#1 PRESCRIBED TREATMENT FOR ATYPICAL-HUS[1,2,a]

Actor Portrayal

ULTOMIRIS for the management of pediatric patients with atypical-HUS

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

SELECT IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

ULTOMIRIS, a complement inhibitor, increases the risk of serious infections caused by *Neisseria meningitidis* [*see Warnings and Precautions (5.1)*] Life-threatening and fatal meningococcal infections have occurred in patients treated with complement inhibitors. These infections may become rapidly life-threatening or fatal if not recognized and treated early.

- **Complete or update vaccination for meningococcal bacteria (for serogroups A, C, W, Y, and B) at least 2 weeks prior to the first dose of ULTOMIRIS, unless the risks of delaying ULTOMIRIS therapy outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against meningococcal bacteria in patients receiving a complement inhibitor. See *Warnings and Precautions (5.1)* for additional guidance on the management of the risk of serious infections caused by meningococcal bacteria.**
- **Patients receiving ULTOMIRIS are at increased risk for invasive disease caused by *Neisseria meningitidis*, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious meningococcal infections and evaluate immediately if infection is suspected.**

Because of the risk of serious meningococcal infections, ULTOMIRIS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called ULTOMIRIS and SOLIRIS REMS [*see Warnings and Precautions (5.2)*].

Atypical-HUS=atypical hemolytic uremic syndrome.
[a]ULTOMIRIS had more than a 50% share of patients with atypical-HUS actively taking Alexion medications every month from August 2021 through August 2023.[1]

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).

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.

Atypical-HUS is a medical emergency that may affect your pediatric patients

Thrombotic microangiopathy (TMA)

A serious medical syndrome characterized by microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and signs of end organ damage, including AKI.[3,4]

Atypical-HUS

A type of TMA caused by complement dysregulation—requires urgent intervention to avoid poor clinical outcomes.[5]

Complement-triggering conditions may lead to manifestation of atypical-HUS[5]:

- Malignant hypertension or hypertensive emergency
- Solid organ or bone marrow transplantation
- Autoimmune diseases (e.g., SLE, APS, scleroderma)
- Pregnancy or postpartum
- Glomerulonephritis
- Malignancy
- Infections
- Certain prescription medications or illicit drugs
- Surgery or trauma

SELECT IMPORTANT SAFETY INFORMATION

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. 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*.

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

Pediatric patients with atypical-HUS often experience early disease onset and poor outcomes[6,7]

Atypical-HUS often manifests early in childhood[6]

42% (89/214)
of patients in a study experienced initial onset of atypical-HUS **before age 16**[6,a]

56% (50/89)
of those children experienced disease onset **before age 2**[6,a]

- Median age of initial atypical-HUS symptoms was **4.7 years** in the ULTOMIRIS 312 study (N=18)[8]

Pediatric patients with atypical-HUS may experience poor outcomes[6,7]

59% (48/81)
Required dialysis during the first episode of atypical-HUS[6,a]

48% (70 patients)
Progressed to **end-stage kidney disease** or death at 3 years, despite plasma therapy[7,b]

Rapidly identify atypical-HUS as the cause of TMA in your pediatric patients to optimize patient outcomes

[a]In a study of 214 patients in a French Nationwide study from 2000 to 2008 who met the diagnostic criteria for atypical-HUS, 89 of which were children at time of onset (defined in this study as ≤16 years of age).[6]
[b]In a study of 273 patients with atypical-HUS who had been registered from 1996 to 2007 within the International Registry of Recurrent and Familial HUS/TTP and had complement abnormalities.[7]
AKI=acute kidney injury; APS=antiphospholipid syndrome; atypical-HUS=atypical hemolytic uremic syndrome; SLE=systemic lupus erythematosus; TTP=thrombotic thrombocytopenic purpura.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont'd)

Serious Meningococcal Infections (cont'd)

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.

Recognize signs and symptoms of atypical-HUS in your pediatric patients

Look for signs of TMA[5]

1. **Thrombocytopenia:**
   - Platelet count <150,000/mm^3 or >25% decrease from baseline
2. **Microangiopathic hemolysis, which may include:**
   - Elevated lactate dehydrogenase
   - Decreased hemoglobin
   - Decreased haptoglobin
   - Schistocytes on blood smear
3. **Signs of organ damage including but not limited to:**
   - Neurological
   - Gastrointestinal
   - Renal (eg, elevated creatinine)

Of children with atypical-HUS at initial presentation

100% (15/15)
reported renal manifestations[9,a]

47% (182/387)
had gastrointestinal symptoms[10,b]

16% (14/89)
experienced neurologic manifestations[6,c]

12% (46/387)
had pulmonary symptoms[10,b]

Signs and symptoms of atypical-HUS can vary between patients; this is not an exhaustive list of all possible symptoms and the percentage for each organ system listed is the high end of the range based on the references cited.

[a]In a Canadian study of 37 patients with atypical-HUS (15 pediatric and 22 adult patients) between February 2014 and May 2017.[9]

[b]In an analysis of 851 patients from the Global aHUS Registry prior to eculizumab treatment, 387 of whom were pediatric and 464 were adults (categorized by age at initial presentation).[10]

[c]In a study of 214 patients in a French nation-wide study from 2000 to 2008 who met the diagnostic criteria for atypical-HUS, 89 of which were children at time of onset (defined in this study as ≤16 years of age).[6]

SELECT IMPORTANT SAFETY INFORMATION

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.

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

Rapidly determine atypical-HUS as the cause of TMA in your pediatric patients

STEP 1 Recognize TMA[5]

Thrombocytopenia
Platelet count <150 x 10^9/L or >25% decrease from baseline

AND

Microangiopathic hemolysis
Schistocytes and/or elevated LDH and/or decreased haptoglobin and/or decreased hemoglobin

Plus 1 or more of the following

Common Symptoms	**Neurological symptoms** Confusion and/or seizures and/or stroke and/or other cerebral abnormalities	**Kidney impairment** Elevated creatinine level and/or decreased eGFR and/or elevated blood pressure and/or abnormal urinalysis result	**Gastrointestinal symptoms** Diarrhea + blood and/or nausea/vomiting and/or abdominal pain and/or gastroenteritis/pancreatitis
Other Symptoms	**Cardiovascular symptoms** Myocardial infarction and/or hypertension and/or arterial stenosis and/or peripheral gangrene	**Pulmonary symptoms** Dyspnea and/or pulmonary hemorrhage and/or pulmonary edema	**Visual symptoms** Pain and blurred vision and/or retinal vessel occlusion and/or ocular hemorrhage

STEP 2 Rapidly determine the cause of TMA[5,b]

Evaluate ADAMTS13 activity and Shiga toxin/EHEC test[a]

While ADAMTS13 results are awaited, a platelet count >30 x 10^9/L and/or sCr >1.7 to 2.3 mg/dL almost eliminates a diagnosis of severe ADAMTS13 deficiency (TTP)

Shiga toxin/EHEC positive	>5% ADAMTS13 activity	≤5%[c] ADAMTS13 activity
↓	↓	↓
STEC-HUS	Atypical-HUS	TTP

Cobalamin C deficiency[11,d]
presenting in neonates or infants

Diacylglycerol kinase epsilon mutations[12,d]
presenting in infants

STEC-HUS is the most frequent cause of TMA in children (64%), followed by atypical-HUS (16%), and TTP (6%)[13]

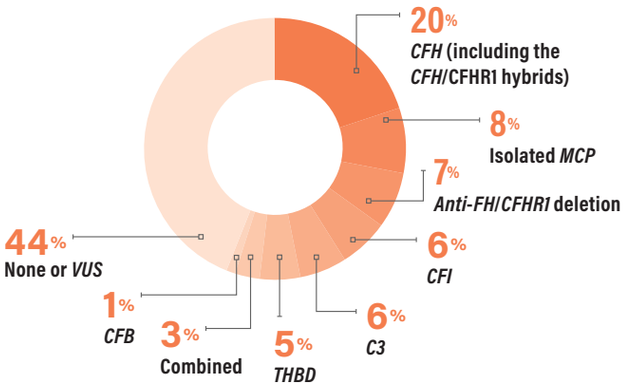
Consider ULTOMIRIS for pediatric patients experiencing TMA caused by atypical-HUS[8]

[a]Shiga toxin/EHEC test is warranted with history/presence of GI symptoms.[5]
[b]This is not an exhaustive list of all causes of TMA that would need to be ruled out.
[c]Range found in published literature is <5%-10%.[5]
[d]Defined as within the first year of life.[12]
ADAMTS13=a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; atypical-HUS=atypical hemolytic uremic syndrome; eGFR=estimated glomerular filtration rate; EHEC=enterohemorrhagic *Escherichia coli*; GI=gastrointestinal; LDH=lactate dehydrogenase; sCr=serum creatinine; STEC-HUS=shiga toxin-producing escherichia coli-associated hemolytic uremic syndrome; TMA=thrombotic microangiopathy; TTP=thrombotic thrombocytopenic purpura.

Assess individual risk factors and genetics to determine patient prognosis

- Pathologic gene mutations that contribute to the underlying complement dysregulation are identified in approximately **60%** to **70%** of patients with atypical-HUS[7,10,14-16]
- **Family history, pediatric onset, and genetic predisposition** are associated with a high risk of TMA recurrence[17-22]

Percentages of genetic mutations identified in adult and pediatric patients with atypical-HUS[7,14,23]



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.

Clinical outcomes of adult and pediatric patients with atypical-HUS carrying identified genetic mutations[24,25,a]

Gene	Risk of death or ESKD within the next year or in the first episode	Risk of TMA recurrence
CFH	50%-70%	50%
MCP	0%-6%	70%-90%
Anti-FH	30%-40%	40%-60%
CFI	50%	10%-30%
C3	60%	50%
THBD	50%	30%
CFB	50%	3/3 without ESKD

Clinical outcomes of patients with unmanaged atypical-HUS. 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.

In a study of genetic/acquired abnormalities in 214 patients with atypical-HUS,

28% (25/89) of children had a *CFH* or *CFI* mutation[6]

56% (11/19) of children with a *CFH* mutation

50% (3/6) of children with a *CFI* mutation

Experienced ESKD or death without intervention at 1 year[26]

- DGKE loss of function mutations are a common cause of atypical-HUS in patients <1 year of age[12]
- Patients with DGKE mutations do not appear to benefit from C5 inhibition therapy[12]

[a]Standalone data for pediatrics is unavailable, therefore this data is reflective of both adult and pediatric populations.

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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.

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

Initiate ULTOMIRIS in your pediatric patients with atypical-HUS

IMMEDIATE

C5 inhibition was observed by the end of the first infusion in pediatric patients in Study 312[2,8,a]

- **100% (18/18)** of pediatric patients in the initial 26-week analysis demonstrated complete C5 inhibition after the first infusion[2,8,a]

COMPLETE

TMA response was achieved in 14 out of 18 pediatric patients taking ULTOMIRIS in Study 312[27,b,c]

Components of Complete TMA Response Observed in Study 312 in the Full Analysis Set at 26 Weeks[27]

Platelet Count Normalization
94% (17/18)
(95% CI: 73%-99%)

LDH Normalization
89% (16/18)
(95% CI: 65%-99%)

≥25% Improvement in Serum Creatinine From Baseline
83% (15/18)
(95% CI: 59%-96%)

Hematologic Normalization[27]
Platelet Count & LDH Normalization
89% (16/18)
(95% CI: 65%-99%)

Complete TMA Response[27]
78% (14/18)
(95% CI: 52%-94%)

- Free C5 serum samples in pediatric patients showed immediate, complete inhibition of C5 throughout the 50-week extension period[27,a,d]

SUSTAINED

Sustained disease control your patients deserve. Of the 78% patients who achieved complete TMA response at Week 26, 100% (14/14) maintained it at Week 50.[8]

Study design[2,8,27]

- **26-week, multicenter, open-label, single-arm study of eculizumab-naïve patients (N=18) with documented diagnosis of atypical-HUS**
- **Select inclusion criteria:** platelet count ≤150 × 10^9/L, evidence of hemolysis such as an elevation in serum LDH, and serum creatinine ≥97.5% percentile at screening or required dialysis
- **Select exclusion criteria:** patients with TMA due to ADAMTS13 deficiency, STEC-HUS, and genetic defect in cobalamin C metabolism
- **Primary endpoint:** complete TMA response, defined as: platelet count normalization (≥150 × 10^9/L), serum LDH normalization (less than upper limit of normal), and ≥25% improvement in serum creatinine from baseline
- **Select secondary endpoints:** time to complete TMA response and complete TMA response status over time, dialysis requirement, CKD stage change, hemoglobin response, and change from baseline in quality of life

Study 312: Select demographics and baseline characteristics

- Mean platelet count was 60.50 x 10^9/L, mean LDH in serum was 2324.11 U/L, mean eGFR was (28.4 mL/min/1.73 m^2)
- 35.7% (5/14) of patients had Stage 5 CKD at baseline as assessed by eGFR
- 7% (1/14) had a history of prior kidney transplant
- 71% (10/14) had extrarenal signs or symptoms of atypical-HUS at baseline

Pediatric extension study

- Pediatric patients with atypical-HUS in the 26-week initial evaluation period could enter an ongoing 4.5-year extension period. Long-term extension data are from an interim analysis with 18 patients at Week 50

The initial interim analysis included in the USPI at the time of approval included 14 pediatric patients with atypical-HUS. The final, published analysis at 26 weeks included 18 patients.[2,8]

[a]As measured by free C5 serum concentration of <0.5 µg/mL.[2]

[b]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.[2]

[c]Primary endpoint.[27]

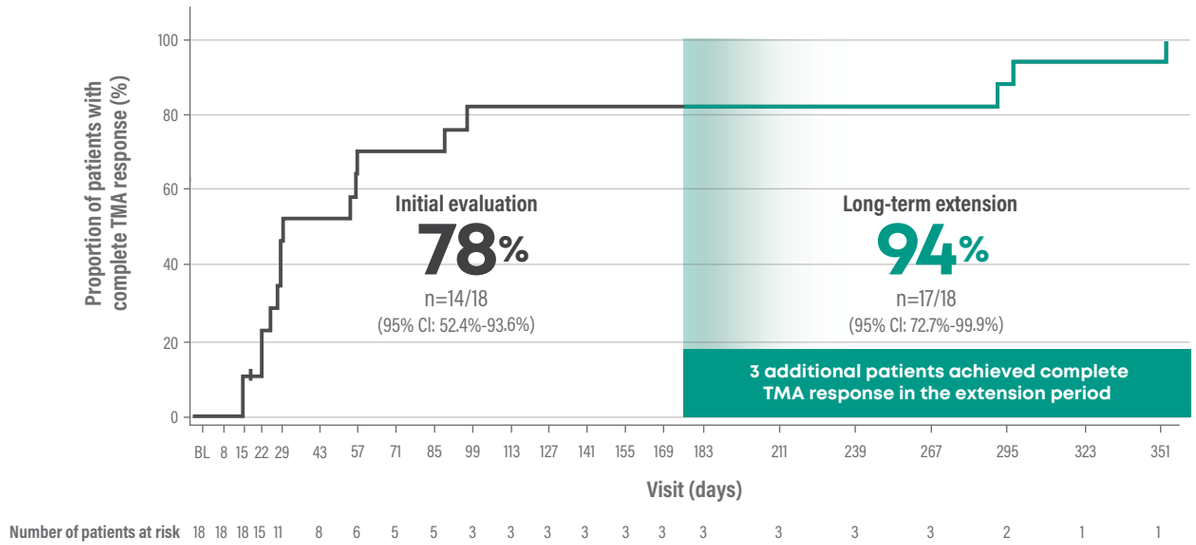
[d]There were individual free C5 outliers noted at 3 time points.[27]

ADAMTS13=a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; atypical-HUS=atypical hemolytic uremic syndrome; C5=complement component 5; CKD=chronic kidney disease; DGKE=diacylglycerol kinase epsilon; eGFR=estimated glomerular filtration rate; ESKD=end stage kidney disease; LDH=lactate dehydrogenase; STEC-HUS=shiga toxin-producing escherichia coli-associated hemolytic uremic syndrome; TMA=thrombotic microangiopathy.

Initiate with ULTOMIRIS to potentially achieve complete TMA response in your pediatric patients with atypical-HUS

Complete TMA response was achieved in 94% of pediatric patients by Week 50[2,8,27]

Time to Complete TMA Response[a]



Median time to complete TMA response was 30.0 days (95% CI: 22.0, 88.0).[8,a] Patients who did not have a response were censored at the date of last visit or study discontinuation at the time when the analysis was performed.[27]

- Of the patients who achieved complete TMA response at 26 weeks (n=14), 100% (14/14) maintained it at Week 50[8]

[a]The initial interim analysis included in the USPI at the time of approval included 14 pediatric patients with atypical-HUS. The final, published analysis at 26 weeks included 18 patients.[2,8]
[b]Secondary endpoint.[27]

SELECT IMPORTANT SAFETY INFORMATION

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.

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

ULTOMIRIS has been shown to maintain or improve kidney function in patients with atypical-HUS[8]

ULTOMIRIS maintained or improved kidney function and offered an opportunity for some pediatric patients to discontinue dialysis[8]

eGFR category stage from baseline to end of initial evaluation period (full analysis set)[8,a]

Baseline eGFR category + eGFR rates (mL/min/1.73 m²)	Post-baseline eGFR category at Day 183 and associated eGFR rates (N=17) (mL/min/1.73 m²)					
	G1 n (%) ≥90	G2 n (%) 60-89	G3a n (%) 45-59	G3b n (%) 30-44	G4 n (%) 15-29	G5 n (%) <15
G1 (n=0) ≥90	0	0	0	0	0	0
G2 (n=1) 60-89	1 (5.9)	0	0	0	0	0
G3a (n=1) 45-59	1 (5.9)	0	0	0	0	0
G3b (n=1) 30-44	1 (5.9)	0	0	0	0	0
G4 (n=8) 15-29	5 (29.4)	1 (5.9)	1 (5.9)	0	1 (5.9)	0
G5 (n=6) <15	3 (17.6)	2 (11.8)	0	0	0	1 (5.9)
TOTAL (n=17)	**11 (64.7)**	**3 (17.6)**	**1 (5.9)**	**0**	**1 (5.9)**	**1 (5.9)**

Improvement vs baseline Worsening vs baseline

eGFR categories were classified based on KDIGO Guidelines for the Evaluation of Chronic Kidney Disease. eGFR values were: Category 1=≥90; Category 2=60 to 89; Category 3a=45 to 59; Category 3b=30 to 44; Category 4=15 to 29; Category 5: <15 [including dialysis].[24,25] The baseline was derived based on last available eGFR before starting treatment. Patients with both baseline and at least 1 value at post-baseline visits were included in the summary. Percentages based on number of patients with non-missing data at both baseline and post-baseline visit.[27-29]

In the 312 clinical trial, CKD staging was defined by eGFR at a certain point in time. Because CKD is defined by KDIGO guidelines as abnormalities of kidney structure or function, such as low eGFR, present for a minimum of 3 months, eGFR categorization was deemed more appropriate. Stage 5 CKD is unlikely to improve.[27-29]

[a]The initial interim analysis included in the USPI at the time of approval included 14 pediatric patients with atypical-HUS. Table presented above is the final, published analysis at 26 weeks, of patients with available data (N=17).[2,8]

[b]Secondary endpoint.[8,27]

Atypical-HUS=atypical hemolytic uremic syndrome; CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; KDIGO=Kidney Disease Improving Global Outcomes; TMA=thrombotic microangiopathy.

Most patients maintained or improved kidney function[8]

Patients with eGFR Categories 1-4

- 91% (10/11) of patients improved their eGFR category[8]
- 100% (11/11) of patients with eGFR ≥15 at baseline maintained or improved their eGFR category[8]

Patients with eGFR Category 5

- 83% (5/6) of patients saw an improvement in eGFR category; of these, all improved to eGFR category 1 or 2[8]

Dialysis discontinuation[8]

AT 26 WEEKS

- 5 of the 6 patients (83%) who required dialysis at study entry were off dialysis by Week 26[8,b]

AT 50 WEEKS

- 6 of the 6 patients (100%) who required dialysis at study entry were off dialysis by Week 50[8]

Potential for recovery of kidney function in your pediatric patients

- Mean eGFR was 108.0 mL/min/1.73 m² at end of study, a 79.6 mL/min/1.73 m² mean increase from baseline[2]

SELECT IMPORTANT SAFETY INFORMATION

Monitoring Disease Manifestations after ULTOMIRIS Discontinuation (cont'd)

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.

Consider ULTOMIRIS and its established safety profile for your pediatric patients with atypical-HUS

Adverse reactions reported in ≥10% of ULTOMIRIS-treated pediatric patients with atypical-HUS at 26 weeks[2]

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

Long-term extension: safety in pediatric patients at 50 weeks (N=21)[8,c]

Event type	Overall (N=21) n (%)	Overall (N=21) Events
Any AE	21 (100.0)	369
Any SAE	14 (66.7)	31
TEAE resulting in drug discontinuation	1 (4.8)	2
TESAE resulting in drug discontinuation	1 (4.8)	2
TEAE resulting in study discontinuation	1 (4.8)	2
TESAE resulting in study discontinuation	1 (4.8)	2
TEAE during study drug infusion	4 (19.0)	7
TESAE during study drug infusion	0 (0)	0
Treatment-related AEs	10 (47.6)	33
Meningococcal infections	0 (0)	0
Deaths	0 (0)	0

- The most frequent adverse reactions reported in ≥20% of pediatric patients treated with ULTOMIRIS were diarrhea, constipation, vomiting, pyrexia, upper respiratory tract infection, headache, and hypertension[2]

[a]Graded per CTCAE v5.0.[2]

[b]Grouped term includes nasopharyngitis, pharyngitis, upper respiratory tract infection, rhinitis, viral upper respiratory tract infection, rhinovirus infection, viral pharyngitis, rhinorrhea, and oropharyngeal pain.[2]

[c]Safety outcomes at the last available follow-up with ULTOMIRIS.[8]

AE=adverse event; BW=body weight; C5=complement component 5; CTCAE=common terminology criteria for adverse events; SAE=serious adverse event; TEAE=treatment-emergent adverse event; TESAE=treatment-emergent serious adverse event.

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

Pharmacodynamic findings showed that free C5 was immediately and completely[a] inhibited in pediatric patients taking ULTOMIRIS[8]

Adapted from Ariceta G, et al. *Kidney Int.* 2021;100(1):225-237.[8]

Box plot of free C5 vs time (semi-log scale). Pharmacodynamics of free C5 in serum concentrations from Ariceta et al, 2021.[8] Dashed line: free C5 concentration of 0.5 µg/mL (denotes complete terminal complement inhibition). Box and whisker plot: the horizontal line in the middle of each box indicates the median, a diamond indicates the mean, and the upper and lower borders of the boxes denote the 75th and 25th percentiles, respectively. The whiskers depict the highest and lowest values within 1.5-fold the interquartile range from the lower and upper quartiles. Outliers are represented by asterisks beyond the whiskers.

By the end of the first infusion, ULTOMIRIS reduced the free C5 serum concentration to <0.5 µg/mL.[8]

[a]Defined as a free serum C5 concentration <0.5 µg/mL.[8]

SELECT IMPORTANT SAFETY INFORMATION

Thromboembolic Event Management

The effect of withdrawal of anticoagulant therapy during treatment with ULTOMIRIS has not been established. Treatment should not alter anticoagulant management.

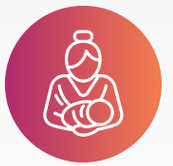
ULTOMIRIS®
(ravulizumab-cwvz)
injection for intravenous use
300 mg/3 mL vial

Consider ULTOMIRIS—preferred by caregivers

Factors for caregivers and patients when selecting their preferred treatment were[30]:

Control of atypical-HUS

Frequency of infusions



Select factors for caregivers and patients

In a survey of 16 caregivers of pediatric patients with atypical-HUS[30,a]

100%
(16/16)

- **Preferred ULTOMIRIS** over eculizumab overall
- **Preferred the frequency of ULTOMIRIS infusions** over eculizumab
- **Preferred quality of life with ULTOMIRIS** vs eculizumab for both patient and caregiver

[a]**A web-based survey which included US caregivers or the legal parents/guardians of pediatrics patients (N=16) with confirmed diagnosis of atypical-HUS who had previously received eculizumab and ≥3 doses of ravulizumab. Mean age of pediatric patients was 10.1 years. Percentages represent the percent of caregivers who preferred ULTOMIRIS vs preferring eculizumab/having no preference.[30]**

Less frequent infusions with ULTOMIRIS[2,31-33]

- Reduces time spent in treatment
- May allow for less time missed at school or work
- May reduce risk of complications from repeated venous access

SELECT IMPORTANT SAFETY INFORMATION

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.

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

Determining optimal duration of therapy for ULTOMIRIS

Per the ULTOMIRIS prescribing information, ULTOMIRIS treatment of atypical-HUS should be for a minimum duration of 6 months. Beyond 6 months, an individualized approach is recommended to determine optimal treatment duration based on clinical response in patients with atypical-HUS; individual risk factors for relapse must be considered[2]

STEP 1 | Evaluate

Evaluate clinical response, including potential kidney recovery. For some patients, complete TMA response may take longer than 6 months[31,34]

STEP 2 | Assess

Assess individual factors such as current kidney function, pediatric onset, genetic variants, ongoing exposure to triggers, family history, and other risk factors for TMA recurrence[17,19,20,22,29,35-37]

Risk factors for TMA recurrence following treatment discontinuation include prior kidney allograft, prior TMA, extrarenal manifestations, childhood onset of disease, anti-CFH autoantibodies, and genetic mutations[19,34,38]

STEP 3 | Decide

Make informed decisions with your patient and confirm their ability to comply with a monitoring plan. If a decision is made to discontinue, monitor for at least 12 months (depending on risk factors, with up to lifelong monitoring in some patients) and be ready to restart when appropriate[2,34]

While platelet levels rapidly[a] improved with ULTOMIRIS, improvements in kidney function may take longer.[31,39]

- Patients with atypical-HUS remain at risk of TMA in the event of new exposure to triggers[19,34,38,40]
- An initial 26-week period of treatment with ULTOMIRIS led to complete TMA response in 78% (14/18) of pediatric patients; the optimal duration of treatment differs for each patient[2,8]

[a]By Day 8.[8]
Atypical-HUS=atypical hemolytic uremic syndrome; TMA=thrombotic microangiopathy.

SELECT IMPORTANT SAFETY INFORMATION

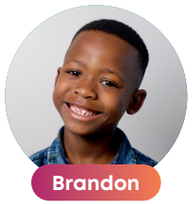
ADVERSE REACTIONS

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.

Adverse reactions reported in ≥20% of pediatric patients treated with ULTOMIRIS were diarrhea, constipation, vomiting, pyrexia, upper respiratory tract infection, decreased vitamin D, headache, cough, rash, and hypertension.

Case Study:
Management of atypical-HUS in pediatric patients <12 years

Overview: Presented to the ED after one episode of hematemesis following a tooth extraction 3 days prior



Baseline:

Age: 6 years old
Height: 109 cm (43 in)
Weight: 28 kg (61 lb)
Race: African American
BMI: 23.6
Blood Pressure: 120/80 mm Hg
Heart Rate: 120 bpm

Medical History

- Asthma (albuterol as needed)
- Family was having trouble managing pain from tooth extraction and presumed hematemesis
- Had been given ibuprofen as prescribed

Family History

- Mother: hypothyroidism
- Father: hypertension

Based on an actual patient case.

Lab values

		Lab values at presentation	Reference values[29,41-44]
Complete Blood Count	White blood cell count (x 10^3 cells/mcL)	7.5	4.5-11
	Hemoglobin (g/dL)	7.5	14-17
	Haptoglobin (mg/dL)	<15	30-200
	Platelet count (x 10^3/mcL)	27	150-350
	LDH (U/L)	3106	60-160
	Reticulocytes (%)	8.4	0.5-1.5
	MCV (fL)	85	80-100
Peripheral Smear	Schistocytes present	Present (+2)	Absent
Coagulation Panel	PT/aPTT/INR (seconds)	12/26/1.1	11-13/25-35/1.0
	D-dimers (ng/mL)	450	≤500
Other Tests	Coombs test	Negative	Negative
	Serum creatinine (mg/dL)	1.4	0.7-1.2
	eGFR (mL/min/1.73 m^2)	29[a]	≥90

At initial presentation in the ED, Brandon continued to experience oral pain and bleeding from the mouth.

- No changes detected on urine output
- Negative for Shiga toxin
- Blood pressure improved after pain control was administered

Brandon was then admitted to the PICU for closer monitoring; active GI bleeding was ruled out and the cause of hematemesis was likely secondary to blood swallowed from tooth extraction. Hematologist recommended PLT and PRBC transfusion.

[a]Calculated using the 2021 Chronic Kidney Disease Epidemiology (CKD-EPI) Collaboration creatinine equation [https://www.niddk.nih.gov/health-information/professionals/clinical-tools-patient-management/kidney-disease/laboratory-evaluation/estimated-gfr-calculators/adults-pediatrics].

SELECT IMPORTANT SAFETY INFORMATION

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.

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

During Days 1 through 3:

- A TMA was suspected and ADAMTS13 activity level test was sent for evaluation
- Oral bleeding was stopped after mouth packing was performed
- Brandon received 2 courses of plasma infusion due to concerns of TTP
- C3 and C4 complements appear normal

On Day 4, ADAMTS13 activity level came back >5%. Atypical-HUS was diagnosed and treatment was started.

- Factor H antibodies came back negative
- **Treatment with ULTOMIRIS was initiated with prophylactic antibiotic use and subsequent meningococcal vaccination was administered in accordance with ULTOMIRIS PI and ACIP guidelines**

Genetic testing for APOL1 and CFH mutations were performed on Day 10.

At Day 13, Brandon was able to be discharged home.

- Genetic testing revealed positive for CFH mutation and negative for APOL1
- Brandon continues to receive ULTOMIRIS infusion as an outpatient

Lab values for Days 1-13

	At admission	Day 3	Day 4	Day 10	Day 13	Reference values[41]
Hemoglobin (g/dL)	7.5	8	8.4	8.7	9.8	14-17
Platelet count (x 10^3/mcL)	27	20	23	62	150	150-350
LDH (U/L)	3106	3178	3500	263	183	60-160
Serum creatinine (mg/dL)	1.4	0.7	0.68	0.7	0.7	0.7-1.2

ACIP=Advisory Committee on Immunization Practices; ADAMTS13=a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; aPTT=activated partial thromboplastin time; atypical-HUS=atypical hemolytic uremic syndrome; ED=emergency department; eGFR=estimated glomerular filtration rate; GI=gastrointestinal; INR=international normalized ratio; LDH=lactate dehydrogenase; MCV=mean corpuscular volume; PICU=pediatric intensive care unit; PLT=platelet; PRBC=packed red blood cell; PT=prothrombin time; TMA=thrombotic microangiopathy; TTP=thrombotic thrombocytopenic purpura.

SELECT IMPORTANT SAFETY INFORMATION

DRUG INTERACTIONS (cont'd)

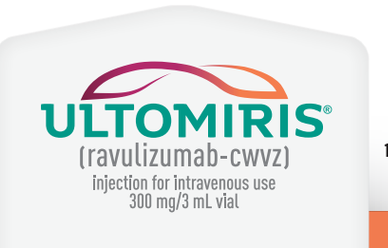
Neonatal Fc Receptor Blockers

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.



Case Study:
Management of atypical-HUS in pediatric patients ≥12 years

Overview: Previously healthy female was brought to the ED following 3 days of fever, poor appetite, fatigue, headache, and body aches

Julia

Baseline:

Age: 14 years old
Height: 157 cm (62 in)
Weight: 45 kg (99 lb)
BMI: 18.1
Blood Pressure: 152/96 mm Hg
Heart Rate: 122 bpm
Respiratory Rate: 20 bpm
Temperature: 39.1° C (102° F)

Medical History

- Mild asthma
- Physical examination is unremarkable other than pallor

Family History

- 3 healthy siblings
- Mother: hypertension
- Father: history of kidney stones
- Maternal uncle developed renal failure of unclear etiology and was on dialysis for 6 years. He received a deceased donor renal transplant, which failed within 3 months

Based on an actual patient case.

Lab values

		Lab values at presentation	Reference values[29,41-44]
Complete Blood Count	White blood cell count (x 10^3 cells/mcL)	12.6	4.5-11
	Hemoglobin (g/dL)	9.1	12-16
	Haptoglobin (mg/dL)	<15	30-200
	Platelet count (x 10^3/mcL)	135	150-350
	LDH (U/L)	3400	60-160
	Reticulocytes (%)	8.4	0.5-1.5
Peripheral Smear	Schistocytes present	Present	Absent
Coagulation Panel	PT/aPTT/INR (seconds)	12/26/1.1	11-13/25-35/1.0
	D-dimers (ng/mL)	450	≤500
Other Tests	Coombs test	Negative	Negative
	Serum creatinine (mg/dL)	1.3	0.5-1.0
	eGFR (mL/min/1.73 m^2)	46[a]	≥90

At initial presentation in the ED, Julia was started on supportive IVF.

- Continued to have elevated blood pressure
- Poor urine output was noted (100 mL/12 hours) and no response was seen to fluid bolus
- Developed generalized tonic-clonic seizure—admitted to PICU

Hematologist and nephrologist were consulted:

- Blood smear was performed, revealing few schistocytes and low platelets
- ADAMTS13 test ordered
- Coombs test was negative
- Stool cultures were negative for EHEC
- Differentials included TMA caused by TTP or atypical-HUS
- Recommendation was to treat with catheter for dialysis and plasmapheresis, and to start C5 complement inhibition therapy once diagnosis is confirmed

On Day 2, Julia experienced another generalized tonic-clonic seizure.

- Blood pressure remained elevated, and nicardipine infusion was started
- Biopsy was delayed due to low platelets
- Julia was anuric with 30 mL of UOP/24 hours

On Day 3, dialysis was begun and PLEX was initiated with a plan for 5 sessions over the next 5-7 days.

- Biopsy was delayed again due to thrombocytopenia
- 1 unit of PRBC transfusion was given

[a]Calculated using the 2021 Chronic Kidney Disease Epidemiology (CKD-EPI) Collaboration creatinine equation [https://www.niddk.nih.gov/health-information/professionals/clinical-tools-patient-management/kidney-disease/laboratory-evaluation/estimated-gfr-calculators/adults-pediatrics].

During Days 4 to 8, Julia continued to be dialysis-dependent.

- Blood pressure remained well controlled on nicardipine and lab parameters were mostly unchanged
- ADAMTS13 activity was >5%. TTP was ruled out and atypical-HUS was strongly suspected
- PLEX was discontinued after ADAMTS13 activity results returned as normal

On Day 9, treatment with ULTOMIRIS was initiated with prophylactic antibiotic use and subsequent meningococcal vaccination in accordance with ULTOMIRIS PI and ACIP guidelines after discussion with the MDT, with a weight-based loading dose of 2400 mg.

- Other immunological evaluations were negative and hemodialysis was continued every other day

At Day 10, no significant changes in status were observed apart from blood pressure improvement.

- Oral antihypertensive medications were administered; blood pressure showed as mildly elevated but continued trending downward overall

By Day 13, Julia was able to be discharged from the hospital and will continue to be monitored and receive ULTOMIRIS infusions in an outpatient setting.

- Dialysis was able to be discontinued at Day 17
- Genetic testing revealed positive pathogenic mutation in C3 gene

Lab values for Days 1-13

	At Admission	Day 2	Day 8	Day 10	Day 13	Reference values[41]
Hemoglobin (g/dL)	9.1	5.4	7.1	8.9	11.1	12-16
Platelet count (x 10^3/mcL)	135	22	31	73	120	150-350
LDH (U/L)	3400	3000	2800	1970	200	60-160
Serum creatinine (mg/dL)	1.3	3.9	3.5	2.8	1.7	0.5-1.0

ACIP=Advisory Committee on Immunization Practices; ADAMTS13=a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; aPTT=activated partial thromboplastin time; atypical-HUS=atypical hemolytic uremic syndrome; C5=complement protein 5; ED=emergency department; eGFR=estimated glomerular filtration rate; EHEC=enterohemorrhagic *Escherichia coli*; INR=international normalized ratio; IVF=intravenous fluid; LDH=lactate dehydrogenase; MDT=multidisciplinary team; PICU=pediatric intensive care unit; PLEX=plasma exchange; PRBC=packed red blood cell; PT=prothrombin time; TMA=thrombotic microangiopathy; TTP=thrombotic thrombocytopenic purpura; UOP=urinary output.

References: 1. Data on file. Atypical-HUS market access dashboard. Alexion Pharmaceuticals, Inc.; 2023. **2.** ULTOMIRIS. Prescribing Information. Alexion Pharmaceuticals, Inc. **3.** Goodship TH, et al. *Kidney Int.* 2017;91(3):539-551. **4.** Agarwal KA, et al. *Kidney Int Rep*. 2020;5(8):1350-1355. **5.** Laurence J, et al. *Clin Adv Hematol Oncol.* 2016;14 Suppl 11(11):2-15. **6.** Frémeaux-Bacci V, et al. *Clin J Am Soc Nephrol*. 2013;8(4):554-562. **7.** Noris M, et al. *Clin J Am Soc Nephrol*. 2010;5(10):1844-1859. **8.** Ariceta G, et al. *Kidney Int*. 2021;100(1):225-237. **9**. Lapeyraque AN, et al. *Can J Kidney Health Dis*. 2020;7:1-9. **10.** Shaefer F, et al. *Kidney Int*. 2018;94(2):408-4181. **11.** Palma LMP, et al. *Pediatr Nephrol*. 2022;37(9):1967-1980. **12.** Lemaire M, et al. *Nat Genet*. 2013;45(5):531-6. **13.** Ashida A, et al. *Clin Exp Nephrol*. 2018;22(4):924-930. **14.** Bresin E, et al. *J Am Soc Nephrol*. 2013;24(3):475-486. **15.** Nester C, et al. *Molecular Immunology*. Published March 12, 2015. **16.** Noris M, et al. In: Adam MP, et al, eds. GeneReviews®. Published November 16, 2007. Updated September 23, 2021. https://www.ncbi.nlm.nih.gov/books/NBK1367/ **17.** Ariceta G, et al. *Clin Kidney J*. 2021;14(9):2075-2084. **18.** Noris M, et al. *N Engl J Med*. 2009;361:1676-1687. **19.** Macia M, et al. *Clin Kidney J*. 2017;10(3):310-319. **20.** Menne J, et al. *BMC Nephrology*. 2019;20(1):125. **21.** Fakhouri F, et al. *Clin J Am Soc Nephrol*. 2017;12(1):50-59. **22.** Noris M, et al. *Nat Rev Nephrol*. 2012;8(11):622-633. **23.** Bruel A, et al. *Clin J Am Soc Nephrol*. 2017;12(8):1237-1247. **24.** Abbas F, et al. *World J Transplant*. 2018;8(5):122–141. **25.** Campistol JM, et al. *Nefrologia*. 2015;35(5):421-447. **26.** Frémeaux-Bacci V, et al. *Clin J Am Soc Nephrol*. 2013;8 Suppl (4):554-562. **27.** Data on file [ALXN1210-aHUS-312CSR]. **28.** Chen TK, Knicely DH, Grams ME. *JAMA*. 2019;322(13):1294-1304. **29.** KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. 2013;3:1:1-150. **30.** Mauch TJ, et al. *J Comp Eff Res*. 2023;12(9):e230036. **31.** Barbour T, et al. *Kidney Int Rep*. (article and supplement) 2021;6(6):1603-1613. **32.** Syed YY. *Drugs*. 2021;81(5):587-594. **33.** Dixon BP, Sabus A. *J Clin Pharm Ther*. 2022;47(7):1081-1087. **34.** Laurence J. *Clin Adv Hematol Oncol*. 2020;18(4):221-230. **35.** Timmermans SAMEG, et al. *J Am Soc Nephrol*. 2018;29(8):2234-2243. **36.** Asif A, et al. *J Nephrol*. 2017;30:347-362. **37.** Fakhouri F, et al. *J Am Soc Nephrol*. 2010;21(5):859-867. **38.** Noris M, Remuzzi G. *Kidney Int Rep*. 2023;8(1):4-7. **39.** Licht C, et al. *Kidney Int*. 2015;87(5):1061-1073. **40.** Chaturvedi S, et al. *Blood Adv*. 2021;5(5):1504-1512. **41.** Merck Manual. Merck & Co. Inc.; Rahway, NJ; 2022. **42.** Zini G, et al. *Int J Lab Hematol*. 2021;43:1264-1271. **43.** Shikdar S, et al. International Normalized Ratio (INR) [Updated 2023 May 1]. StatPearls Publishing; 2024. https://www.ncbi.nlm.nih.gov/books/NBK507707/ **44.** Theis S, et al. Coombs Test. *NCBI* Bookshelf. September 12, 2022. Bookshelf ID: NBK547707.

Alexion: a long-standing history of commitment to supporting healthcare professionals and their patients

For Patients

ONESOURCE®
Personalized Patient Support from Alexion

We created OneSource™ to support your patients every step of the way

OneSource is a complimentary, personalized patient support program available for patients, families, and caregivers facing complement-mediated diseases to help them start and stay on the treatment as prescribed.

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

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 patients eligible to be reimbursed by government insurance programs[b] 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** or **OneSource@Alexion.com** for more information on patient eligibility

[a]Based on typical commercial patient out-of-pocket deductible limits. Additional terms and conditions apply. Please contact OneSource with additional questions.
[b]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.
Atypical-HUS=atypical hemolytic uremic syndrome; FDA=Food and Drug Administration.

SELECT IMPORTANT SAFETY 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.

For HCPs

ALEXION ACCESS NAVIGATOR

Alexion Access Navigator

A dedicated resource where US healthcare professionals and their offices can find downloadable access and reimbursement materials, including indication-specific coding and billing guides, sample letters of medical necessity, and a link to the REMS program.
AlexionAccessNavigator.com/Ultomiris

Utilize atypical-HUS ICD-10 codes to avoid coverage challenges

D59.32 Hereditary hemolytic uremic syndrome
Atypical hemolytic uremic syndrome with an identified genetic cause
Code also, if applicable
- **Defects in the complement system (D84.1)**
- **Methylmalonic acidemia (E71.120)**

D59.39 Other hemolytic uremic syndrome
Atypical (nongenetic) hemolytic uremic syndrome
Secondary hemolytic uremic syndrome
Code first, if applicable, any associated:
- **COVID-19 (U07.1)**
- **Complications of liver transplant (T86.4-)**
- **Complications of kidney transplant (T86.1-)**
- **Complications of heart transplant (T86.2-)**

Code also, if applicable, any associated condition, such as:
- **Hypertensive emergency (I16.1)**
- **Systemic lupus erythematosus (M32.-)**
- **Malignant neoplasm (C00-C96)**

Use Additional code, if applicable, for adverse effect to identify drug
(T36-T50 with fifth or sixth character 5)

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.

ALEXION®
AstraZeneca Rare Disease