

#1 PRESCRIBED  
TREATMENT  
for  
atypical-HUS<sup>1,2\*</sup>

Consider a treatment used for more than 1,000 patients with atypical-HUS,<sup>1†</sup> and more than 9,000 patient-years across all ULTOMIRIS indications<sup>3‡</sup>

ULTOMIRIS<sup>®</sup>  
(ravulizumab-cwvz)

Immediate, complete, and sustained<sup>§</sup> C5 inhibition with ULTOMIRIS in adult and pediatric patients with atypical-HUS<sup>2,4,5</sup>

## 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.

## SELECT IMPORTANT SAFETY INFORMATION

### 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.

### 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.

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.

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.

### ULTOMIRIS REMS

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

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](http://www.ultomirisrems.com) or 1-888-765-4747.

\*ULTOMIRIS had more than a 50% share of patients with atypical-HUS actively taking Alexion medications every month from August 2021 through August 2023.<sup>1</sup>

<sup>†</sup>Reflects the number of patients with atypical-HUS currently on ULTOMIRIS as of August 2023.<sup>1</sup>

<sup>‡</sup>Based on a cumulative search of the Alexion safety database for real-world ravulizumab data from December 2018 to December 2022 across all indications.<sup>3</sup> See all indications at [UltomirisHCP.com](http://UltomirisHCP.com).

<sup>§</sup>In the majority (93%) of adult and pediatric patients with atypical-HUS throughout the entire 26-week treatment period.<sup>2</sup>

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

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

# ULTOMIRIS IS THE FIRST AND ONLY C5 INHIBITOR FOR ATYPICAL-HUS LASTING UP TO 8 WEEKS<sup>2</sup>

For adult and pediatric patients 1 month of age and older  
with atypical-HUS to inhibit complement-mediated TMA<sup>2\*</sup>

## IMMEDIATE

**100% (n=70) of adult and pediatric patients**

had complete C5 inhibition at the end of the first infusion of ULTOMIRIS.<sup>2,4-6</sup>

## COMPLETE

**54% (n=30/56; 95% CI: 40%-67%) of adult and 71% (n=10/14; 95% CI: 42%-92%) of pediatric patients** met the composite endpoint of complete TMA response with ULTOMIRIS by 26 weeks.<sup>2†‡</sup>

Four additional adult patients who did not achieve a complete TMA response at 26 weeks did so with continued ULTOMIRIS treatment at 52 weeks.<sup>2,6</sup>

## SUSTAINED

**Up to 8 weeks of sustained C5 inhibition and the possibility to live dialysis-free in adult and pediatric patients.<sup>2§</sup>**

**ULTOMIRIS has a minimum treatment duration of 6 months;  
treatment beyond 6 months should be individualized per each patient's need<sup>2</sup>**

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 SOLIRIS® (eculizumab), administer the loading dose of ULTOMIRIS at the time of the next scheduled SOLIRIS dose.

ULTOMIRIS treatment of atypical-HUS should be a minimum duration of 6 months

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

\*Limitation of Use: ULTOMIRIS is not indicated for the treatment of patients with STEC-HUS.<sup>2</sup>

†Complete TMA response was defined as normalization of hematological parameters (platelet count and LDH) and  $\geq 25\%$  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.<sup>2</sup>

‡Interim results of a 26-week, multicenter, open-label, single-arm study of 14 SOLIRIS-naïve patients with documented diagnosis of atypical-HUS.<sup>2</sup>

§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).<sup>2</sup>

C5=complement protein 5; LDH=lactate dehydrogenase; STEC-HUS=Shiga toxin *E. coli*-related hemolytic uremic syndrome; TMA=thrombotic microangiopathy.

**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.**

## SELECT IMPORTANT SAFETY INFORMATION (continued)

### 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

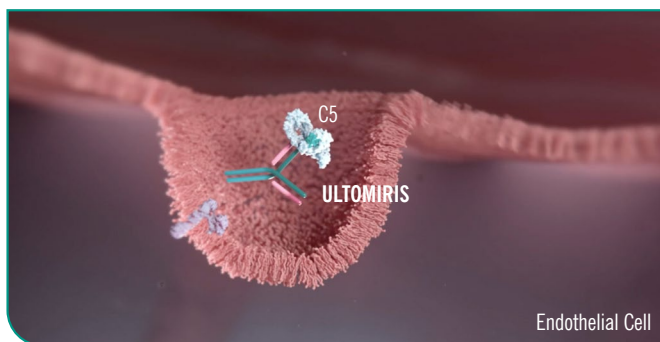
27% (23/84) of patients treated with subcutaneous administration of ULTOMIRIS experienced injection site reactions which included application site rash, device allergy, infusion site pain, infusion site reaction, injection site bruising, injection site erythema, injection site hematoma, injection site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

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# ULTOMIRIS BINDS TO C5 FOR IMMEDIATE, COMPLETE, AND SUSTAINED C5 INHIBITION

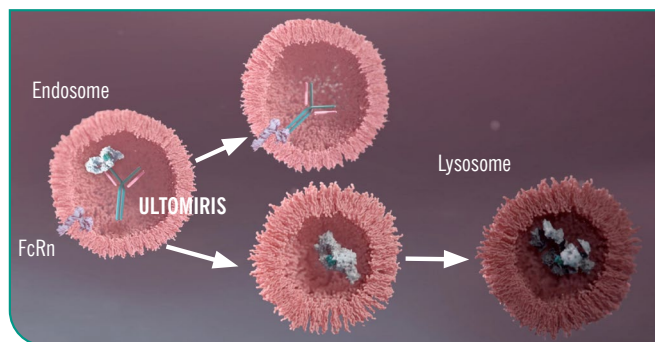
1

**ULTOMIRIS** binds to C5 in the bloodstream to prevent its activation.<sup>2</sup>



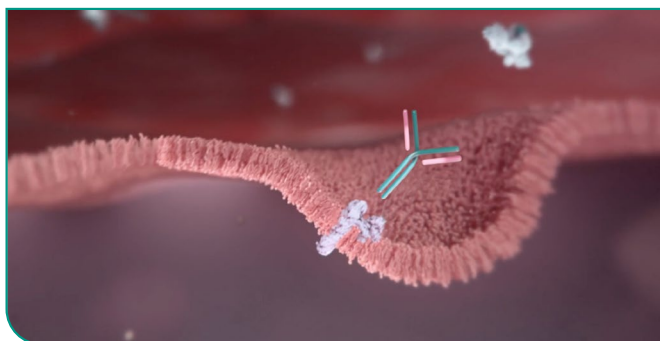
2

**ULTOMIRIS** is engineered to release C5 in the endosome as pH levels drop and use FcRn to recycle back to the bloodstream, leaving C5 to be degraded by the lysosome.<sup>7</sup>



3

**ULTOMIRIS** has also been engineered to bind to FcRn to provide immediate, complete, and sustained\* inhibition of C5 for up to 8 weeks.<sup>2,6,7</sup>



\*In the majority (93%) of adult and pediatric patients with atypical-HUS throughout the entire 26-week treatment period.<sup>2</sup>  
FcRn=neonatal Fc receptor.

Please see additional Important Safety Information throughout and accompanying full [Prescribing Information \(UltomirisHCP.com/PI\)](https://www.ultomirishcp.com/PI) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening meningococcal infections/sepsis.

## SELECT IMPORTANT SAFETY INFORMATION (continued)

### Injection Site Reactions-Subcutaneous administration (continued)

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.

### 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  $\geq 20\%$ ) 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 ( $\geq 10\%$ ) 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.

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Injection for intravenous use  
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# STUDY 311: ULTOMIRIS IN ADULT PATIENTS WITH ATYPICAL-HUS

**IMMEDIATE** C5 inhibition was observed on Day 1 in adult patients<sup>2,4</sup>

**100% (56/56)** of adult patients in the 26-week Study 311 demonstrated complete C5 inhibition after the first infusion<sup>2,4\*</sup>

**COMPLETE** TMA response was achieved in the majority of adult patients taking ULTOMIRIS in Study 311<sup>2</sup>

## Components of Complete TMA Response Observed in Study 311<sup>2</sup>

**84%**

(95% CI: 72%-92%)  
n=47

Platelet Count  
Normalization

**77%**

(95% CI: 64%-87%)  
n=43

LDH Normalization

**59%**

(95% CI: 45%-72%)  
n=33

≥25% Improvement in Serum  
Creatinine From Baseline

## Hematologic Normalization

**73%**

(95% CI: 60%-84%)  
n=41

Platelet Count  
& LDH Normalization

## Complete TMA Response<sup>†</sup>

**54%**

(95% CI: 40%-67%)  
n=30

- **100% (30/30)** of complete TMA responses were maintained through all available follow-up in adult patients<sup>2‡</sup>
- **>99.5%** of all free C5 serum samples in adult patients showed complete inhibition of C5 throughout the 6-month study period with ULTOMIRIS<sup>4\*</sup>

**SUSTAINED:** ULTOMIRIS demonstrated **8 weeks** of sustained C5 inhibition in Study 311, creating opportunity to discontinue dialysis in adult patients<sup>2</sup>

## At 26 weeks

### An opportunity for your adult patients to discontinue dialysis

- 17 of the 29 patients (59%) who required dialysis at study entry discontinued dialysis by the end of available follow-up<sup>2†</sup>
- 21 of 27 patients (78%) who were off dialysis were still not on dialysis at last available follow-up<sup>2†</sup>

### Potential for recovery of kidney function in your adult patients

- Mean eGFR was 51.8 mL/min/1.73 m<sup>2</sup> at end of study, a 35.9 mL/min/1.73 m<sup>2</sup> (227%) mean increase from baseline<sup>2†</sup>
- Normalization of mean platelet count (an individual component of complete TMA response) occurred by Day 8 of treatment with ULTOMIRIS. In contrast, improvements in renal function occurred more gradually over the 26-week treatment evaluation period, and in some patients continued in the 52-week extension period<sup>6,8</sup>

## Study 311 assessed efficacy and safety of ULTOMIRIS in adult patients<sup>2,4,8</sup>

- 26-week, open-label, single-arm study of adult patients (N=56)<sup>2</sup>
- Inclusion: platelet count  $\leq 150 \times 10^9/L$ , evidence of hemolysis such as an elevation in serum LDH, and serum creatinine above the upper limits of normal or required dialysis<sup>2</sup>
- Exclusion: patients with TMA due to ADAMTS13 deficiency, STEC-HUS, and genetic defect in cobalamin C metabolism<sup>2</sup>
- 8 patients were immediately postpartum, 48 had received pretreatment PE/PI, and 27 had been in the ICU<sup>4</sup>
- Primary endpoint: complete TMA response,<sup>†</sup> which comprised: platelet count normalization ( $\geq 150 \times 10^9/L$ ), serum LDH normalization ( $\leq 246 U/L$ ), and  $\geq 25\%$  improvement in serum creatinine from baseline<sup>2,4</sup>
- Select secondary endpoints: time to complete TMA response and complete TMA response status over time, dialysis requirement and CKD stage as evaluated by eGFR, hemoglobin response, and change from baseline in quality of life<sup>8</sup>

\*As measured by free C5 serum concentration of  $<0.5$  mcg/mL.<sup>2</sup>

<sup>†</sup>Complete TMA response was defined as normalization of hematological parameters (platelet count and LDH) and  $\geq 25\%$  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.<sup>2</sup>

<sup>‡</sup>Secondary endpoint.<sup>8</sup>

ADAMTS13=a disintegrin and metalloproteinase with a thrombospondin type 1 motif member 13; CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; ICU=intensive care unit; PE/PI=plasma exchange/plasma infusion; STEC-HUS=Shiga toxin *E. coli*-related hemolytic uremic syndrome; TMA=thrombotic microangiopathy.

# STUDY 311: SAFETY PROFILE OF ULTOMIRIS IN ADULT PATIENTS WITH ATYPICAL-HUS

## Adverse Reactions Reported in $\geq 10\%$ of ULTOMIRIS-Treated Adult Patients With Atypical-HUS<sup>2</sup>

Body System Adverse Reaction	Adult Patients (N=58)	
	All Grades <sup>‡</sup> (n=53) n (%)	$\geq$ Grade 3 (n=14) n (%)
<b>Blood and lymphatic system disorders</b>		
Anemia	8 (14)	0 (0)
<b>Gastrointestinal disorders</b>		
Diarrhea	18 (31)	2 (3)
Nausea	15 (26)	2 (3)
Vomiting	15 (26)	2 (3)
Constipation	8 (14)	1 (2)
Abdominal pain	7 (12)	1 (2)
<b>General disorders and administration site conditions</b>		
Pyrexia	11 (19)	1 (2)
Edema peripheral	10 (17)	0 (0)
Fatigue	8 (14)	0 (0)
<b>Infections and infestations</b>		
Upper respiratory tract infection*	15 (26)	0 (0)
Urinary tract infection	10 (17)	5 (9)
Gastrointestinal infection <sup>†</sup>	8 (14)	2 (3)
<b>Metabolism and nutrition disorders</b>		
Hypokalemia	6 (10)	1 (2)
<b>Musculoskeletal and connective tissue disorders</b>		
Arthralgia	13 (22)	0 (0)
Back pain	7 (12)	1 (2)
Muscle spasms	6 (10)	0 (0)
Pain in extremity	6 (10)	0 (0)
<b>Nervous system disorders</b>		
Headache	23 (40)	1 (2)
<b>Psychiatric disorders</b>		
Anxiety	8 (14)	1 (2)
<b>Respiratory, thoracic, and mediastinal disorders</b>		
Cough	10 (17)	0 (0)
Dyspnea	10 (17)	1 (2)
<b>Skin and subcutaneous tissue disorders</b>		
Alopecia	6 (10)	0 (0)
Dry skin	6 (10)	0 (0)
<b>Vascular disorders</b>		
Hypertension	14 (24)	7 (12)

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The most frequent adverse reactions reported in  $\geq 20\%$  of adult patients treated with ULTOMIRIS were<sup>2</sup>:

- diarrhea
- upper respiratory tract infection
- headache
- nausea
- arthralgia
- hypertension
- vomiting

Clinically relevant adverse reactions include viral tonsillitis (in  $<10\%$  of patients) and infusion-related reactions (in 3% of patients).<sup>2</sup>

Serious adverse reactions were reported in 42 (57%) adult and pediatric patients with atypical-HUS receiving ULTOMIRIS. The most frequent serious adverse reactions reported in more than 2 patients (2.7%) treated with ULTOMIRIS were<sup>2</sup>:

- hypertension
- pneumonia
- abdominal pain

Four patients died during the adult atypical-HUS study. Patient deaths were determined by study investigators as unrelated to study drug; the cause of death was sepsis in two patients and intracranial hemorrhage in one patient. The fourth patient, who was excluded from the trial after a diagnosis of STEC-HUS, died due to pretreatment cerebral arterial thrombosis.<sup>2,8</sup>

\*Grouped term includes nasopharyngitis, pharyngitis, upper respiratory tract infection, rhinitis, viral upper respiratory tract infection, rhinovirus infection, viral pharyngitis, rhinorrhea, and oropharyngeal pain.

<sup>†</sup>Grouped term includes gastroenteritis, gastrointestinal infection, enterocolitis infection, infectious colitis, and enterocolitis.

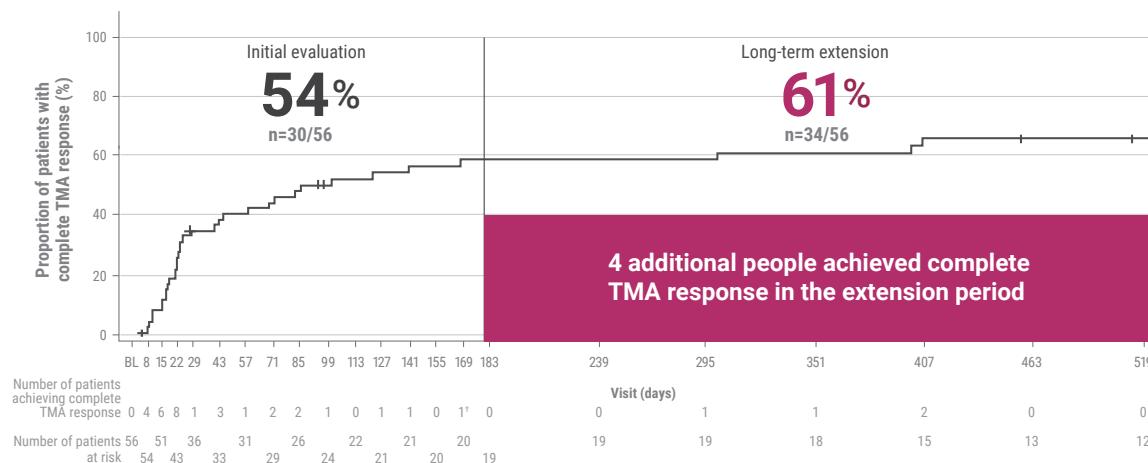
<sup>‡</sup>Graded per CTCAE v5.0.

CTCAE=Common Terminology Criteria for Adverse Events.

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# 52-WEEK EXTENSION OF STUDY 311 FOR ULTOMIRIS IN ADULT PATIENTS WITH ATYPICAL-HUS

**COMPLETE** TMA response was achieved in the majority of adult patients taking ULTOMIRIS<sup>6\*</sup>



**SUSTAINED** at 52 weeks: an opportunity for your adult patients to discontinue dialysis<sup>6</sup>

- 100% of patients who discontinued dialysis (17/17) stayed off dialysis

**The extension period aimed to assess the safety and efficacy of ULTOMIRIS over a longer period of time for adults who completed the initial evaluation period<sup>2,6,8</sup>**

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](http://UltomirisHCP.com/aHUS).

**Safety outcomes at the last available follow-up with ULTOMIRIS (n=58)<sup>6</sup>**

Event Type	Day 1-183		Day 1 until last available follow-up	
	n (%)	Events	n (%)	Events
<b>Any AE</b>	58 (100.0)	696	58 (100.0)	986
Treatment related	19 (32.8)	50	20 (34.5)	66
Not treatment related	58 (100.0)	646	58 (100.0)	920
<b>Any SAE</b>	28 (48.3)	60	33 (56.9)	84
<b>Fatal TEAEs</b>	3 (5.2)	3	3 (5.2)	3
<b>Study discontinuation owing to</b>				
TEAEs	3 (5.2)	3	3 (5.2)	3
TESAEs	3 (5.2)	3	3 (5.2)	3
<b>Drug discontinuation owing to</b>				
TEAEs	3 (5.2)	3	3 (5.2)	3
TESAEs	3 (5.2)	3	3 (5.2)	3
<b>SAEs during study drug infusion</b>	0 (0)	0	0 (0)	0
<b>Meningococcal infections</b>	0 (0)	0	0 (0)	0

At the last available follow-up, all patients experienced one or more AEs; 20 patients (34.5%) experienced treatment-related AEs, most often headache, diarrhea, and vomiting.<sup>4</sup>

A total of 33 patients (56.9%) experienced serious AEs, most often hypertension and pneumonia (5.2% each).<sup>6</sup>

\*Complete TMA response was defined as normalization of hematological parameters (platelet count and LDH) and  $\geq 25\%$  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.<sup>2</sup>

Patients who did not have a response were censored at the date of last visit when the analysis was performed.<sup>4,8</sup>

<sup>†</sup>The patient achieved initial complete TMA response measurement at Day 169; however, confirmatory measurement was not achieved until the extension period (Day 239).<sup>6</sup>

AE=adverse event; HUS=hemolytic uremic syndrome; SAE=serious adverse event; TEAE=treatment-emergent adverse event; TESAE=treatment-emergent serious adverse event.



# ASSESS RISK FACTORS TO INDIVIDUALIZE TREATMENT DURATION

Minimum  
**6**  
months

ULTOMIRIS treatment of atypical-HUS should be a minimum duration of 6 months, after which time the treatment duration should be individualized<sup>2\*</sup>

A longer treatment duration may be considered with these factors:

1

Patient has not achieved complete TMA response after a minimum 6-month treatment with complement inhibitor<sup>2,9</sup>

OR

2

Having high risk factors for TMA recurrence (eg, genetic mutations, clinical history of TMA, family history, transplant, pediatric onset, complement biomarkers/levels, exposure to triggers)<sup>10-17</sup>

OR

3

Exhibiting clinical/individual needs for maintaining therapy/disease management<sup>2,6,9</sup>

Minimum  
**12**  
months

After ULTOMIRIS discontinuation, continue following up with your patient and monitor for clinical symptoms and laboratory signs of TMA complications for at least 12 months<sup>2†</sup>

With untreated atypical-HUS, the risk of TMA complications may be lifelong<sup>14</sup>

TMA complications post-discontinuation can be identified if any of the following is observed<sup>2</sup>:

- Clinical symptoms of TMA, including changes in mental status, seizures, angina, dyspnea, thrombosis, or increasing blood pressure
- In addition, at least 2 of the following laboratory signs observed concurrently with results 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
  - An increase in serum LDH of 25% or more as compared to baseline or to nadir during ULTOMIRIS treatment

Of the patients who have had a TMA manifestation and have discontinued C5 inhibition therapy, approximately **25% to 30% will experience relapse**<sup>11,15</sup>

There are no specific data on ULTOMIRIS discontinuation<sup>2</sup>

If TMA complications occur after ULTOMIRIS discontinuation, consider reinitiating ULTOMIRIS treatment or initiating appropriate organ-specific supportive measures<sup>2</sup>

\*Due to the heterogeneous nature of atypical-HUS events and patient-specific risk factors.<sup>2</sup>

†Assess discontinuation of ULTOMIRIS based on clinical judgment, including TMA relapse risk and complete TMA response. There are no specific data on ULTOMIRIS discontinuation.<sup>2</sup>

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# STUDY 312: ULTOMIRIS IN PEDIATRIC PATIENTS WITH ATYPICAL-HUS

**IMMEDIATE** C5 inhibition was observed on Day 1 in pediatric patients in the 26-week Study 312<sup>2,5\*</sup>

**100% (14/14)** of pediatric patients in the 26-week Study 312 demonstrated complete C5 inhibition after the first infusion<sup>2,5</sup>

**COMPLETE** TMA response was achieved in 10 out of 14 pediatric patients taking ULTOMIRIS in Study 312<sup>2†</sup>

## Components of Complete TMA Response Observed in Study 312<sup>2</sup>

**93%**

(95% CI: 66%-99%)  
n=13

Platelet Count  
Normalization

**86%**

(95% CI: 57%-98%)  
n=12

LDH Normalization

**79%**

(95% CI: 49%-95%)  
n=11

≥25% Improvement in Serum  
Creatinine From Baseline

## Hematologic Normalization<sup>2</sup>

**86%**

(95% CI: 57%-98%)  
n=12

Platelet Count  
& LDH Normalization

## Complete TMA Response<sup>2</sup>

**71%**

(95% CI: 42%-92%)  
n=10

- **100% (10/10)** of complete TMA responses were maintained through all available follow-up in pediatric patients<sup>2‡</sup>
- Free C5 serum samples in pediatric patients showed immediate, complete inhibition of C5 sustained throughout the 26-week period<sup>2,5\*</sup>

**SUSTAINED:** ULTOMIRIS demonstrated **4 or 8 weeks** (depending on body weight) of sustained C5 inhibition in Study 312, creating opportunity to discontinue dialysis in pediatric patients<sup>2</sup>

## At 26 weeks

### An opportunity for your pediatric patients to discontinue dialysis

- 4 of the 5 patients (80%) who required dialysis at study entry discontinued dialysis after the first month in study and for the duration of ULTOMIRIS treatment<sup>2‡</sup>
- No patient started dialysis during the study<sup>2‡</sup>

### Potential for recovery of kidney function in your pediatric patients

- Mean eGFR was 108.0 mL/min/1.73 m<sup>2</sup> at end of study, a 79.6 mL/min/1.73 m<sup>2</sup> (280%) mean increase from baseline<sup>2‡</sup>

## Study 312 assessed efficacy and safety of ULTOMIRIS in pediatric patients<sup>2,18</sup>

- 26-week, multicenter, open-label, single-arm study of eculizumab-naïve patients (N=14) with documented diagnosis of atypical-HUS<sup>2</sup>
- Inclusion: platelet count  $\leq 150 \times 10^9/L$ , evidence of hemolysis such as an elevation in serum LDH, and serum creatinine  $\geq 97.5\%$  percentile at screening or required dialysis<sup>2</sup>
- Exclusion: patients with TMA due to ADAMTS13 deficiency, STEC-HUS, and genetic defect in cobalamin C metabolism<sup>2</sup>
- Primary endpoint: complete TMA response,<sup>‡</sup> which comprised: platelet count normalization ( $\geq 150 \times 10^9/L$ ), serum LDH normalization (less than upper limit of normal), and  $\geq 25\%$  improvement in serum creatinine from baseline<sup>2</sup>
- Select secondary endpoints: time to complete TMA response and complete TMA response status over time, dialysis requirement, and CKD stage as evaluated by eGFR, hemoglobin response, and change from baseline in quality of life<sup>18</sup>

Data reported here are the interim analysis results of Study 312 in the cohort of eculizumab inhibitor-naïve patients, included in the US ULTOMIRIS Prescribing Information.<sup>2</sup>

\*As measured by free C5 serum concentration of  $<0.5$  mcg/mL<sup>2</sup>

†Complete TMA response was defined as normalization of hematological parameters (platelet count and LDH) and  $\geq 25\%$  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.<sup>2</sup>

‡Secondary endpoint.<sup>18</sup>

ADAMTS13=a disintegrin and metalloproteinase with a thrombospondin type 1 motif member 13; CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; LDH=lactate dehydrogenase; STEC-HUS=Shiga toxin *E. coli*-related hemolytic uremic syndrome; TMA=thrombotic microangiopathy.

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# STUDY 312: SAFETY PROFILE OF ULTOMIRIS IN PEDIATRIC PATIENTS WITH ATYPICAL-HUS

## Adverse Reactions Reported in $\geq 10\%$ of ULTOMIRIS-Treated Pediatric Patients With Atypical-HUS<sup>2</sup>

Body System Adverse Reaction	Pediatric Patients (N=16)	
	All Grades <sup>†</sup> (n=16) n (%)	$\geq$ Grade 3 (n=6) n (%)
<b>Blood and lymphatic system disorders</b>		
Anemia	2 (13)	1 (6)
Lymphadenopathy	2 (13)	0 (0)
<b>Gastrointestinal disorders</b>		
Diarrhea	6 (38)	0 (0)
Constipation	4 (25)	0 (0)
Vomiting	4 (25)	1 (6)
Abdominal pain	3 (19)	0 (0)
Nausea	2 (13)	0 (0)
<b>General disorders and administration site conditions</b>		
Pyrexia	8 (50)	0 (0)
<b>Infections and infestations</b>		
Upper respiratory tract infection*	7 (44)	1 (6)
Gastroenteritis viral	2 (13)	2 (13)
Pneumonia	2 (13)	1 (6)
Tonsillitis	2 (13)	0 (0)
<b>Injury, poisoning, and procedural complications</b>		
Contusion	3 (19)	0 (0)
<b>Investigations</b>		
Vitamin D decreased	3 (19)	0 (0)
<b>Metabolism and nutrition disorders</b>		
Decreased appetite	2 (13)	0 (0)
Iron deficiency	2 (13)	0 (0)
<b>Musculoskeletal and connective tissue disorders</b>		
Myalgia	3 (19)	0 (0)
Pain in extremity	2 (13)	0 (0)
<b>Nervous system disorders</b>		
Headache	5 (31)	0 (0)
<b>Respiratory, thoracic, and mediastinal disorders</b>		
Cough	3 (19)	0 (0)
Dyspnea	2 (13)	0 (0)
<b>Skin and subcutaneous tissue disorders</b>		
Rash	3 (19)	0 (0)
<b>Vascular disorders</b>		
Hypertension	4 (25)	1 (6)
Hypotension	2 (13)	0 (0)



The most frequent adverse reactions reported in  $\geq 20\%$  of pediatric patients treated with ULTOMIRIS were<sup>2</sup>:

- diarrhea
- constipation
- vomiting
- pyrexia
- upper respiratory tract infection
- headache
- hypertension

Clinically relevant adverse reactions in  $< 10\%$  of patients included viral infection.<sup>2</sup>

Serious adverse reactions were reported in 42 (57%) adult and pediatric patients with atypical-HUS receiving ULTOMIRIS. The most frequent serious adverse reactions reported in more than 2 patients (2.7%) treated with ULTOMIRIS were<sup>2</sup>:

- hypertension
- pneumonia
- abdominal pain

\*Grouped term includes nasopharyngitis, pharyngitis, upper respiratory tract infection, rhinitis, viral upper respiratory tract infection, rhinovirus infection, viral pharyngitis, rhinorrhea, and oropharyngeal pain.

<sup>†</sup>Graded per CTCAE v5.0.

CTCAE=Common Terminology Criteria for Adverse Events.

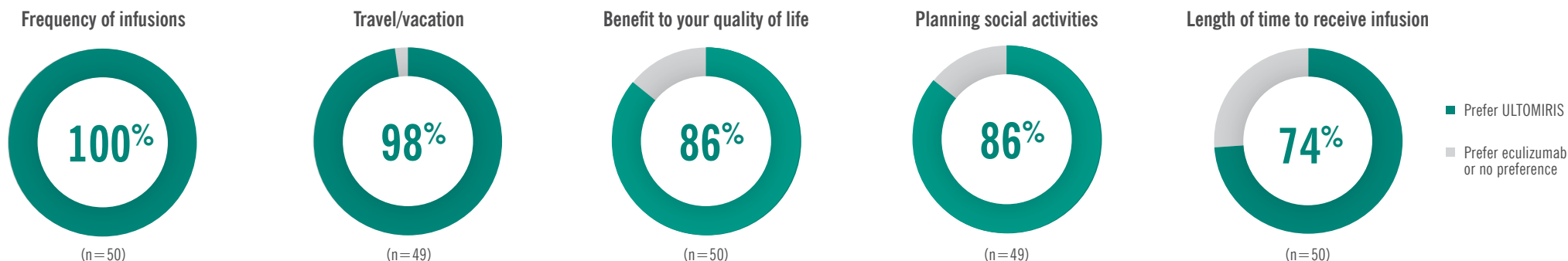
Please see additional Important Safety Information throughout and accompanying full Prescribing Information ([UltomirisHCP.com/PI](http://UltomirisHCP.com/PI)) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening meningococcal infections/sepsis.

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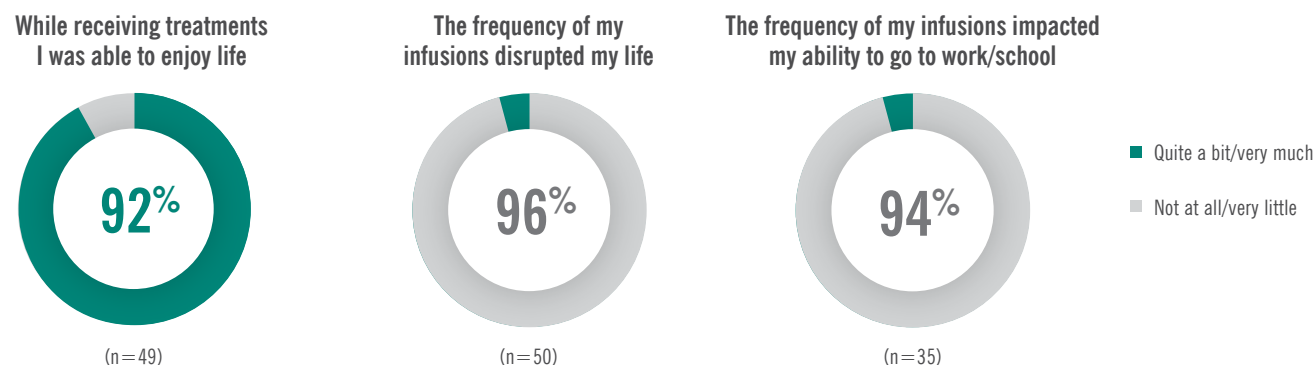
# PATIENTS PREFERRED ULTOMIRIS

In a survey of adult US patients (N=50) with confirmed atypical-HUS who had previously received eculizumab and  $\geq 3$  doses of ULTOMIRIS<sup>19\*</sup>

## Patient-reported survey: proportion of patients (%) who preferred ULTOMIRIS regarding specific parameters<sup>19</sup>



## ULTOMIRIS impacted patients: Adult patients were asked how ULTOMIRIS impacted the following domains, based on their experience during their treatment with SOLIRIS and after switching to ULTOMIRIS<sup>19</sup>



• For the same questions, results seen with eculizumab were 66% (n=50), 28% (n=50), and 40% (n=35), respectively

## ULTOMIRIS is more affordable

The average annual cost of ongoing ULTOMIRIS treatment for atypical-HUS is at least **22% less** than SOLIRIS treatment<sup>20</sup>

These figures are based on average wholesale acquisition cost (WAC) for patients  $\geq 40$  kg. Actual costs for individual patients will vary.

Patients treated with ULTOMIRIS require fewer maintenance infusions than those treated with eculizumab (for patients weighing  $> 20$  kg), at 7 vs 26 infusions per year<sup>2,21</sup>

For patients who responded "not applicable," responses were excluded from the percentage calculation for each question. Mean durations of eculizumab and ULTOMIRIS treatment were 46.9 and 12.9 months, respectively.<sup>19</sup>

\*A web-based survey of US adults (N=50) with confirmed diagnosis of atypical-HUS who had previously received eculizumab and  $\geq 3$  doses of ravulizumab.<sup>19</sup>

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

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- OneSource is a complimentary, personalized patient support program that connects patients, families, and caregivers facing complement-mediated diseases with a dedicated team of support professionals and advocates

## Copay assistance

- OneSource will provide financial assistance by covering eligible patients' out-of-pocket medication and infusion costs associated with ULTOMIRIS
- 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‡ or other federal or state programs (including any state prescription drug assistance programs)
- Additional requirements may apply. Contact Alexion **OneSource** at [1.888.765.4747](tel:18887654747) or [OneSource@Alexion.com](mailto:OneSource@Alexion.com) for more information on patient eligibility

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[AlexionAccessNavigator.com/Ultomiris](http://AlexionAccessNavigator.com/Ultomiris)

\*Based on typical commercial patient out-of-pocket deductible limits.

†Additional terms and conditions apply. Please contact OneSource with additional questions.

‡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.

REMS=Risk Evaluation and Mitigation Strategies.

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**#1** PRESCRIBED  
TREATMENT  
for  
atypical-HUS<sup>1,2\*</sup>

Consider a treatment used for more than  
1,000 patients with atypical-HUS,<sup>1†</sup> and more  
than 9,000 patient-years across all  
ULTOMIRIS indications<sup>3‡</sup>

Immediate, complete, and sustained<sup>§</sup> C5 inhibition with  
ULTOMIRIS in adult and pediatric patients with atypical-HUS<sup>2,4,5</sup>

IMMEDIATE

100% (n=70) of adult and pediatric patients

had complete C5 inhibition at the end of the first infusion of ULTOMIRIS.<sup>2,4-6</sup>

COMPLETE

54% (n=30/56; 95% CI: 40%-67%) of adult and 71% (n=10/14; 95% CI: 42%-92%) of pediatric patients

met the composite endpoint of complete TMA response with ULTOMIRIS by 26 weeks.<sup>2||¶</sup> Four additional adult patients  
who did not achieve a complete TMA response at 26 weeks did so with continued ULTOMIRIS treatment at 52 weeks.<sup>2,6</sup>

SUSTAINED

Up to 8 weeks of sustained C5 inhibition and the possibility to live dialysis-free in  
adult and pediatric patients.<sup>2#</sup>



For more information on support resources for atypical-HUS,  
please visit [UltomirisHCP.com/aHUS](https://UltomirisHCP.com/aHUS)

\*ULTOMIRIS had more than a 50% share of patients with atypical-HUS actively taking Alexion medications every month from August 2021 through August 2023.<sup>1</sup>

†Reflects the number of patients with atypical-HUS currently on ULTOMIRIS as of August 2023.<sup>1</sup>

‡Based on a cumulative search of the Alexion safety database for real-world ravulizumab data from December 2018 to December 2022 across all indications.<sup>3</sup> See all indications at [UltomirisHCP.com](https://UltomirisHCP.com).

§In the majority (93%) of adult and pediatric patients with atypical-HUS throughout the entire 26-week treatment period.<sup>2</sup>

||Complete TMA response was defined as normalization of hematological parameters (platelet count and LDH) 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.<sup>2</sup>

¶Interim results of a 26-week, multicenter, open-label, single-arm study of 14 SOLIRIS-naïve patients with documented diagnosis of atypical-HUS.<sup>2</sup>

#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).<sup>2</sup>

**References:** 1. Data on file. Atypical-HUS market access dashboard. Alexion Pharmaceuticals, Inc.; 2023. 2. ULTOMIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. 3. Fam S, et al. Poster presented at: The 9th Congress of the European Academy of Neurology (EAN); July 1-4, 2023; Budapest, Hungary. 4. Rondeau E, et al. *Kidney Int.* 2020;97(6):1287-1296. 5. Ariceta G, et al. *Kidney Int.* 2021;100:225-237. 6. Barbour T, et al. *Kidney Int Rep.* (article and supplement) 2021;6(6):1603-1613. 7. Sheridan D, et al. *PLoS One.* 2018;13(4):e0195909. 8. Data on file [ALXN1210-aHUS-311CSR]. 9. Laurence J. *Clin Adv Hematol Oncol.* 2020;18(4):221-230. 10. Noris M, Mescala F, Remuzzi G. *Nat Rev Nephrol.* 2012;8:622-633. 11. Menne J, et al. *BMC Nephrol.* 2019;20(1):125. 12. Ariceta G, et al. *Clin Kidney J.* 2021;14(9):2075-2084. 13. Duineveld C, et al. *Kidney Int Rep.* 2023;8(4):715-726. 14. Asif A, Nayer A, Haas CS. *J Nephrol.* 2017;30(3):347-362. 15. Macia M, et al. *Clin Kidney J.* 2017;10(3):310-319. 16. Timmermans SAMEG, et al. *J Am Soc Nephrol.* 2018;29(8):2234-2243. 17. Fakhouri F, et al. *J Am Soc Nephrol.* 2010;21(5):859-867. 18. Data on file [ALXN1210-aHUS-312CSR]. 19. Mauch T, et al. *J Comp Eff Res.* 2023;12(9):e230036. 20. Data on file. aHUS ULTOMIRIS Calculator. Alexion Pharmaceuticals, Inc.; 2023. 21. SOLIRIS. Prescribing information. Alexion Pharmaceuticals, Inc.

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#### 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.



Please see additional Important  
Safety Information throughout and  
accompanying full Prescribing Information  
([UltomirisHCP.com/PI](https://UltomirisHCP.com/PI)) for ULTOMIRIS,  
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