels ≤1.5 x ULN (246 U/L) at screening (Study 302). After the primary evaluation period (26 weeks), patients initiated on ULTOMIRIS continued on maintenance treatment, while patients initiated with eculizumab switched from eculizumab to ULTOMIRIS for the open-label extension (OLE). During the OLE, patients received weight-based dosing of ULTOMIRIS every 8 weeks. Outcomes of interest included change in LDH level from baseline and the proportion of patients experiencing breakthrough IVH and major adverse vascular events.[2,4,5]

[‡]Major adverse vascular events reported through the end of study were peripheral arterial thrombosis, coronary artery disease, cerebrovascular accident, angina unstable, deep vein thrombosis, acute myocardial infarction, pulmonary embolism, and cerebral venous thrombosis.[1]

[§]Breakthrough IVH was defined as at least 1 new or worsening symptom or sign of IVH in the presence of elevated LDH ≥2 x ULN, after prior LDH reduction to <1.5 x ULN on therapy.[1]

IVH=intravascular hemolysis; LDH=lactate dehydrogenase; PNH=paroxysmal nocturnal hemoglobinuria; ULN=upper limit of normal; U/L=units per liter.

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)*].

CONTRAINDICATIONS

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

Please see additional Important Safety Information throughout and full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

KEEP PNH UNDER CONTROL WITH ULTOMIRIS[1-4]

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

- **Durable disease control[1-4]**
  1 infusion every 8 weeks for PNH disease control[4,*]
- **#1 prescribed treatment for PNH[1,4,†]**
  Standard of care treatment for PNH[4,6]
- **Rapid and sustained terminal complement control[4,5,7]**
  Complete C5 inhibition reduced the risk of organ damage and thrombosis[2,5,6,8,9]

No new safety signals reported through more than 5 years of treatment[1]
An established and **consistent safety profile**[1]

Studied in the longest and largest PNH trial to date[1,2,4]
More than 5 years of **clinical evidence and real-world experience**[1,4]

26-week primary evaluation period (n=222)[4]

Most frequent adverse reactions (≥10%) with ULTOMIRIS: upper respiratory tract infection[‡] (39%), headache (32%)

5.6 years (entire study period): safety outcomes reported in the safety population (N=244)[1]

Most common TEAEs (≥10%) with ULTOMIRIS: headache (28.7%), upper respiratory tract infection (24.6%), pyrexia (19.7%), nasopharyngitis (18.9%), COVID-19 (17.2%), arthralgia (15.2%)

*Starting 2 weeks after the initial loading dose, maintenance doses are administered every 4 or 8 weeks (depending on body weight).[4]
†Based on US market share data.
‡Includes the preferred terms nasopharyngitis, upper respiratory tract infection, oropharyngeal pain, viral upper respiratory tract infection, rhinitis, respiratory tract infection, rhinorrhea, pharyngitis, and upper respiratory tract inflammation.[4]
ACIP=Advisory Committee on Immunization Practices; C5=complement protein 5; PNH=paroxysmal nocturnal hemoglobinuria; TEAE=treatment-emergent adverse event.

SELECT IMPORTANT SAFETY INFORMATION
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.

Please see additional Important Safety Information throughout and full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

INITIATING ULTOMIRIS
for the treatment of PNH

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

Patients starting ULTOMIRIS with no prior treatment[4]

Starting 2 weeks after the initial loading dose, maintenance doses are administered once every 4 or 8 weeks (depending on body weight).

ULTOMIRIS → Loading dose

ULTOMIRIS → Maintenance dose **EVERY 4 OR 8 WEEKS** (depending on body weight)

Patients switching from eculizumab to ULTOMIRIS[4]

The loading dose of ULTOMIRIS should be administered at the time of the next scheduled eculizumab dose. Maintenance doses are administered once every 4 or 8 weeks (depending on body weight), starting 2 weeks after the loading dose.

Eculizumab → Last eculizumab infusion

ULTOMIRIS → Loading dose **AT TIME OF NEXT SCHEDULED ECULIZUMAB DOSE**

ULTOMIRIS → Maintenance dose **EVERY 4 OR 8 WEEKS** (depending on body weight)

Determining the ULTOMIRIS dose and schedule[4,*]

Body weight range (kg)[†]	Loading dose (mg)	Maintenance dose (mg) and dosing interval	
5 to <10	600	300	Every 4 weeks
10 to <20	600	600	
20 to <30	900	2,100	Every 8 weeks
30 to <40	1,200	2,700	
40 to <60	2,400	3,000	
60 to <100	2,700	3,300	
100 or greater	3,000	3,600	

Monitor patients who discontinue ULTOMIRIS[4]:

- For at least 16 weeks to detect hemolysis and other reactions

Consider restarting treatment with ULTOMIRIS[4]:

- If signs and symptoms of hemolysis occur after discontinuation, including elevated LDH

» Sustain clinical benefits through continuation of ULTOMIRIS in appropriate patients.[4]

*The dosing schedule is allowed to occasionally vary within 7 days of the scheduled infusion day (except for the first maintenance dose of ULTOMIRIS), but the subsequent doses should be administered according to the original schedule.[4]
[†]Body weight at time of treatment.
LDH=lactate dehydrogenase; PNH=paroxysmal nocturnal hemoglobinuria.

SELECT IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS (continued)
Serious Meningococcal Infections (continued)
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*.

Please see additional Important Safety Information throughout and full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

For adult patients with PNH experiencing EVH,

GIVE THEM THE POWER OF PLUS

Voydeya® (danicopan) 50mg·100mg tablets

VOYDEYA® is designed to address extravascular hemolysis (EVH) without giving up backbone therapy with ULTOMIRIS®.[10,*]

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.

When added to ULTOMIRIS backbone therapy, VOYDEYA may help adult patients[4,10,11,†]:

- Increase hemoglobin levels
- Reduce the need for transfusion
- Feel less fatigue[‡]

SAFETY WAS ASSESSED IN THE 12-WEEK RANDOMIZATION PERIOD OF THE ALPHA CLINICAL TRIAL[10]

The most common adverse reaction (≥10%) with VOYDEYA was headache. Adverse reactions reported in ≥5% of VOYDEYA-treated patients with PNH and greater than placebo[§,‖] were headache, vomiting,[¶] pyrexia,[¶] increase in alanine aminotransferase, hypertension, and pain in extremity.[10]

VOYDEYA safety was similar through 72 weeks, with no discontinuations due to hemolysis.[12,#]

*VOYDEYA may also be taken with SOLIRIS® (eculizumab) to address EVH.[10]

†In a multiple-region, randomized, double-blind phase 3 study, adult patients with PNH experiencing EVH received either VOYDEYA (n=42) or placebo (n=21) in addition to their stable dose (≥6 months) of ULTOMIRIS or SOLIRIS for 12 weeks. After 12 weeks, patients on placebo were switched to VOYDEYA and patients in the VOYDEYA arm continued treatment for a total of 24 weeks. All patients continued to receive background therapy with either ULTOMIRIS or SOLIRIS. At the end of the treatment periods (Week 24), patients were offered to enter a long-term extension (LTE) period. The primary endpoint was the change in hemoglobin levels from baseline to Week 12.[10]

‡Fatigue was self-assessed using the FACIT-Fatigue Scale.[10]

§Clinically relevant adverse reactions in <5% of patients include increased serum triglycerides.[10]

‖Common Toxicity Criteria Adverse Events (CTCAE).[10]

¶Represents a composite of multiple, related adverse reactions.[10]

#Overall, there were 7 TEAEs of BTH in 5 participants (6 events per 100 patient-years). All BTH events were considered unrelated to danicopan treatment and were resolved rapidly without trial discontinuation, dose adjustment, or need for transfusion.[12]

BTH=breakthrough hemolysis; FACIT=Functional Assessment of Chronic Illness Therapy; PNH=paroxysmal nocturnal hemoglobinuria; TEAE=treatment-emergent adverse event.

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.

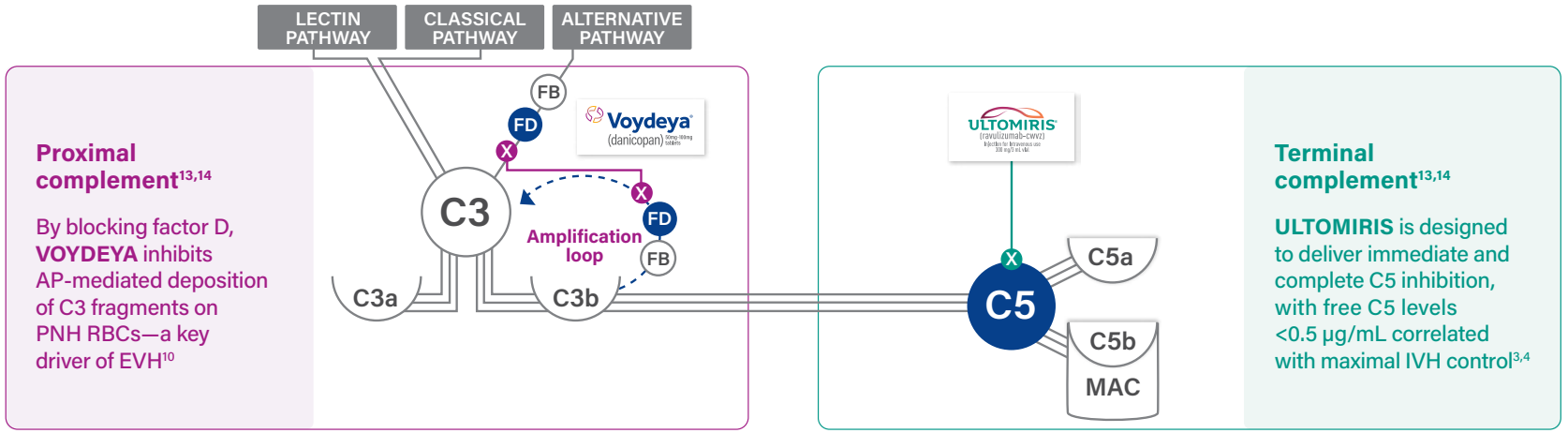
- **Complete or update vaccination for encapsulated bacteria specifically, *Neisseria meningitidis* and *Streptococcus pneumoniae* at least 2 weeks prior to the first dose of VOYDEYA, unless the risks of delaying therapy with VOYDEYA outweigh the risk of developing a serious infection. Comply with the 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 additional Important Safety Information throughout and full Prescribing Information for VOYDEYA, including Boxed WARNING regarding serious and life-threatening or fatal infections.

ADDING VOYDEYA TO ULTOMIRIS* IS DESIGNED TO PROVIDE DUAL INHIBITION OF COMPLEMENT[4,10]

For appropriate adult patients, adding AP-mediated proximal complement inhibition with VOYDEYA to targeted terminal complement inhibition with ULTOMIRIS† provides dual inhibition to help manage IVH* and EVH‡ for those who need it.[4,10]



*Free C5 levels of <0.5 µg/mL were correlated with maximal IVH control and complete terminal complement inhibition in patients with PNH.[4]
†VOYDEYA may also be taken with SOLIRIS® (eculizumab) to address EVH.[10]
‡VOYDEYA is designed to prevent the AP-mediated deposition of C3 fragments on PNH RBCs; such deposition is a key cause of the EVH that is observed in a subset of patients with PNH on treatment with a C5 inhibitor.[10]
AP=alternative pathway; C3=complement protein 3; C5=complement protein 5; EVH=extravascular hemolysis; FB=factor B; FD=factor D; IVH=intravascular hemolysis; MAC=membrane attack complex; PNH=paroxysmal nocturnal hemoglobinuria; RBC=red blood cell.

SELECT IMPORTANT SAFETY INFORMATION

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.

Please see additional Important Safety Information throughout and full Prescribing Information for VOYDEYA, including Boxed WARNING regarding serious and life-threatening or fatal infections.

Voydeya® (danicopan) 50mg·100mg tablets

VOYDEYA IS AN ADD-ON TO ULTOMIRIS TO ADDRESS EVH

RAPID AND SUSTAINED IMPROVEMENTS IN HEMOGLOBIN LEVELS[10,11,*]

2.9 g/dL (±0.211)‡

Primary endpoint
Patients who took VOYDEYA achieved a **clinically meaningful† and statistically significant increase of 2.9 (±0.211)‡ g/dL in mean hemoglobin levels** compared with 0.5 (±0.313) g/dL for placebo (*P*=0.0007) at 12 weeks.[1,10,11]

Sustained Hgb control
Hemoglobin improvements were maintained through Week 72[12]

REDUCED NEED FOR TRANSFUSION[12]

Statistically significant improvements seen at Week 12 and sustained through Week 72 in key secondary endpoints[10,12]

78.9% n=45/57 **of patients were transfusion-free from baseline to Week 12 (*P*≤0.001)** compared with 27.6% of patients (n=8/29) on placebo.[12]

37.4% **reduction in absolute reticulocyte count from baseline to Week 12 (*P*<0.0001)** compared with a 0.4% reduction for patients on placebo.[12,§]

INITIATING VOYDEYA FOR THE TREATMENT OF PNH

VOYDEYA is an oral, TID, add-on treatment to ULTOMIRIS or SOLIRIS[10]

VOYDEYA is a round, white oral tablet and is available in 2 dosage strengths[10]:

- The recommended starting dosage of VOYDEYA for adult patients is 150 mg TID
- Depending on clinical response, dosage can be increased to 200 mg TID
- VOYDEYA should not be administered as monotherapy

Among study participants, 73.8% were escalated to the maximum dose of 200 mg TID.[12]

ULTOMIRIS continues to provide critical PNH control even if your patient misses a dose of VOYDEYA.[4]

*Baseline disease characteristics between the 2 treatment groups were generally balanced and were indicative of EVH.[1,10]
†A change in hemoglobin of ≥2 g/dL is considered clinically meaningful.[1]
‡Data presented as LS mean (± SE).[1]
§Significantly reduced absolute reticulocyte count from baseline at Week 12 compared to placebo, with a treatment difference of -92.5 x 10^9/L (SEM: 8.2) (*P*<0.0001).[12]
EVH=extravascular hemolysis; Hgb=hemoglobin; LS=least squares; PNH=paroxysmal nocturnal hemoglobinuria; SE=standard error; SEM=standard error of the mean; TID=3 times a day.

SELECT IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS (continued)
Serious Infections Caused by Encapsulated Bacteria (continued)
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.

Please see additional Important Safety Information throughout and full Prescribing Information for VOYDEYA, including Boxed WARNING regarding serious and life-threatening or fatal infections.

ONESOURCE®
Personalized Patient Support from Alexion

SUPPORTING YOUR PATIENTS WITH PNH IN EVERY WAY

Patients and healthcare providers can expect the same level of patient support and resources with ULTOMIRIS, VOYDEYA, and SOLIRIS, with access to a dedicated Alexion representative and OneSource™ partner. Enrollment in OneSource will also allow patients to take advantage of various programs that Alexion offers in the event of delays or denials.

Help your patients get started on treatment without delay

On average, patients enrolled in OneSource start ULTOMIRIS within a week after receiving consent.[1,*]

Financial assistance is available

No matter what kind of insurance your patient has, we can provide information about resources available that may be able to help cover some of the costs of their Alexion treatment.

Alexion OneSource CoPay Program

The CoPay Program provides financial assistance by covering the out-of-pocket treatment costs for eligible patients.[†,‡]

$0
in out-of-pocket costs for eligible patients[‖,¶]

Access Programs (VOYDEYA ONLY)

Free Limited Supply[§]

If your patient is commercially insured and their prescription is delayed by 5 or more days, they may be eligible for a 30-day supply, plus one refill (if needed).

Free Trial

If your patient has not yet tried VOYDEYA to treat EVH, they may be eligible for a free 30-day trial.

» Contact your OneSource team at 1-888-765-4747 or visit AlexionOneSource.com for more information.

*Includes patients with PNH enrolled in OneSource from March 2021 to August 2023.[1]
†The Program is valid only for patients with commercial insurance who have a valid prescription for an FDA-approved indication of ULTOMIRIS or VOYDEYA. The Program is not valid for patients eligible to be reimbursed by government insurance programs or other federal or state programs (including any state prescription drug assistance programs). Additional requirements may apply.
‡The Program provides financial assistance by covering eligible patients' out-of-pocket medication and infusion costs associated with ULTOMIRIS up to $15,000 US dollars per calendar year.
§Exclusions may apply.
‖Based on typical commercial patient out-of-pocket deductible limits.
¶Additional terms and conditions apply. Please contact OneSource with additional questions.
EVH=extravascular hemolysis; PNH=paroxysmal nocturnal hemoglobinuria.

Please see full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections, and full Prescribing Information for VOYDEYA, including Boxed WARNING regarding serious and life-threatening or fatal infections.

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

IMPORTANT SAFETY INFORMATION FOR ULTOMIRIS® (ravulizumab-cwvz) (continued)

WARNINGS AND PRECAUTIONS (continued)

Serious Meningococcal Infections (continued)

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.

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

IMPORTANT SAFETY INFORMATION FOR VOYDEYA® (danicopan) (continued)

WARNINGS AND PRECAUTIONS (continued)

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.

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

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

Voydeya®
(danicopan) 50mg·100mg tablets

Choose Sustained PNH Control with ULTOMIRIS[1-4] »

Rapid and sustained terminal complement control[4,5,7]

Complete C5 inhibition reduced the risk of organ damage and thrombosis[2,5,6,8,9]

Consistent safety profile[1]

No new safety signals reported through more than **5 years of treatment**

Convenient patient-preferred dosing[4,15]

Durable disease control with **1 infusion every 8 weeks**[1-4,*]

Discover more at SustainedControl.com

For adult patients with PNH experiencing EVH,

GIVE THEM THE POWER OF PLUS

VOYDEYA is designed to address extravascular hemolysis (EVH) without giving up backbone therapy with ULTOMIRIS.[10,†]

Discover more at TreatEVHsymptoms.com

*Starting 2 weeks after the initial loading dose, maintenance doses are administered every 4 or 8 weeks (depending on body weight).[4]
†VOYDEYA may also be taken with SOLIRIS to address EVH.[10]
C5=complement protein 5; EVH=extravascular hemolysis; PNH=paroxysmal nocturnal hemoglobinuria.

Please see full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections, and full Prescribing Information for VOYDEYA, including Boxed WARNING regarding serious and life-threatening or fatal infections.

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