ULTOMIRIS®
(ravulizumab-cwvz)
injection for intravenous use
300 mg/30 mL vial

DO YOU HAVE PNH PATIENTS LIKE JONATHAN & JENNIFER?

Learn about their stories and the types of PNH patients that may be appropriate for treatment with ULTOMIRIS® (ravulizumab-cwvz).

Actor portrayals

Only ULTOMIRIS has demonstrated efficacy to reduce the risk of life-threatening vascular events for more than 5 years.[1-4,a]

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

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

INDICATION & IMPORTANT SAFETY INFORMATION

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)*].

[a]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 lactate dehydrogenase (LDH) levels <1.5 x the upper limit of normal (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]
[b]Study was a Phase 3, open-label, randomized, active-controlled, multicenter study to evaluate the safety and efficacy of ravulizumab versus eculizumab administered by IV infusion to adult patients with PNH who were naïve to complement inhibitor treatment. The study was to enroll approximately 214 patients. In addition, patients rolled over from other ongoing studies of ravulizumab IV in patients with PNH into the Extension Period to receive ravulizumab.[1]

IV, intravenous; IVH, intravascular hemolysis; PNH, paroxysmal nocturnal hemoglobinuria.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information (UltomirisHCP.com/PI) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

PNH Patient Naive to Therapy

Jonathan[a]: a 35-year-old male, naïve to complement inhibition, complains of erectile dysfunction, fatigue and dyspnea. When he was diagnosed with PNH 5 years ago, he was reluctant to start treatment with eculizumab due to the need for frequent infusions and his busy work schedule. Jonathan is currently managed by his PCP with supportive care measures, but he is considering a new alternative since his symptoms have worsened and are causing limitations at work.

Only 6 to 7 doses per year[2,c]
Reduced opportunity for missed dosing

Jonathan's Diagnostic Journey[1,2,6]

2011

Patient History

Age: 30

Clinical Presentation
Erectile dysfunction, thrombocytopenia, and modest anemia

Lab Values
Hb, g/dL: 10
PLT, x 10^9/L: 90
WBC, x 10^9/L: 3.6
LDH, U/L: 650
Coombs Test: Negative

Diagnosis
Owing to the presence of Coombs-negative hemolytic anemia, HSFC was performed on peripheral blood to evaluate for PNH, and a 34% granulocyte clone size was identified

Management
Against medical advice, the patient declined treatment with eculizumab for personal reasons at this time. He was started on supportive care with iron, B12, and folic acid supplementation, and was subsequently lost to follow up when he moved away for work

Late 2016

Current Visit

December
Age: 35

Clinical Presentation
Recurrent erectile dysfunction, fatigue, and dyspnea on exertion

Lab Values
Hb, g/dL: 9.6
PLT, x 10^9/L: 87
WBC, x 10^9/L: 2.7
LDH, U/L: 1552

PNH Monitoring
HSFC was performed on peripheral blood to monitor the PNH granulocyte clone size, which had increased from 34% to 56% in 5 years

Management
Jonathan was still concerned about a frequent infusion schedule. However, since he was **naïve to complement inhibition**, he was considered for inclusion in the 301 study. After counseling and meningococcal vaccination, he was randomized to receive ULTOMIRIS® (ravulizumab-cwvz) infusions Q8W[b]

2017

May

(Study 301 Entry Point)
Age: 36

Study Entry Pre-Screen Clinical Presentation
Persistent erectile dysfunction, fatigue, and dyspnea have worsened

Pre-Screen Lab Values
Hb, g/dL: 7.1
PLT, x 10^9/L: 80
WBC, x 10^9/L: 2.7
LDH, U/L: 1783

PNH Monitoring
Granulocyte clone: 63%
Monocyte clone: 77.9%
Erythrocyte clone: 56.0%

FACIT-Fatigue[d] Score
29.7

Management
Started on ULTOMIRIS; patient was transfusion independent

August

(Study 301-3 Month Follow-Up[e])
Age: 36

Clinical Presentation
Dyspnea and fatigue improved and erectile dysfunction resolved

Lab Values
Hb, g/dL: 12.3
PLT, x 10^9/L: 89
WBC, x 10^9/L: 3.1
LDH, U/L: 258

FACIT-Fatigue Score
34.3

Adverse Events
Patient experienced headache after the first and second ULTOMIRIS infusions

Management
ULTOMIRIS

November

(Study 301-6 Month Follow-Up)
Age: 36

Clinical Presentation
Fatigue continued to improve, daily activities and work schedule have normalized

Lab Values
Hb, g/dL: 11.0
PLT, x 10^9/L: 70
WBC, x 10^9/L: 3.2
LDH, U/L: 232

PNH Monitoring
Granulocyte clone: 74.6%
Monocyte clone: 80.1%
Erythrocyte clone: 73.0%

FACIT-Fatigue Score
35.7

Adverse Events
Patient experienced upper respiratory tract infection during Week 22

Management
ULTOMIRIS

2018

May

(Study 301-12 Month Follow-Up[f])
Age: 37

Clinical Presentation
Reduction of hemolysis and improvements of clinical parameters observed and sustained within 1 year of ULTOMIRIS treatment

Pre-Screen Lab Values
Hb, g/dL: 11.7
PLT, x 10^9/L: 74
WBC, x 10^9/L: 3.2
LDH, U/L: 193

PNH Monitoring
Granulocyte clone: 79.8%
Monocyte clone: 83.5%
Erythrocyte clone: 80.0%

FACIT-Fatigue Score
36.5

Adverse Events
No additional adverse events reported

Management
ULTOMIRIS; patient remained transfusion independent

Individual results may vary

Reference Ranges[g]: **Hb, g/dL:** 13.2-17.1 **PLT, x 10^9/L:** 140-400 **WBC x 10^9/L:** 3.8-10.8 **LDH, U/L:** 246 U/L

[a]The narrative was adapted from an actual patient case from the ULTOMIRIS naïve (301) clinical trial.[1] [b]Starting 2 weeks after the initial loading dose, maintenance doses are administered every 8 weeks for adult patients and every 4 or 8 weeks for pediatric patients (depending on body weight).[2] [c]The mean (SD) terminal elimination half-life and clearance of ULTOMIRIS in patients with PNH are 49.6 (9.08) days and 0.08 (0.02) L/day, respectively.[2] [d]FACIT-Fatigue scores ranges from 0-52, with lower scores indicating more severe fatigue.[6] FACIT-Fatigue is self-reported, and patients were not blinded to treatment assignment. [e]Lab values were taken routinely throughout the trial. Efficacy endpoints were evaluated at 26 weeks. [f]Based on physician follow up with patient.[1] The randomized clinical trial concluded at 26 weeks. Individual results may vary. [g]Reference ranges for Hb, PLT, and WBC from Quest Diagnostics; reference range for LDH from study 301.

FACIT, Functional Assessment of Chronic Illness Therapy; Hb, hemoglobin; HSFC, high-sensitivity flow cytometry; LDH, lactate dehydrogenase; PCP, primary care physician; PLTs, platelets; PNH, paroxysmal nocturnal hemoglobinuria; Q2W, every 2 weeks; Q8W, every 8 weeks; SD, standard deviation; U/L, upper limit of normal; WBC, white blood cell.

IMPORTANT SAFETY INFORMATION (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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information (UltomirisHCP.com/PI) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

PNH Patient Currently on Eculizumab

Jennifer[a]: a 56-year-old female, with PNH diagnosis and a history of anemia and Budd-Chiari syndrome. She was on the maintenance dose of eculizumab for the past 2 years. Jennifer is concerned about managing a busy work and travel schedule around biweekly infusions with eculizumab and wants to discuss whether she is a candidate for a reduced infusion frequency with ULTOMIRIS® (ravulizumab-cwvz).

Deliver 8 weeks of PNH control with each dose of ULTOMIRIS.[2,b]

Jennifer's Diagnostic Journey[2,7]

2 years

Patient history (Age: 53)

Clinical presentation

Anemia, severe upper quadrant abdominal pain

Lab values

Hb: 10 g/dL
Reticulocytes: 4.9%
WBC: 3.9 x 10^9/L
PLTs: 100 x 10^9/L
LDH: 900 U/L
Bilirubin: 3 mg/dL
AST: 90 U/L
ALT: 75 U/L
D-dimer: 2400 ng/mL
Coombs Test: Negative result
Spiral CT of the Abdomen: Hepatic vein thrombosis (Budd-Chiari syndrome)

Diagnosis

PNH

Owing to evidence of Coombs-negative hemolytic anemia, HSFC—performed on peripheral blood—identified PNH clone (granulocytes, 67%)

Management

Eculizumab (concurrent with meningococcal vaccination and prophylactic antibiotics) and anticoagulant therapy were started[7]

Adverse events

Headache

3 months

Clinical presentation

The patient has been treated with eculizumab for the past two years.

Lab values

PNH granulocyte clone: 68%

Management

Eculizumab; anticoagulant therapy discontinued per patient request

The effect of withdrawal of anticoagulant therapy during eculizumab treatment has not been established. Therefore, treatment with eculizumab should not alter anticoagulant management[7]

Adverse events

No adverse event reported

4 months

Current visit (Age: 56) switched to ULTOMIRIS

Clinical presentation

Patient remains on eculizumab but has expressed interest in less frequent infusions. She comes in for a routine visit and to discuss whether she is a candidate for a reduced infusion frequency with ULTOMIRIS

Lab values before switching to ULTOMIRIS

Hb: 10.8 g/dL
Reticulocytes: 5.1%
WBC: 3.5 x 10^9/L
PLTs: 135 x 10^9/L
LDH: 225 U/L
Bilirubin: 1.0 mg/dL

Management

ULTOMIRIS was started at the time of next scheduled SOLIRIS dose

Adverse events

Headache

10 months

Clinical presentation

The patient was safely and effectively switched from eculizumab to ULTOMIRIS and has been clinically stable for the past 6 months

6-month post-ULTOMIRIS lab values

Hb: 11 g/dL
Reticulocytes: 5.2%
WBC: 4.2 x 10^9/L
PLTs: 140 x 10^9/L
LDH: 225 U/L
Bilirubin: 1.0 mg/dL
PNH granulocyte clone: 72%

Adverse events

Nausea

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Serious Meningococcal Infections (CONT'D)

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.

Individual results may vary

Reference Ranges:			
	ALT, U/L: 6-29	**D-dimer, ng/mL:** <500	**PLT, x 10^9/L:** 140-400
	AST, U/L: 10-35	**Hb (female), g/dL:** 11.7-15.5	**Reticulocytes, %:** 0.5-1.5
	Bilirubin, mg/dL: 0.2-1.2	**LDH, U/L:** 246	**WBC, x 10^9/L:** 3.8-10.8

Reference ranges for Hb, PLT, WBC, D-dimer, bilirubin, AST, and ALT from Quest Diagnostics; reference range for reticulocytes from MedlinePlus; reference for LDH from study 302.

[a]This patient narrative was deidentified and adapted from an actual patient case. [b]Starting 2 weeks after the initial loading dose, maintenance doses are administered every 8 weeks for adult patients and every 4 or 8 weeks for pediatric patients (depending on body weight).[2]

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CT, computed tomography; Hb, hemoglobin; HSFC, high-sensitivity flow cytometry; lab, laboratory; LDH, lactate dehydrogenase; PLTs, platelets; PNH, paroxysmal nocturnal hemoglobinuria; WBC, white blood cell.

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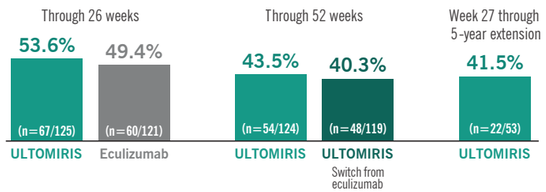
Robust and sustained efficacy across all endpoints for more than 5 years

ULTOMIRIS® (ravulizumab-cwvz) Demonstrated Robust LDH Normalization[2-5,8]

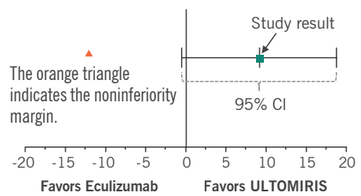
ULTOMIRIS was noninferior to eculizumab across all endpoints during the randomized treatment period (Week 0 to Week 26) in complement inhibitor naïve and experienced patients[2,4,5]

LDH Normalization in Complement Inhibitor–Naïve Patients[2-4,8]



Reflects adjusted prevalence within each treatment.
Adjusted odds ratio: 1.19 (95% CI, 0.80, 1.77; P_{int}<0.0001).

LDH Mean Percent Change From Baseline in Complement Inhibitor–Experienced Patients[5,9]



ULTOMIRIS (N=97)	Eculizumab (N=98)	Difference (95% CI)[a]
-0.82	8.39	9.21 (-0.42,18.84)[b]

ULTOMIRIS **achieved noninferiority**[c] compared to eculizumab for the primary endpoint, percent change in LDH from baseline to Day 183, in complement inhibitor–experienced patients[5,9]

Efficacy was maintained through the 5-year extension period of the complement inhibitor–naïve study, during which all patients received ULTOMIRIS[8]

[a]Difference (95% CI) was based on estimated difference in percent with 95% CI.[6] [b]Treatment difference was estimated for eculizumab–ravulizumab.[6] [c]A conclusion of noninferiority indicates the noninferiority margin is larger or smaller than the lower or upper bound of the 95% CI indicated.[5,9]

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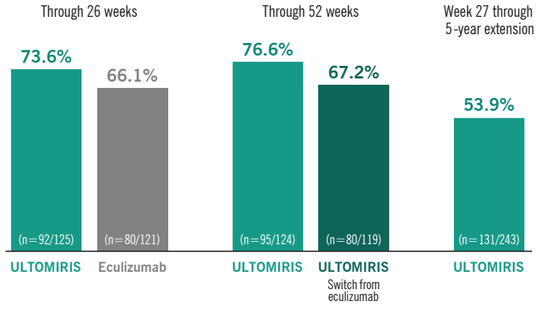
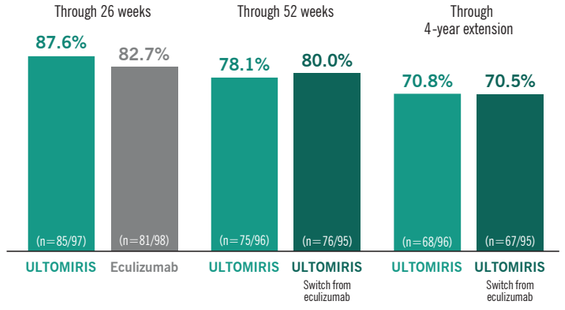
ULTOMIRIS Treatment Helped Minimize Transfusions[1-5]

Transfusion Avoidance in Complement Inhibitor–Naïve Patients[1-4]



Transfusion Avoidance in Complement Inhibitor–Experienced Patients[1,2,5]



Difference in rate: 6.8% (95% CI, -4.66, 18.14; P_{int}<0.0001). Based on estimated differences in percent with 95% CI.

CI, confidence interval; LDH, lactate dehydrogenase.

ULTOMIRIS Reduced the Risk of Thromboembolic Events and Improved Hemoglobin

In Complement Inhibitor–Naïve Patients[1,4]

Safety assessed, 26-week, 5.6 years, no new safety, and in the phase 3 clinical trials

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

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

68%	70%	45%
Weeks 1-26 (n=85/125)[e]	Weeks 27-52 (n=169/243)[f]	Week 27 through 5-year extension (n=110/243)[f]

Achieved hemoglobin stabilization[1,3,4,g]

In Complement Inhibitor–Experienced Patients[1,5]

98% Of patients did not experience **major adverse vascular events** through **more than 4 years** (n=188/191)[1]

92% Of patients did not experience **breakthrough IVH** through **more than 4 years** (n=176/191)[1]

76%	81%	62%
Weeks 1-26 (n=74/97)	Weeks 27-52 (n=155/191)	Week 27 through 4-year extension (n=120/191)

Achieved hemoglobin stabilization[1,5,10]

26-week primary evaluation period (n=222)[2]

Most frequent adverse reactions reported (≥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 (≥15%) with ULTOMIRIS: headache (28.7%), upper respiratory tract infection (24.6%), pyrexia (19.7%), nasopharyngitis (18.9%), COVID-19 (17.2%), arthralgia (15.2%)

[a]Major adverse vascular events through 5+ years[1,3,4]: Weeks 1-26: 1.6% (n=2/125); Weeks 27-52: 0.4% (n=1/243); entire study period: 4.5% (n=11/244). 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] [b]MAVE was defined as thrombophlebitis/deep vein thrombosis, renal vein/arterial thrombosis, mesenteric/visceral vein thrombosis, mesenteric/visceral arterial thrombosis, hepatic/portal vein thrombosis (Budd-Chiari syndrome), dermal thrombosis, acute peripheral vascular disease occlusion, cerebral arterial occlusion/cerebrovascular accident, cerebral venous occlusion, and pulmonary embolus. Nonthromboembolisms include myocardial infarction, transient ischemic attack, unstable angina, amputation (nontraumatic, nondiabetic), and gangrene (nontraumatic, nondiabetic).[1] [c]Breakthrough IVH through the 5-year extension period[1,3,4]: Weeks 1-26: 4.0% (n=5/125); Weeks 27-52: 2.4% (n=6/243); entire extension period: 14% (n=34/243).[1,3] [d]Breakthrough IVH was defined as at least 1 new or worsening symptom or sign of IVH in the presence of elevated LDH ≥2 × ULN, after prior LDH reduction to <1.5 × ULN on therapy.[1] [e]Full analysis set (all patients who received ≥1 dose of ULTOMIRIS and had ≥1 efficacy assessment after the first infusion).[3] [f]Extension set (all patients who entered the extension period).[3] [g]Defined as avoidance ≥2 g/dL decrease in hemoglobin level from baseline in the absence of a transfusion.[4]

IVH, intravascular hemolysis; LDH, Lactate dehydrogenase; TEAEs, treatment-emergent adverse events; ULN, upper limit of normal.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

Scan for full Prescribing Information

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 additional Important Safety Information throughout and accompanying full Prescribing Information (UltomirisHCP.com/PI) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

Image is not of an actual patient

ULTOMIRIS® (ravulizumab-cwvz) is the #1 prescribed treatment for PNH[2,10]

Help your patients with PNH get started on ULTOMIRIS

Fill out the Patient & Prescriber Start Form

Order the meningococcal vaccination series, provide a prescription for ULTOMIRIS, and enroll your patient in OneSource for support services.

Talk to your patients about copay assistance

$0 in out-of-pocket costs for eligible patients[a,b]

- The Alexion OneSource™ CoPay 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
- Valid only for patients with commercial insurance who have a valid prescription for a US FDA–approved indication of ULTOMIRIS. Not valid for costs eligible to be reimbursed by government insurance programs[c] or other federal or state programs (including any state prescription drug assistance programs)
- Additional requirements may apply. Contact Alexion OneSource for more information on patient eligibility

Enroll in the Risk Evaluation and Mitigation Strategy (REMS) program

Due to the risk of meningococcal infections, ULTOMIRIS is available only through a restricted program under REMS.

Scan to enroll in the REMS Program and see additional requirements. You can also call 1-888-765-4747 for more information.

[a]Based on typical commercial patient out-of-pocket deductible limits. [b]Additional terms and conditions apply. Please contact OneSource with additional questions. [c]Includes Medicaid, Medicare (including Medicare Part D), Medicare Advantage Plans, Medigap, Veterans Affairs, Department of Defense, or TRICARE. Patients residing in Massachusetts or Rhode Island are eligible for assistance with medication costs but are not eligible for assistance with infusion costs.

FDA, Food and Drug Administration; PNH, paroxysmal nocturnal hemoglobinuria.

References: 1. Data on file. Alexion Pharmaceuticals, Inc.; 2019. **2.** ULTOMIRIS. Prescribing Information. Alexion Pharmaceuticals, Inc. **3.** Schrezenmeier H, et al. *Ther Adv Hematol.* 2020;11:2040620720966137. **4.** Lee JW, et al. *Blood.* 2019;133(6):530-539. **5.** Kulasekararaj AG, et al. *Blood.* 2019;133(6):540-549. **6.** Cella D, et al. *J Pain Symptom Manage.* 2002;24(6):547-561. **7.** SOLIRIS. Prescribing Information. Alexion Pharmaceuticals, Inc. **8.** Data on file. ALXN1210-PNH-301 Clinical Study Report. Alexion Pharmaceuticals, Inc. **9.** Data on file. ALXN1210-PNH-302 Clinical Study Report. Alexion Pharmaceuticals, Inc. **10.** Data on file. Alexion Pharmaceuticals, Inc.

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ALEXION
AstraZeneca Rare Disease