
Actor portrayal

ALEXION
AstraZeneca Rare Disease

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

RISKS OF TMA RECURRENCE

Individualizing treatment duration decisions for your patients with atypical-HUS

Maintain appropriate duration of C5 inhibition for your patients with atypical-HUS

Assess the risk of TMA recurrence

Understanding patient prognosis through clinical history, complement biomarkers, transplant history, or genetic mutations will help in assessing the risk.[1-5]

Individualize C5 inhibition treatment

Based on your assessment and monitoring, continue C5 inhibition as appropriate for your patients to reduce the risk of relapse.[6]

Consider ULTOMIRIS

Switch to or restart ULTOMIRIS for immediate, complete, and sustained C5 inhibition. Following the minimum 6-month treatment duration, ULTOMIRIS use should be individualized.[6]

C5=complement protein 5; HUS=hemolytic uremic syndrome; TMA=thrombotic microangiopathy.

SELECT IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

Life-threatening meningococcal infections/sepsis have occurred in patients treated with ULTOMIRIS. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.

- **Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.**
- **Immunize patients with meningococcal vaccines at least 2 weeks prior to administering the first dose of ULTOMIRIS, unless the risks of delaying ULTOMIRIS therapy outweigh the risk of developing a meningococcal infection. See *Warnings and Precautions* for additional guidance on the management of the risk of meningococcal infection.**
- **Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Monitor patients for early signs of 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 REMS.

INDICATION

ULTOMIRIS is indicated for the treatment of adult and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).

Limitation of Use:
ULTOMIRIS is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

Subcutaneous Use in Adult Patients with aHUS
Subcutaneous administration of ULTOMIRIS is not approved for use in pediatric patients.

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 meningococcal infections/sepsis.

THE LIFE-THREATENING RISK OF TMA MAY BE CONTINUOUS[7,8]

Understanding TMA in atypical-HUS

Atypical-HUS is a life-threatening condition driven by overactivation of the complement system. Following discontinuation of a C5 inhibitor, patients may be at risk for complement-mediated TMA recurrence, which can have life-threatening consequences.[2,5,7-9]

Certain factors may increase the risk for TMA recurrence in patients with atypical-HUS

Identified genetic mutation

Mutations in complement genes have been associated with higher risk of TMA[1,2,5,10]

Clinical history of TMA

Multiple TMA manifestations may suggest high risk for subsequent TMAs in the presence of complement-triggering conditions[1,2,5]

Family history of TMA or renal disease

Unmanaged patients with a family history of TMA or renal disease have a higher risk of TMA recurrence[1,11]

History of renal transplant

Patients with certain genetic mutations are at a higher risk for TMA recurrence following renal transplantation[4,12,13]

Pediatric onset

Children are considered to be at high risk due to the increased frequency of complement-triggering events such as infections and vaccinations; TMA recurrence was reported to be high in unmanaged pediatric-onset patients[2,9]

Complement biomarkers/levels

Increased serum C5b-9 plasma levels after C5 inhibitor discontinuation in patients with atypical-HUS have been associated with a higher risk of relapse[3]

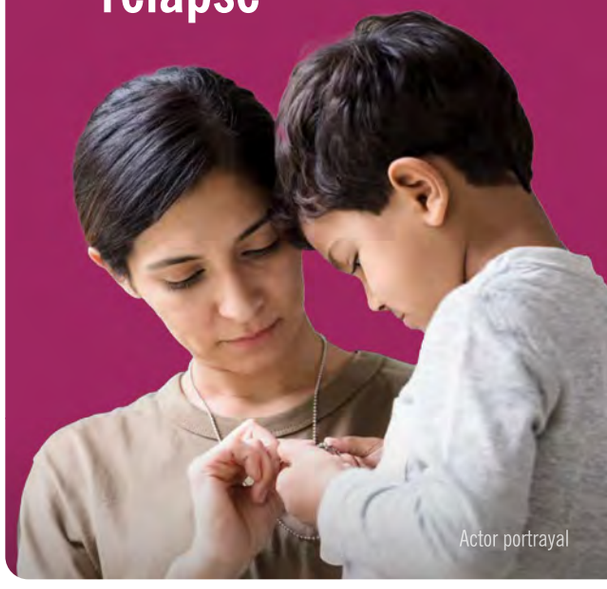
Exposure to triggers

Malignant hypertension or complications from pregnancy, including miscarriages, preeclampsia, HELLP syndrome, and others, may increase risk for recurrent TMA[14,15]

C5=complement protein 5; HELLP=hemolysis, elevated liver enzymes, low platelet counts; HUS=hemolytic uremic syndrome; TMA=thrombotic microangiopathy.

Of those patients who have had a TMA manifestation and have discontinued C5 inhibition therapy, approximately

25% to 30% will experience relapse[2,9]



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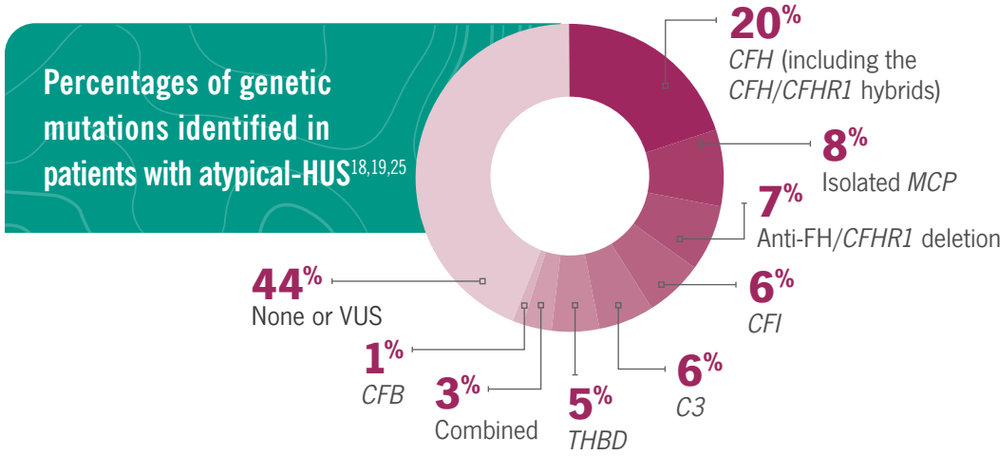
UNDERSTAND THE ROLE OF GENETICS IN ATYPICAL-HUS MANAGEMENT

Certain genetic mutations and related autoantibodies may play a role in the development of atypical-HUS[7,16-19]

- Atypical-HUS develops because of a **predisposition for complement dysregulation** and/or exposure to **factors that trigger complement activation**[8,20-22]
- Pathologic gene mutations that contribute to the underlying complement dysregulation are identified in **approximately 60% to 70% of patients with atypical-HUS**[7,16-19]
- In **approximately 30% to 40% of patients with atypical-HUS**, no underlying genetic mutations have been identified[17]
- However, as **mutations continue to be discovered**, some of these individuals may prove to have a genetic component[23,24]



Adapted from Noris M, et al. *Clin J Am Soc Nephrol*. 2010;5(10):1844-1859; Bresin E, et al. *J Am Soc Nephrol*. 2013;24(3):475-486; and Bruel A, et al. *Clin J Am Soc Nephrol*. 2017;12(8):1237-1247.

Certain genetic mutations put some patients at high risk for poor outcomes[4,12]

- **Patients with certain identified mutations are associated with a higher risk** of TMA recurrence, ESRD progression, and death within the next year after the first episode[4,12,26]
- **The risk of TMA recurrence is increased after a renal transplant** in certain mutations[4,12]

Clinical outcomes of patients with atypical-HUS carrying identified genetic mutations[4,12,a]

Gene	Risk of death or ESRD within the next year after first episode	Risk of TMA recurrence	Risk of TMA recurrence after renal transplant
CFH	50%-70%	50%	75%-90%
MCP	0%-6%	70%-90%	<20%
Anti-FH	30%-40%	40%-60%	Higher with increased antibody titers
CFI	50%	10%-30%	45%-80%
C3	60%	50%	40%-70%
THBD	50%	30%	1 patient
CFB	50%	3/3 without ESRD	100%

[a]Clinical outcomes of patients with atypical-HUS who were not treated with C5 inhibitors.
Adapted from Abbas F, et al. *World J Transplant*. 2018;8(5):122-141 and Campistol JM, et al. *Nefrologia*. 2015;35(5):421-447.

Genetic testing may be a valuable prognostic tool for managing patients with atypical-HUS.[8,20] However, as **about 30% to 40% of patients with atypical-HUS** do not have an identified genetic mutation, using genetic testing for diagnosis can have limitations.[17]

anti-FH=anti-complement factor H antibody; *C3*=complement component 3; *CFB*=complement factor B; *CFH*=complement factor H; *CFHR1*=complement factor H-related protein 1; *CFI*=complement factor I; ESRD=end-stage renal disease; HUS=hemolytic uremic syndrome; *MCP*=membrane cofactor protein; *THBD*=thrombomodulin; TMA=thrombotic microangiopathy; VUS=variants of unknown significance.

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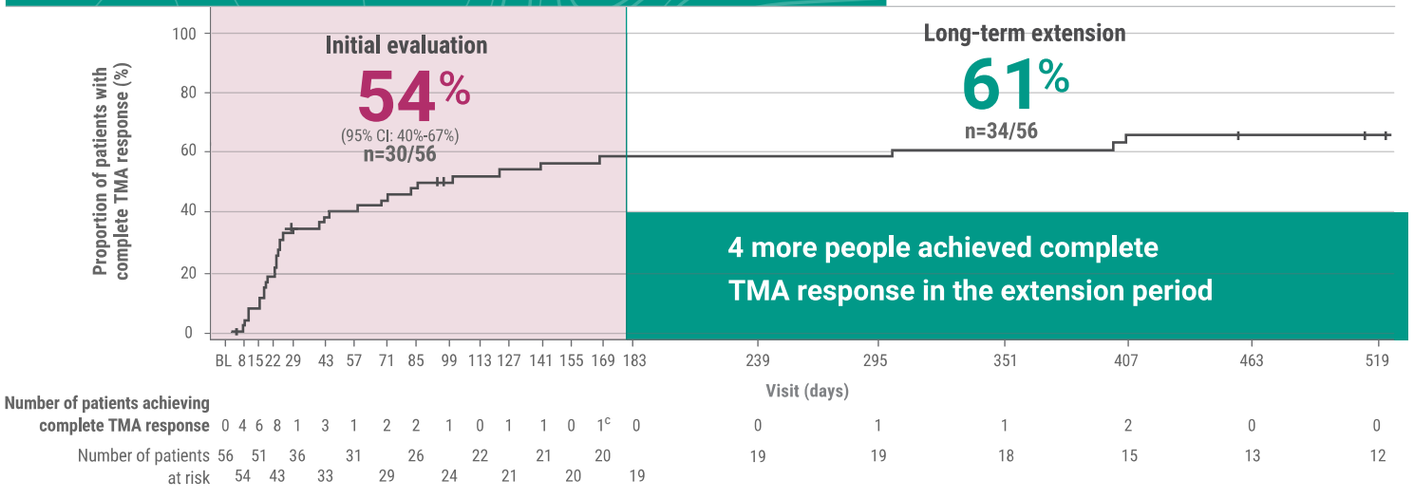
UNDERSTANDING COMPLETE TMA RESPONSE AND SUSTAINED HEMATOLOGIC MARKERS

Ongoing C5 inhibitor treatment—for example, with ULTOMIRIS—has been associated with sustained improvements in hematologic markers of atypical-HUS.[27,a]

Complete adult TMA response with ULTOMIRIS® (ravulizumab-cwvz)[27,b]



Study design[27]

A total of 56 adult patients with atypical-HUS who were naïve to complement inhibitor treatment prior to study entry were evaluated for efficacy. Of these, 49 patients completed the 26-week initial evaluation period. These patients entered the extension period of up to 4.5 years, with an interim analysis at 52 weeks. See complete study design at UltomirisHCP.com/ahus.

ULTOMIRIS has been established in helping patients achieve and maintain a complete TMA response[27]

Learn more about ULTOMIRIS safety and efficacy

bit.ly/3IVxehc

ULTOMIRIS has a minimum treatment duration of 6 months[6]

At 6 months, individualize treatment duration based on factors such as family history, clinical history, and risk of TMA recurrence.[1,2,5,11]

[a]As demonstrated through clinical trial extension period. [b]Complete TMA response was defined as normalization of hematological parameters (platelet count and lactate dehydrogenase) and ≥25% improvement in serum creatinine from baseline during the 26-week initial evaluation period. Patients had to meet all criteria at 2 separate assessments obtained at least 4 weeks (28 days) apart and any measurement in between.[1] Patients that did not have a response were censored at the date of last visit or study discontinuation at the time when the analysis was performed.[2] [c]Patients achieved initial complete TMA response measurement at day 169; however, confirmatory measurement was not achieved until the extension period (day 239).[27]
BL=baseline; C5=complement protein 5; HUS=hemolytic uremic syndrome; TMA=thrombotic microangiopathy.

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

CONTRAINDICATIONS

- Patients with unresolved *Neisseria meningitidis* infection.
- Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying ULTOMIRIS treatment outweigh the risks of developing a meningococcal infection.

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 meningococcal infections/sepsis.

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CONSIDER RISK OF TMA RECURRENCE WHEN DETERMINING TREATMENT DURATION

Discontinuation of C5 inhibitors increases the risk of TMA recurrence[2,5,9,a-c]

Among patients with atypical-HUS who discontinued C5 inhibitors[2,5,9]:

Approximately **25% to 30%** experienced TMA recurrence[2,5,9]

7.5 months
Median time to relapse, according to one study[2,5,9]

Risks of C5 inhibitor discontinuation include:

- TMA recurrence[5]
- Reduced renal function[5]
- Acute kidney injury[5,28]
- Irreversible CKD[28]
- Dialysis reinitiation[1,9]
- ESRD[9]
- Neurologic manifestations[9]
- Cardiovascular manifestations[9]
- Death[9]

TMA recurrence may lead to irreversible renal damage in some patients. Timely reintroduction of treatment may help improve renal function[1,5]

Talk to your patients

- Evaluate risk factors through discussion with your patients and performing tests such as genetic testing
- Understand their medical and family history, genetics, and how susceptible they are to triggers
- ULTOMIRIS has a minimum treatment duration of 6 months
- Plan to enable immediate reinitiation of C5 inhibition if needed

If you and your patient decide to discontinue C5 inhibition therapy, follow the important safety information regarding discontinuation within the Prescribing Information.

In patients with atypical-HUS, relapses could necessitate a longer duration of C5 inhibition therapy.[29]

The risk is approximately **2 to 3 times higher** in patients with a genetic pathogenic variant, especially particular variants[2,5,9,30,31]

[a]A long-term, prospective, observational, multicenter, follow-up study of 93 patients with atypical-HUS who were treated with at least 1 infusion of eculizumab in any of the 5 previously conducted parent studies.[2]
[b]Using the French atypical-HUS registry, 108 patients treated with eculizumab were identified, some of whom discontinued eculizumab.[5]
[c]Data from the global atypical-HUS registry, 5 clinical trials, and long-term extension study in 357 patients with atypical-HUS who discontinued eculizumab.[9]
C5=complement protein 5; CKD=chronic kidney disease; ESRD=end-stage renal disease; HUS=hemolytic uremic syndrome; TMA=thrombotic microangiopathy.

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

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

Life-threatening meningococcal infections have occurred in patients treated with ULTOMIRIS. The use of ULTOMIRIS increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis). Meningococcal disease due to any serogroup may occur.

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 meningococcal infections/sepsis.

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CAREFUL MONITORING FOLLOWING C5 INHIBITOR DISCONTINUATION

Education and ongoing monitoring are key to managing patients who discontinue C5 inhibitor treatment

Educate your patients on early TMA symptoms. Patients should check their blood pressure regularly and self-administer urine dipstick tests 3 times every week to monitor proteinuria or hematuria.[1,29]

MONITORING

TMA clinical signs and symptoms

Following C5 inhibitor discontinuation, monitor patients for signs and symptoms of TMA complications. The ULTOMIRIS® (ravulizumab-cwvz) label specifies a minimum of 12 months for such monitoring.[1,2] Consider the following:

- Changes in mental status
- Seizures
- Angina
- Dyspnea
- Thrombosis
- Increasing blood pressure

Follow up every 2 to 4 weeks, depending on whether a genetic mutation is found.

When to consider reinstitution of C5 inhibitor

If TMA complications occur after C5 inhibitor discontinuation, consider reinstitution of C5 inhibitor treatment or appropriate organ-specific supportive measures.[6]

Ask your patients to call immediately

if they experience a sudden increase in blood pressure, changes in their urine, or any other sign that could indicate a TMA manifestation or exposure to a trigger.

Laboratory tests for monitoring patients with atypical-HUS following C5 inhibitor discontinuation[2,6]

Monitor for laboratory signs of TMA after C5 inhibitor discontinuation (occurrence of 2 or repeated measurement of any of the following):

- ↓ **A decrease in platelet count by ≥25% and < LLN** compared to baseline or the peak platelet count during C5 inhibitor treatment
- ↑ **An increase in serum creatinine by ≥25% and > ULN** compared to baseline or nadir during C5 inhibitor treatment
- ↑ **An increase in serum LDH by ≥25% and > ULN** compared to baseline or nadir during C5 inhibitor treatment

C5=complement protein 5; HUS=hemolytic uremic syndrome; LDH=lactate dehydrogenase; LLN=lower limit of normal; TMA=thrombotic microangiopathy; ULN=upper limit of normal.

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

Serious Meningococcal Infections (continued)

Vaccinate or revaccinate for meningococcal disease according to the most current ACIP recommendations for patients with complement deficiencies. Immunize patients without history of meningococcal vaccination at least 2 weeks prior to the first dose of ULTOMIRIS. Patients who initiate ULTOMIRIS treatment less than 2 weeks after receiving meningococcal vaccine(s) must receive appropriate prophylactic antibiotics until 2 weeks after vaccination.

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 meningococcal infections/sepsis.

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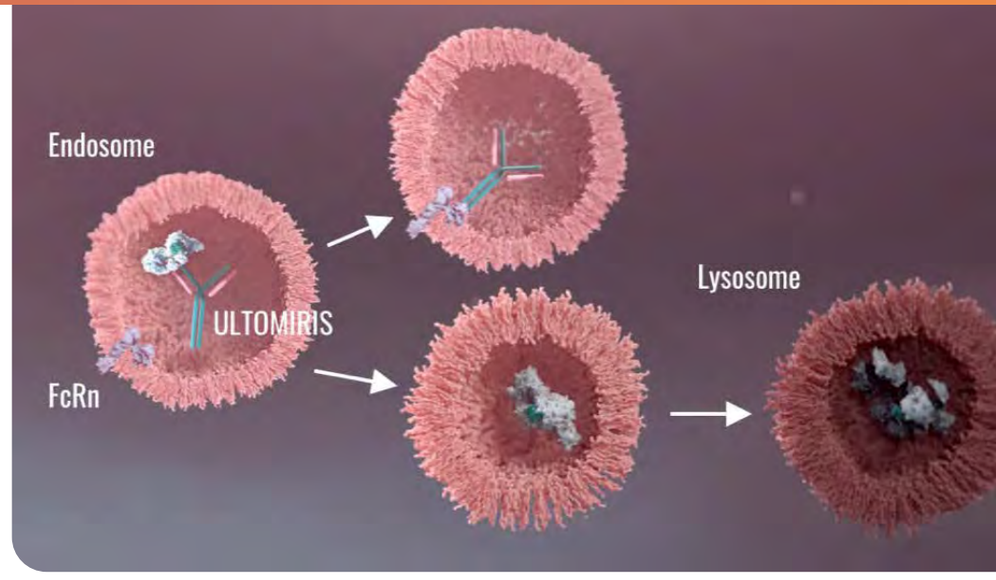
ULTOMIRIS TREATMENT IN PATIENTS WITH ATYPICAL-HUS

ULTOMIRIS provides immediate, complete, and sustained inhibition of C5 for up to 8 weeks[6,a]

- Engineered to bind to FcRn with greater affinity than eculizumab[6,27,32,b]
- Delivers long-acting treatment with a half-life approximately 4x longer than eculizumab[6,33,c]

Determine the risk factors for your patients with atypical-HUS to have a TMA recurrence. For certain patients, consider rapidly transitioning them to or restarting them on ULTOMIRIS, the first and only long-acting complement inhibitor.



Moving to a long-acting C5 inhibitor

6 months
minimum duration

ULTOMIRIS treatment of atypical-HUS should be a minimum duration of 6 months, after which treatment duration should be individualized.[6]

Extended
treatment duration

A longer treatment duration may be considered if patients do not achieve a complete TMA response by the end of 26 weeks, they may have high risk factors for TMA relapse, or they may exhibit clinical or individual needs for maintaining therapy for disease management.[6,27]

[a]Starting 2 weeks after the intravenous loading dose, maintenance doses are infused intravenously every 8 weeks for adult patients and every 4 or 8 weeks for pediatric patients (depending on body weight).[6] [b]Targeted engineering to incorporate 4 amino acid substitutions designed to reduce target-mediated drug disposition and enhance FcRn-mediated recycling of eculizumab led to the generation of ULTOMIRIS, which exhibited an extended duration of action in preclinical models relative to eculizumab.[6] [c]The mean (SD) terminal elimination half-life and clearance of intravenous ULTOMIRIS in patients with atypical-HUS are 51.8 (16.2) days and 0.08 (0.04) L/day, respectively. Half-life of eculizumab is 11.25 to 17.25 days.[6]
C5=complement protein 5; FcRn=neonatal Fc receptor; HUS=hemolytic uremic syndrome; SD=standard deviation; TMA=thrombotic microangiopathy.

SELECT IMPORTANT SAFETY INFORMATION

Serious Meningococcal Infections (continued)

The benefits and risks of antibiotic prophylaxis for prevention of meningococcal infections in patients receiving ULTOMIRIS have not been established. Consider discontinuation of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection.

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 meningococcal infections/sepsis.

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TRANSITIONING TO OR RESTARTING ULTOMIRIS

Steps for transitioning patients to or restarting patients on ULTOMIRIS

1. Discuss transitioning from eculizumab

Have a conversation with your patients and obtain their consent. Talk about the risks and benefits of transition, the dosing regimen, adverse reactions they may experience during infusion, and how frequently they will be monitored during treatment.

2. Enroll in the ULTOMIRIS REMS

Due to the risk of meningococcal infections, prescribers must enroll in the Risk Evaluation and Mitigation Strategy (REMS) program to obtain ULTOMIRIS.

To learn more and enroll, call 1-888-765-4747 or visit UltomirisREMS.com.

NOTE: The ULTOMIRIS REMS program is independent of the eculizumab REMS program and requires its own enrollment.

3. Connect patients with OneSource™

This complimentary, personalized patient support program can provide disease education and help with health insurance navigation, community connections, and ongoing support.

ONESOURCE®
Personalized Patient Support from Alexion

Contact OneSource at 1-888-765-4747 or visit AlexionOneSource.com.

Pay as low as

$0 in out-of-pocket costs for eligible people[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 patients covered 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

[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.

SELECT IMPORTANT SAFETY INFORMATION

ULTOMIRIS REMS

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

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 meningococcal infections/sepsis.

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Steps for transitioning patients to or restarting patients on ULTOMIRIS (continued)

4. Check vaccination status and vaccinate as needed

Ensure that patients are up to date on meningococcal vaccines and boosters. The 2022 Advisory Committee on Immunization Practices (ACIP) recommends meningococcal vaccines in patients receiving complement inhibitors, including those receiving ULTOMIRIS. Immunize patients without a history of meningococcal vaccination at least 2 weeks prior to receiving the first dose of ULTOMIRIS. Patients who initiate ULTOMIRIS treatment less than 2 weeks after receiving meningococcal vaccine(s) must receive appropriate prophylactic antibiotics until 2 weeks after vaccination.[6]

5. Initiate ULTOMIRIS treatment

Starting 2 weeks after the intravenous loading dose, maintenance doses are infused intravenously every 8 weeks for adult patients and every 4 or 8 weeks for pediatric patients (depending on body weight). For patients transitioning from eculizumab, administer the loading dose of ULTOMIRIS at the time of the next scheduled eculizumab dose.[6]

Monitor for adverse reactions during and after ULTOMIRIS administration

- The infusion may be slowed or stopped at the physician's discretion[6]
- Monitor patients during the infusion and for at least 1 hour following completion for signs or symptoms of an infusion-related reaction[6]
- Interrupt ULTOMIRIS infusion and institute appropriate supportive measures if signs of cardiovascular instability or respiratory compromise occur[6]

Learn more about ULTOMIRIS dosing

bit.ly/3wgGjtf

ALEXION ACCESS NAVIGATOR

Take advantage of a dedicated resource for information on access and reimbursement—designed exclusively for healthcare professionals and their offices.

Find the information you need at AlexionAccessNavigator.com

Actor portrayal

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ULTOMIRIS REMS (continued)

Under the ULTOMIRIS REMS, prescribers must enroll in the program. Prescribers must counsel patients about the risk of meningococcal infection/sepsis, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccines.

Additional information on the REMS requirements is available at www.ultomirisrems.com or 1-888-765-4747.

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 meningococcal infections/sepsis.

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SELECT IMPORTANT SAFETY INFORMATION AND INDICATION

SELECT IMPORTANT SAFETY INFORMATION

Other Infections

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 guidelines.
If ULTOMIRIS is administered to patients with active systemic infections, monitor closely for worsening infection.

Monitoring Disease Manifestations after ULTOMIRIS Discontinuation

ULTOMIRIS treatment of aHUS should be a minimum duration of 6 months. Due to heterogeneous nature of aHUS events and patient-specific risk factors, treatment duration beyond the initial 6 months should be individualized. There are no specific data on ULTOMIRIS discontinuation. After discontinuing treatment with ULTOMIRIS, patients should be monitored for clinical symptoms and laboratory signs of TMA complications for at least 12 months.

TMA complications post-discontinuation can be identified if any of the following is observed: Clinical symptoms of TMA include changes in mental status, seizures, angina, dyspnea, thrombosis or increasing blood pressure. In addition, at least two of the following laboratory signs observed concurrently and results should be confirmed by a second measurement 28 days apart with no interruption: a decrease in platelet count of 25% or more as compared to either baseline or to peak platelet count during ULTOMIRIS treatment; an increase in serum creatinine of 25% or more as compared to baseline or to nadir during ULTOMIRIS treatment; or, an increase in serum LDH of 25% or more as compared to baseline or to nadir during ULTOMIRIS treatment. If TMA complications occur after discontinuation, consider reinitiation of ULTOMIRIS treatment or appropriate organ-specific supportive measures.

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

Intravenous or subcutaneous 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% of patients treated with ULTOMIRIS. These events included lower back pain, drop in blood pressure, elevation in blood pressure, limb discomfort, drug hypersensitivity (allergic reaction), dysgeusia (bad taste), and drowsiness. These reactions did not require discontinuation of ULTOMIRIS. If signs of cardiovascular instability or respiratory compromise occur, interrupt ULTOMIRIS infusion and institute appropriate supportive measures.

Injection Site Reactions-Subcutaneous administration

27% (23/84) of patients treated with subcutaneous administration of ULTOMIRIS experienced injection site reactions which included application site rash, device allergy, infusion site pain, infusion site reaction, injection site bruising, injection site erythema, injection site hematoma, injection site induration, injection site inflammation, injection site pain, injection site pruritus, injection site rash, injection site reaction, injection site swelling, injection site urticaria, medical device site bruise, medical device site erythema, medical device site hematoma, medical device site induration, medical device site pruritus, medical device site rash, and medical device site reaction.

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SELECT IMPORTANT SAFETY INFORMATION AND INDICATION (CONTINUED)

Allergies to Acrylic Adhesives

The on-body injector of ULTOMIRIS uses acrylic adhesive. For patients with a known allergy to acrylic adhesive, use of this product may result in an allergic reaction. Premedication can be considered, and supportive measures should be instituted if signs of allergy appear.

ADVERSE REACTIONS

Most common adverse reactions in patients with aHUS (incidence ≥20%) were upper respiratory tract infection, diarrhea, nausea, vomiting, headache, hypertension and pyrexia. Serious adverse reactions were reported in 42 (57%) patients with aHUS receiving ULTOMIRIS. The most frequent serious adverse reactions reported in more than 2 patients (2.7%) treated with ULTOMIRIS were hypertension, pneumonia and abdominal pain. In clinical studies, clinically relevant adverse reactions in <10% of patients include viral tonsillitis in adults and viral infection in pediatric patients and in 3% of adult patients include infusion-related reactions.

Adverse Reactions for Subcutaneous Administration of ULTOMIRIS

Most common adverse reactions (≥10%) with ULTOMIRIS subcutaneous administration via On Body Injector in adult patients with PNH were local injection site reactions, diarrhea, and headache.

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.

INDICATION

ULTOMIRIS is indicated for the treatment of adult and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).

Limitation of Use:

ULTOMIRIS is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

Subcutaneous Use in Adult Patients with aHUS

Subcutaneous administration of ULTOMIRIS is not approved for use in pediatric patients.

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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 meningococcal infections/sepsis.

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

MANAGING POTENTIAL TMA RECURRENCE WITH ONGOING C5 INHIBITION

Know the risk of recurrence for your patients with atypical-HUS

Through proper assessment, you can gain a better understanding of your patients' risk of TMA recurrence.[1,2,4,5,17]

Make a plan

For appropriate patients, consider developing an individualized plan for monitoring and C5 inhibition treatment based on the specific needs of your patients with atypical-HUS. After discontinuing treatment with ULTOMIRIS, patients should be monitored for clinical symptoms and laboratory signs of TMA complications for at least 12 months.[6]

Restart or transition to ULTOMIRIS

For some patients, treatment with ULTOMIRIS may be appropriate beyond the minimum 6-month treatment duration.[6,27]

Discover the benefits of transitioning patients to ULTOMIRIS

Learn more about the immediate, complete, and sustained benefits of ULTOMIRIS.

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Actor portrayal

C5 = complement protein 5; HUS = hemolytic uremic syndrome; TMA = thrombotic microangiopathy.

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