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

For Nurses

WIDEN THEIR WORLD

INFUSE YOUR PATIENTS WITH ATYPICAL-HUS WITH UP TO 8 WEEKS OF FREEDOM[1,a]

[a]Starting 2 weeks after the intravenous loading dose, maintenance doses are infused intravenously every 8 weeks for adult patients and every 4 or 8 weeks for pediatric patients (depending on body weight).

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)*].

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:

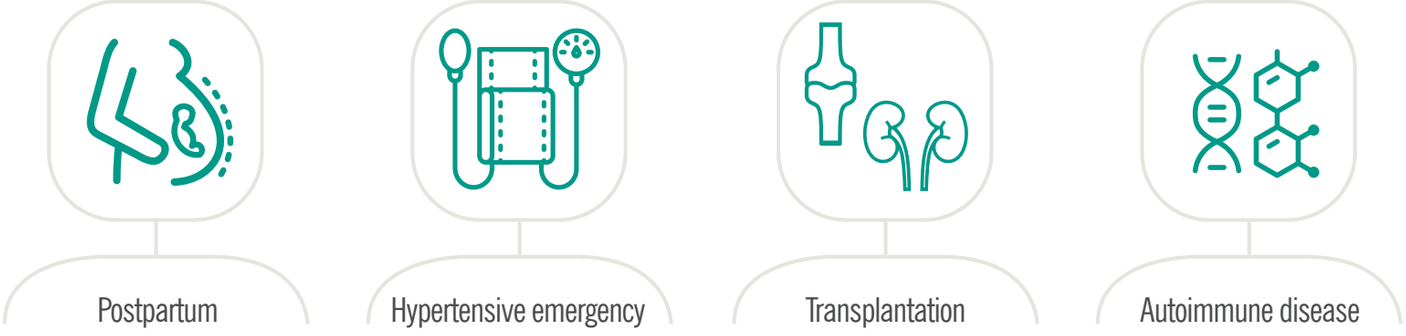
ULTOMIRIS is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

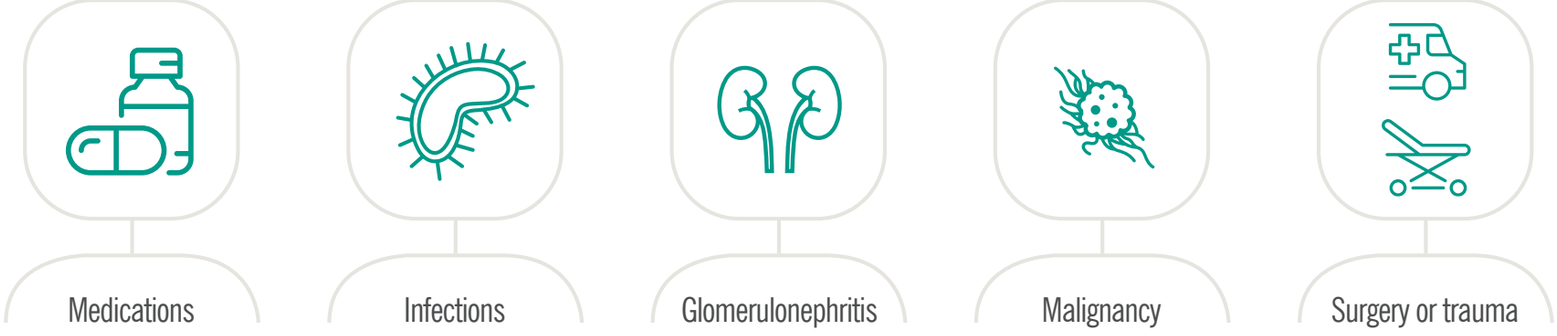
Please see additional Important Safety Information throughout and accompanying full Prescribing Information (UltomirisHCP.com/PI) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

THROMBOTIC MICROANGIOPATHY (TMA) CAN BE ASSOCIATED WITH VARIOUS TRIGGERS[2]

- Atypical-HUS is a disease caused by dysregulation of the alternative pathway of the complement system, leading to excessive complement activation and TMA[3,4]
  - Atypical-HUS may be triggered by conditions that activate complement[2]
  - Persistence of TMA despite treatment of associated conditions may suggest atypical-HUS[5]

Triggers that may accelerate activation of the complement system[2]





DIFFERENTIAL DIAGNOSIS OF TMA, INCLUDING ATYPICAL-HUS[2,3,5,6]

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**

Renal impairment
Elevated creatinine level and/or **decreased eGFR** and/or **elevated blood pressure** and/or **abnormal urinalysis results**

GI symptoms
Diarrhea ± blood and/or **nausea/vomiting** and/or **abdominal pain** and/or **gastroenteritis/pancreatitis**

OTHER SYMPTOMS

CV symptoms
MI 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**

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).
If STEC-HUS and TTP are ruled out, a diagnosis of atypical-HUS should be considered.

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

[a]Shiga toxin/EHEC test is warranted with history/presence of gastrointestinal symptoms.
[b]Range found in published data is 5%-10%.
ADAMTS13=a disintegrin and metalloproteinase with a thrombospondin type 1 motif member 13; CV=cardiovascular; EHEC=enterohemorrhagic *E coli*; eGFR=estimated glomerular filtration rate; GI=gastrointestinal; LDH=lactate dehydrogenase; MI=myocardial infarction; sCr=serum creatinine; STEC-HUS=Shiga toxin–producing *E coli* hemolytic uremic syndrome; TMA=thrombotic microangiopathy; TTP=thrombotic thrombocytopenic purpura.

ULTOMIRIS WAS ASSESSED IN AN OPEN-LABEL, SINGLE-ARM STUDY OF 56 ADULT PATIENTS WITH ATYPICAL-HUS[1]

Adult Study

- The efficacy of ULTOMIRIS was assessed in an open-label, single-arm study of 56 adult patients who displayed signs of TMA and were naive to complement inhibitor therapy prior to study entry[1]
- Patients were required to have a platelet count ≤150 x 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[1]
- Enrollment criteria excluded patients with TMA due to ADAMTS13 deficiency, STEC-HUS, and genetic defect in cobalamin C metabolism[1]
- The study consisted of a 26-week initial evaluation period. Mean age at time of first infusion was 42.2 years; 66.1% of patients were female; 51.8% were White, 26.8% were Asian, and 21.4% were unknown or other race[1]

Primary end point[1,7]	Select secondary end points[7]
• Complete TMA response[a], comprising - Platelet count normalization (≥150 × 10^9/L) - Serum LDH normalization (≤246 U/L) - ≥25% improvement in serum creatinine from baseline	• Time to complete TMA response • Complete TMA response status over time • Dialysis requirement • CKD stage as evaluated by eGFR • Hemoglobin response • Change from baseline in quality of life

Select Demographics and Baseline Characteristics (N=56)[1,7]

- More than half, 51% (27/53), represented a critically ill population[b]
- Mean platelet count was 118.52 x 10^9/L
- Mean LDH in serum was 702.38 U/L
- Mean eGFR was 15.86 mL/min/1.73 m^2
- 71.4% (40/56) had Stage 5 CKD as assessed by eGFR
- 14% (8/56) had a history of transplant
- 14% (8/56) had evidence of TMA >3 days after childbirth
- 93% (52/56) had extra-renal signs or symptoms of atypical-HUS at baseline

[a]Patients had to meet all criteria at 2 separate assessments obtained at least 4 weeks (28 days) apart and any measurement in between.[1]
[b]Percentage of patients who had received ICU-level care prior to the start of screening based on the total number of patients who had any ER visits or hospitalizations due to atypical-HUS prior to the start of screening.[7]
CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; ER=emergency room; LDH=lactate dehydrogenase; STEC-HUS=Shiga toxin–producing *E coli* hemolytic uremic syndrome; TMA=thrombotic microangiopathy.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

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IN A 26-WEEK STUDY, THE MAJORITY OF ADULT PATIENTS TAKING ULTOMIRIS ACHIEVED COMPLETE TMA RESPONSE[1]

Adult Study (N=56)[1]

Components of Complete TMA Response

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

54%
(95% CI: 40%-67%)
n=30

Select secondary end points

- **100% (30/30)** of complete TMA responses were maintained through all available follow-up[1]
- 17 of the 29 patients (59%) who required dialysis at study entry discontinued dialysis by the end of available follow-up; 6 of 27 patients who were off dialysis at baseline were on dialysis at last available follow-up[1]
- Mean eGFR was 51.8 mL/min/1.73 m^2 at end of study, a 35.9 mL/min/1.73 m^2 (227%) mean increase from baseline[1]

>99.5% of all free C5 serum samples in adult patients showed complete inhibition of C5 throughout the 6-month study period[7,a]

[a]As measured by free C5 serum concentration of <0.5 mcg/mL.[1]

C5=complement protein 5; CI=confidence interval; eGFR=estimated glomerular filtration rate; LDH=lactate dehydrogenase; TMA=thrombotic microangiopathy.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

ULTOMIRIS, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by meningococcal bacteria (septicemia and/or meningitis) in any serogroup, including non-groupable strains. Life-threatening and fatal meningococcal infections have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors.

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ULTOMIRIS WAS ASSESSED IN AN OPEN-LABEL, SINGLE-ARM STUDY OF 14 PEDIATRIC PATIENTS WITH ATYPICAL-HUS[1]

Pediatric Study

- The efficacy of ULTOMIRIS was assessed in a 26-week ongoing, multicenter, open-label, single-arm study of 14 pediatric patients with documented diagnosis of atypical-HUS who were eculizumab-naive[1]
- Patients were required to have a platelet count ≤150 x 10^9/L, evidence of hemolysis such as an elevation in serum LDH, and serum creatinine level ≥97.5% percentile at screening or required dialysis[1]
- Enrollment criteria excluded patients with TMA due to ADAMTS13 deficiency, STEC-HUS, and genetic defect in cobalamin C metabolism[1]
- The median age at time of first infusion was 5.2 years; 64.3% of patients were female; 50.0% were White, 28.6% were Asian, 14.3% were Black or African American, 7.1% were American Indian or Alaskan Native, and 7.1% were of unknown race[1]

Primary end point[1,8]

- Complete TMA response[a], comprising
  - Platelet count normalization (≥150 × 10^9/L)
  - Serum LDH normalization (less than upper limit of normal)
  - ≥25% improvement in serum creatinine from baseline

Select secondary end points[8]

- Time to complete TMA response
- Complete TMA response status over time
- Dialysis requirement
- CKD stage as evaluated by eGFR
- Hemoglobin response
- Change from baseline in quality of life

Select Demographics and Baseline Characteristics (N=14, interim)[1,8]


Actor portrayal

- 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 extra-renal signs or symptoms of atypical-HUS at baseline

[a]Patients had to meet all criteria at 2 separate assessments obtained at least 4 weeks (28 days) apart and any measurement in between.[1]

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–producing *E coli* hemolytic uremic syndrome; TMA=thrombotic microangiopathy.

SELECT IMPORTANT SAFETY INFORMATION

Serious Meningococcal Infections (continued)

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

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IN A 26-WEEK STUDY, NEARLY 3 OUT OF 4 PEDIATRIC PATIENTS TAKING ULTOMIRIS ACHIEVED COMPLETE TMA RESPONSE[1]

Pediatric Study (N=14, interim)[1]

Components of Complete TMA Response

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

86%
(95% CI: 57%-98%)
n=12
Platelet Count & LDH Normalization

Complete TMA Response

71%
(95% CI: 42%-92%)
n=10

Select secondary end points

- **100% (10/10)** of complete TMA responses were maintained through all available follow-up[1]
- 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; no patient started dialysis during the study[1]
- Mean eGFR was 108.0 mL/min/1.73 m^2 at end of study, a 79.6 mL/min/1.73 m^2 (280%) mean increase from baseline[1]

99.6% of all free C5 serum samples in pediatric patients showed complete inhibition of C5 throughout the 6-month study period[8,a]

[a]As measured by free C5 serum concentration of <0.5 mcg/mL.[1]

C5=complement protein 5; CI=confidence interval; eGFR=estimated glomerular filtration rate; LDH=lactate dehydrogenase; TMA=thrombotic microangiopathy.

SELECT IMPORTANT SAFETY INFORMATION

Serious Meningococcal Infections (continued)

drug regimens for prophylaxis and their efficacy have not been studied in unvaccinated or vaccinated patients receiving complement inhibitors, including ULTOMIRIS. The benefits and risks of treatment with ULTOMIRIS, as well as those associated with antibacterial drug prophylaxis in unvaccinated or vaccinated patients, must be considered against the known risks for serious infections caused by *Neisseria meningitidis*.

Vaccination does not eliminate the risk of serious meningococcal infections, despite development of antibodies following vaccination.

Closely monitor patients for early signs and symptoms of meningococcal infection and evaluate patients immediately if infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if they occur. Promptly treat known infections. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection depending on the risks of interrupting treatment in the disease being treated.

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SAFETY PROFILE OF ULTOMIRIS IN ADULT PATIENTS WITH ATYPICAL-HUS[1]

Adverse Reactions Reported in ≥10% of ULTOMIRIS-Treated Adult Patients With Atypical-HUS[1]

BODY SYSTEM ADVERSE REACTION	ADULT PATIENTS (N=58)	
	All Grades*** (n=53) n (%)	≥Grade 3 (n=14) n (%)
Blood and lymphatic system disorders		
Anemia	8 (14)	0 (0)
Gastrointestinal disorders		
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)
General disorders and administration site conditions		
Pyrexia	11 (19)	1 (2)
Edema peripheral	10 (17)	0 (0)
Fatigue	8 (14)	0 (0)
Infections and infestations		
Upper respiratory tract infection*	15 (26)	0 (0)
Urinary tract infection	10 (17)	5 (9)
Gastrointestinal infection**	8 (14)	2 (3)
Metabolism and nutrition disorders		
Hypokalemia	6 (10)	1 (2)
Musculoskeletal and connective tissue disorders		
Arthralgia	13 (22)	0 (0)
Back pain	7 (12)	1 (2)
Muscle spasms	6 (10)	0 (0)
Pain in extremity	6 (10)	0 (0)
Nervous system disorders		
Headache	23 (40)	1 (2)
Psychiatric disorders		
Anxiety	8 (14)	1 (2)
Respiratory, thoracic, and mediastinal disorders		
Cough	10 (17)	0 (0)
Dyspnea	10 (17)	1 (2)
Skin and subcutaneous tissue disorders		
Alopecia	6 (10)	0 (0)
Dry skin	6 (10)	0 (0)
Vascular disorders		
Hypertension	14 (24)	7 (12)

The most frequent adverse reactions reported in ≥20% of adult patients treated with ULTOMIRIS were upper respiratory tract infection, diarrhea, nausea, vomiting, headache, hypertension, and arthralgia.[1]

Clinically relevant adverse reactions in <10% of patients included viral tonsillitis.[1]

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 hypertension, pneumonia, and abdominal pain.[1]

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.[1]

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

**Grouped term includes gastroenteritis, gastrointestinal infection, enterocolitis infection, infectious colitis, and enterocolitis.

***Graded per CTCAE v5.0.

CTCAE=Common Terminology Criteria for Adverse Events; STEC-HUS=Shiga toxin–producing *E coli* hemolytic uremic syndrome.

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SAFETY PROFILE OF ULTOMIRIS IN PEDIATRIC PATIENTS WITH ATYPICAL-HUS[1]

Adverse Reactions Reported in ≥10% of ULTOMIRIS-Treated Pediatric Patients With Atypical-HUS[1]

BODY SYSTEM ADVERSE REACTION	PEDIATRIC PATIENTS (N=16)	
	All Grades** (n=16) n (%)	≥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*	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)

The most frequent adverse reactions reported in ≥20% of pediatric patients treated with ULTOMIRIS were upper respiratory tract infection, diarrhea, constipation, vomiting, headache, hypertension, and pyrexia.[1]

Clinically relevant adverse reactions in <10% of patients included viral infection.[1]

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 hypertension, pneumonia, and abdominal pain.[1]

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

**Graded per CTCAE v5.0.

CTCAE=Common Terminology Criteria for Adverse Events.

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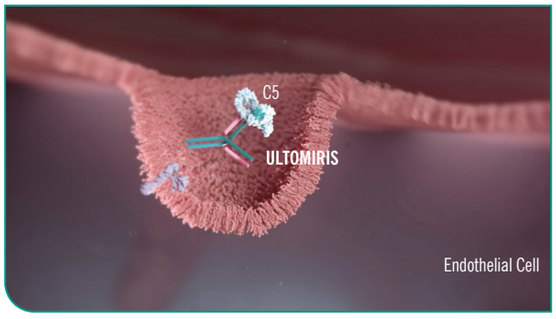
ULTOMIRIS, BUILT ON THE FOUNDATION OF ECULIZUMAB, HAS AN ~4X LONGER HALF-LIFE[a,b]

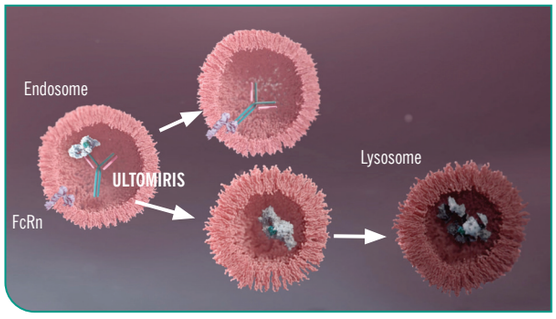
1

Both **ULTOMIRIS** and eculizumab bind to C5 in the bloodstream to prevent its activation.[1,9]



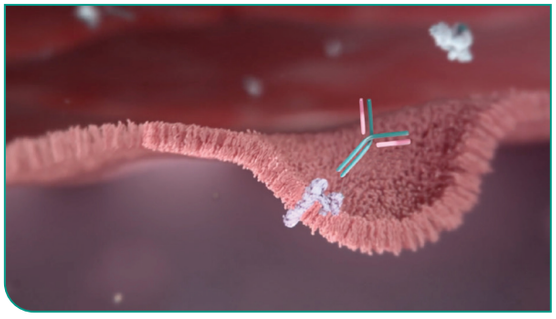
2

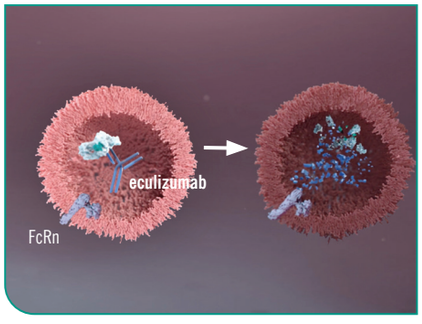
ULTOMIRIS is engineered to release C5 in the endosome as pH levels drop and use FcRn to recycle back to the bloodstream, leaving C5 to be degraded by the lysosome.[10]



3

ULTOMIRIS has also been engineered to bind to FcRn with greater affinity with a half-life ~4x longer than eculizumab to provide immediate, complete, and sustained inhibition of C5 for up to 8 weeks.[9,10,c]





ULTOMIRIS differs from eculizumab in how it behaves after binding to C5. For eculizumab, binding to C5 inhibits FcRn-mediated recycling, leading to its lysosomal degradation along with C5.[10]

[a]The mean (SD) terminal elimination half-life and clearance of intravenous ULTOMIRIS in patients with atypical-HUS are 51.8 (16.2) days and 0.08 (0.04) L/day, respectively. Half-life of eculizumab is 11.25 to 17.25 days.[1,9]

[b]Targeted engineering to incorporate 4 amino acid substitutions designed to reduce TMDD and enhance FcRn-mediated recycling of eculizumab led to the generation of ULTOMIRIS, which exhibited an extended duration of action in preclinical models relative to eculizumab.[10]

[c]In the majority (93%) of adult and pediatric patients with atypical-HUS throughout the entire 26-week treatment period.[1]

C5=complement protein 5; FcRn=neonatal Fc receptor; SD=standard deviation; TMDD=target-mediated drug disposition.

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.

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ULTOMIRIS IS ADMINISTERED ONCE EVERY 4 OR 8 WEEKS, DEPENDING ON BODY WEIGHT[1]

THE RECOMMENDED DOSING REGIMEN CONSISTS OF A LOADING DOSE FOLLOWED BY MAINTENANCE DOSES[1]	
ADULT PATIENTS WITH ATYPICAL-HUS	**PEDIATRIC PATIENTS ≥1 MONTH OF AGE WITH ATYPICAL-HUS WEIGHING ≥5 KG**
Starting 2 weeks after the initial loading dose, maintenance doses are administered **once every 8 weeks**	**Starting 2 weeks after the initial loading dose,** maintenance doses are administered **once every 4 or 8 weeks, depending on body weight**

ULTOMIRIS WEIGHT-BASED DOSING REGIMEN[1]

Body Weight Range (kg)	Loading Dose (mg)	Maintenance Dose (mg) and Dosing Interval	
≥5 to <10	600	300	Every 4 weeks
≥10 to <20	600	600	
≥20 to <30	900	2,100	Every 8 weeks
≥30 to <40	1,200	2,700	
≥40 to <60	2,400	3,000	
≥60 to <100	2,700	3,300	
100 or greater	3,000	3,600	

For adult and pediatric patients with atypical-HUS transitioning from eculizumab to ULTOMIRIS[1]

- Loading dose of ULTOMIRIS should be infused intravenously at the time of the next scheduled eculizumab 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), starting 2 weeks after the intravenous loading dose

Dosing considerations[1]

- The dosing schedule is allowed to occasionally vary within 7 days of the scheduled infusion day (except for the first maintenance dose of ULTOMIRIS), but subsequent doses should be administered according to the original schedule

SELECT IMPORTANT SAFETY INFORMATION

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 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.

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

ULTOMIRIS 100 mg/mL IS ADMINISTERED AS A LOADING DOSE FOLLOWED BY MAINTENANCE DOSES[1]

ULTOMIRIS 100 mg/mL WEIGHT-BASED DOSING[1]

	Body weight range[a] (kg)	ULTOMIRIS volume		Volume of 0.9% NaCl[b]		Total volume (dose)	Minimum infusion time (hr)	Maximum infusion rate (mL/hr)
Loading dose administration	5 to <10	**6 mL**	+	**6 mL**	=	**12 mL** (600 mg)	**1.4**	**9**
	10 to <20	**6 mL**	+	**6 mL**	=	**12 mL** (600 mg)	**0.8**	**15**
	20 to <30	**9 mL**	+	**9 mL**	=	**18 mL** (900 mg)	**0.6**	**30**
	30 to <40	**12 mL**	+	**12 mL**	=	**24 mL** (1,200 mg)	**0.5**	**48**
	40 to <60	**24 mL**	+	**24 mL**	=	**48 mL** (2,400 mg)	**0.8**	**60**
	60 to <100	**27 mL**	+	**27 mL**	=	**54 mL** (2,700 mg)	**0.6**	**90**
	100 or greater	**30 mL**	+	**30 mL**	=	**60 mL** (3,000 mg)	**0.4**	**150**

[a]Body weight at time of treatment.
[b]Dilute ULTOMIRIS only using 0.9% Sodium Chloride Injection, USP.

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. In addition, at least two of the

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.

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

ULTOMIRIS 100 mg/mL MAINTENANCE DOSES ARE ADMINISTERED ONCE EVERY 4 OR 8 WEEKS, DEPENDING ON BODY WEIGHT[1]

ULTOMIRIS 100 mg/mL WEIGHT-BASED DOSING[1]

	Body weight range[a] (kg)	ULTOMIRIS volume		Volume of 0.9% NaCl[b]		Total volume (dose)	Minimum infusion time (hr)	Maximum infusion rate (mL/hr)
Maintenance dose administration	5 to <10	**3 mL**	+	**3 mL**	=	**6 mL** (300 mg)	**0.8**	**8**
	10 to <20	**6 mL**	+	**6 mL**	=	**12 mL** (600 mg)	**0.8**	**15**
	20 to <30	**21 mL**	+	**21 mL**	=	**42 mL** (2,100 mg)	**1.3**	**33**
	30 to <40	**27 mL**	+	**27 mL**	=	**54 mL** (2,700 mg)	**1.1**	**50**
	40 to <60	**30 mL**	+	**30 mL**	=	**60 mL** (3,000 mg)	**0.9**	**67**
	60 to <100	**33 mL**	+	**33 mL**	=	**66 mL** (3,300 mg)	**0.7**	**95**
	100 or greater	**36 mL**	+	**36 mL**	=	**72 mL** (3,600 mg)	**0.5**	**144**

[a]Body weight at time of treatment.
[b]Dilute ULTOMIRIS only using 0.9% Sodium Chloride Injection, USP.

SELECT IMPORTANT SAFETY INFORMATION

Monitoring Disease Manifestations after ULTOMIRIS Discontinuation (continued)

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.

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.

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

ORDERING ULTOMIRIS 100 mg/mL VIALS FOR PATIENTS WITH ATYPICAL-HUS

The ULTOMIRIS 100 mg/mL formulation comes in 2 single-dose vials, 1,100 mg/11 mL (aqua cap) and 300 mg/3 mL (lavender cap), and is a translucent, clear to yellowish color solution. With ULTOMIRIS 100 mg/mL, there is an optimal vial mix (3 mL and 11 mL) for each patient weight cohort, ensuring there is no product wastage

NUMBER OF VIALS NEEDED FOR ULTOMIRIS WEIGHT-BASED DOSING: 100 mg/mL FORMULATION[1]

	Body weight range (kg)	ULTOMIRIS volume	ULTOMIRIS vial combinations	
			1,100 mg/11 mL	300 mg/3 mL
Loading dose administration	5 to <10	6 mL		2
	10 to <20	6 mL		2
	20 to <30	9 mL		3
	30 to <40	12 mL		4
	40 to <60	24 mL		8
	60 to <100	27 mL		9
	100 or greater	30 mL		10

100 mg/mL (3 mL vial): J code, J1303; National Drug Code, NDC 25682-025-01

100 mg/mL (11 mL vial): J code, J1303; National Drug Code, NDC 25682-028-01

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.

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.

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

ORDERING ULTOMIRIS 100 mg/mL VIALS FOR PATIENTS WITH ATYPICAL-HUS (CONTINUED)

NUMBER OF VIALS NEEDED FOR ULTOMIRIS WEIGHT-BASED DOSING: 100 mg/mL FORMULATION[1]

	Body weight range (kg)	ULTOMIRIS volume	ULTOMIRIS vial combinations	
			1,100 mg/11 mL	300 mg/3 mL
Maintenance dose administration	5 to <10	3 mL		1
	10 to <20	6 mL		2
	20 to <30	21 mL		7
	30 to <40	27 mL		9
	40 to <60	30 mL		10
	60 to <100	33 mL	3	
	100 or greater	36 mL	3	1

100 mg/mL (3 mL vial): J code, J1303; National Drug Code, NDC 25682-025-01

100 mg/mL (11 mL vial): J code, J1303; National Drug Code, NDC 25682-028-01

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 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.

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

SUPPLEMENTAL DOSE OF ULTOMIRIS

Plasma exchange (PE), plasmapheresis (PP), and intravenous immunoglobulin (IVIg) treatment have been shown to reduce ULTOMIRIS serum levels. A supplemental dose of ULTOMIRIS is required in the setting of PE, PP, or IVIg.[1]

SUPPLEMENTAL DOSE OF ULTOMIRIS AFTER PE, PP, or IVIg[1]

	Body weight range[a] (kg)	**Most recent ULTOMIRIS dose** (mg)	**Supplemental dose** (mg) **following each PE or PP intervention**	**Supplemental dose** (mg) **following completion of an IVIg cycle**
Supplemental dose administration	40 to <60	2,400	1,200	600
		3,000	1,500	
	60 to <100	2,700	1,500	600
		3,300	1,800	
	100 or greater	3,000	1,500	600
		3,600	1,800	
	Timing of ULTOMIRIS supplemental dose		Within 4 hours following each PE or PP intervention	Within 4 hours following completion of an IVIg cycle

[a]Body weight at time of treatment.

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.

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

SUPPLEMENTAL DOSE OF ULTOMIRIS (CONTINUED)

ULTOMIRIS SUPPLEMENTAL DOSE REFERENCE TABLE: 100 mg/mL FORMULATION[1]

	Body weight range[a] (kg)	Supplemental dose (mg)	ULTOMIRIS volume		Volume of 0.9% NaCl[b]		Total volume	Minimum infusion time (hr)	Maximum infusion rate (mL/hr)
Supplemental dose administration	40 to <60	600	6 mL	+	6 mL	=	12 mL	0.25	48
		1,200	12 mL	+	12 mL	=	24 mL	0.42	57
		1,500	15 mL	+	15 mL	=	30 mL	0.50	60
	60 to <100	600	6 mL	+	6 mL	=	12 mL	0.20	60
		1,500	15 mL	+	15 mL	=	30 mL	0.36	83
		1,800	18 mL	+	18 mL	=	36 mL	0.42	86
	100 or greater	600	6 mL	+	6 mL	=	12 mL	0.17	71
		1,500	15 mL	+	15 mL	=	30 mL	0.25	120
		1,800	18 mL	+	18 mL	=	36 mL	0.28	129

[a]Body weight at time of treatment.
[b]Dilute ULTOMIRIS only using 0.9% Sodium Chloride Injection, USP.

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.

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.

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

PREPARING AND ADMINISTERING ULTOMIRIS[1]

1. Weigh patient

2. Determine **how many ULTOMIRIS vials are needed based on patient weight and prescribed dose** (see pages 12-15 for reference)
   - Vials should be stored under refrigeration at 2°C-8°C (36°F-46°F) in the original carton to protect from light. Do not freeze. Do not shake
   - Each vial of ULTOMIRIS is intended for single-dose only

3. Visually inspect each ULTOMIRIS vial to be sure there is no particulate matter or precipitate (if either, do not use)

4. Using aseptic technique, **withdraw the volume of ULTOMIRIS (corresponding to the prescribed dose) from the appropriate number of vials and add to an equal volume (1:1) of 0.9% Sodium Chloride Injection, USP,** in an infusion bag (see pages 12-15 for reference)
   - ULTOMIRIS is supplied in two single-dose vials (1,100 mg/11 mL and 300 mg/3 mL) to enable an optimal vial mix for each weight cohort, ensuring there is no product wastage
   - ULTOMIRIS requires dilution to a final concentration of 50 mg/mL for the 3 mL and 11 mL vials

5. **Gently mix** the solution by swirling (do not shake or introduce air bubbles) and protect from light

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS (continued)

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.

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.

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injection for intravenous use
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PREPARING AND ADMINISTERING ULTOMIRIS (CONTINUED)[1]

6. Prior to administration, allow the admixture to adjust to room temperature (18°C-25°C, 64°F-77°F). Do not heat the admixture in a microwave or with any heat source other than ambient air temperature

7. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit

8. Administer the solution immediately to the patient through a **0.2 or 0.22 micron filter**
   - If the solution is not administered immediately, the solution can be stored under refrigeration at 2°C-8°C (36°F-46°F) for ≤24 hours, taking into account the expected infusion time. Do not freeze the solution
   - When administering stored (refrigerated) solution, be sure to bring to room temperature naturally before administering, and be sure to administer within 4 hours

9. The **length of infusion time will vary** based on the dose as determined by the patient's weight, but the rate of infusion should not exceed the maximum for each dose (see pages 12-15 for reference)

10. **Monitor patient for at least 1 hour following infusion** to ensure no signs or symptoms of an infusion-related reaction occur
    - If an adverse reaction occurs during the administration of ULTOMIRIS, the infusion may be slowed or stopped at the discretion of the physician. Interrupt ULTOMIRIS infusion and institute appropriate supportive measures if signs of cardiovascular instability or respiratory compromise occur
    - Some signs of infusion-related reaction include lower back pain, drop in blood pressure, elevation in blood pressure, limb discomfort, drug hypersensitivity (allergic reaction), dysgeusia (bad taste), and drowsiness

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 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.

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

What is atypical-HUS?

Atypical-HUS (atypical hemolytic uremic syndrome) is a complex disease of uncontrolled complement activation that causes severe, progressive organ damage or death. Atypical-HUS manifests as TMA in either the presence or absence of an identified trigger.[11,12]

What is TMA?

TMA (thrombotic microangiopathy) is a disorder characterized by thrombocytopenia, microangiopathic hemolytic anemia, and organ dysfunction in which ischemic organ injury can occur to the brain, kidneys, heart, pancreas, liver, lungs, eyes, and skin.[5]

What is a trigger?

A trigger is a condition that activates the complement system and may unmask atypical-HUS. Triggers can include hypertensive emergency, pregnancy/postpartum, autoimmune disease, infection, medications, and transplant (solid organ/bone marrow). If treatment of the trigger does not resolve the TMA, one should consider a diagnosis of unmasked atypical-HUS.[2]

How is atypical-HUS diagnosed?

Atypical-HUS is diagnosed following laboratory confirmation of TMA – ie, thrombocytopenia (low platelet count), microangiopathic hemolysis (eg, high LDH), and evidence of organ involvement (often the kidney) – and performing additional tests to exclude other common causes of TMA (disseminated intravascular coagulation [DIC], thrombotic thrombocytopenic purpura [TTP], and Shiga toxin–producing E. coli hemolytic uremic syndrome [STEC-HUS]). There is no specific test for atypical-HUS.[2,3,5]

LDH = lactate dehydrogenase.

What causes atypical-HUS?

Atypical-HUS is a genetic disease caused by a mutation that affects the complement system. The disease can develop at any age and is lifelong.[3,11]

What are the symptoms of atypical-HUS?

The signs and symptoms of atypical-HUS are varied and may be associated with TMA manifestations: abnormal bleeding, bruising, headaches, blood in urine/stool (signs of thrombocytopenia); fatigue, dark urine, back pain, jaundice, paleness (signs of hemolysis); edema, low urine output, listlessness, confusion, nausea/vomiting, weight loss or weight gain (signs of kidney dysfunction).[13-16]

Who gets atypical-HUS?

Atypical-HUS may be inherited (approximately 20% of cases are familial) or develop sporadically (no family history of the disease).[11]

What laboratory values are important in atypical-HUS?

Labs that are commonly measured to track the disease include platelet count, LDH (released when red blood cells are destroyed in a hemolytic process), and measures of kidney function including serum creatinine and estimated glomerular filtration rate (eGFR).[2]

Can atypical-HUS go away?

Atypical-HUS is a lifelong disease, and patients are always at risk of TMA complications.[3]

What is ULTOMIRIS?

ULTOMIRIS is a prescription medicine for adult and pediatric patients (≥1 month of age) with atypical-HUS. ULTOMIRIS is the first long-acting complement inhibitor approved by the US Food and Drug Administration for atypical-HUS and is dosed once every 4 or 8 weeks, depending on body weight.[1]

What do patients need to know before taking ULTOMIRIS?

ULTOMIRIS is a medicine that affects the immune system and can lower the ability of the immune system to fight infections. ULTOMIRIS increases the chance of getting serious and life-threatening meningococcal infections. Patients must receive a meningococcal vaccination at least 2 weeks before their first dose of ULTOMIRIS unless their vaccine is up to date. If urgent treatment with ULTOMIRIS is needed, patients should receive a meningococcal vaccination as soon as possible.[1]

How is ULTOMIRIS administered?

ULTOMIRIS is administered through intravenous infusion, starting with a loading dose followed by maintenance doses once every 4 or 8 weeks, depending on body weight. Please refer to pages 18-19 of this brochure for additional information on preparation and administration of ULTOMIRIS.[1]

How long is the infusion time for ULTOMIRIS?

ULTOMIRIS has weight-based dosing, and the infusion times vary slightly based on respective weight category. As shown on pages 11-13 of this brochure, minimum infusion times are dependent upon body weight.[1]

What is the difference between the dosing and administration for ULTOMIRIS and eculizumab?

ULTOMIRIS can offer extended control of atypical-HUS between infusions and is infused once every 4 or 8 weeks, depending on body weight, vs once every 2 weeks with eculizumab. ULTOMIRIS infusion times vary based on patient weight (see pages 11-13). Eculizumab is usually infused over 35 minutes in adults and 1 to 4 hours in pediatric patients.[1,9]

What should patients expect after taking ULTOMIRIS?

Results for each atypical-HUS patient taking ULTOMIRIS may be different. After each infusion, patients should be monitored for 1 hour for allergic reactions.[1]

How long should patients be maintained on ULTOMIRIS?

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.[1]

Will insurance cover ULTOMIRIS?

Through OneSource™, Alexion Patient Liaisons and Patient Navigators may answer your patients' questions about atypical-HUS, health insurance, financial resources, and community resources available.

SELECT IMPORTANT SAFETY INFORMATION

USE IN SPECIFIC POPULATIONS

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ULTOMIRIS during pregnancy. Healthcare providers and patients may call 1-833-793-0563 or go to www.UltomirisPregnancyStudy.com to enroll in or to obtain information about the registry.

To report SUSPECTED ADVERSE REACTIONS, contact Alexion Pharmaceuticals, Inc. at 1-844-259-6783 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see 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.

ULTOMIRIS®
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OneSource™ is here to help

ONESOURCE®
Personalized Patient Support from Alexion

Contact OneSource at 1-888-765-4747

Alexion Patient Liaisons and Patient Navigators, with advanced atypical-HUS disease education experience and health insurance information, will be assigned to each patient to provide complimentary education and support.

With 20 years of complement research experience and over a decade of providing complement inhibition in the clinical setting, ALEXION is committed to bringing therapies to patients with rare diseases

For more information on support resources for atypical-HUS, please visit:

• AlexionOneSource.com • ULTOMIRISHCP.com/aHUS • UltSolREMS.com

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

Alexion's support programs connect patients, families, and caregivers facing complement-mediated diseases with a dedicated team of support professionals and advocates.

Copay assistance

- The Alexion OneSource CoPay Program provides financial assistance by covering eligible patients' out-of-pocket medication and infusion costs associated with ULTOMIRIS up to $15,000 US dollars per calendar year
- Valid only for patients with commercial insurance who have a valid prescription for a US FDA–approved indication of ULTOMIRIS. Not valid for patients covered by government insurance programs[c] or other federal or state programs (including any state prescription drug assistance programs)
- Additional requirements may apply. Contact Alexion OneSource for more information on patient eligibility

[a]Based on typical commercial patient out-of-pocket deductible limits.

[b]Additional terms and conditions apply. Please contact OneSource with additional questions.

[c]Includes Medicaid, Medicare (including Medicare Part D), Medicare Advantage Plans, Medigap, Veterans Affairs, Department of Defense, or TRICARE. Patients residing in Massachusetts or Rhode Island are eligible for assistance with medication costs but are not eligible for assistance with infusion costs.

ALEXION®
AstraZeneca Rare Disease

Alexion Patient Liaisons and Patient Navigators assist with:

Education

- Providing patients with educational and supporting materials related to atypical-HUS and/or Alexion therapy, such as brochures and website resources
- Safety education regarding Alexion therapy and vaccination support when applicable
- Education and coordination of treatment logistics

Health Insurance Navigation

- Helping patients understand their health insurance coverage for the Alexion therapy
- Providing information on external funding resources for out-of-pocket costs and exploring alternative options for gaps in coverage and funding issues or concerns
- Supporting patients in locating infusion sites or home infusion options based on patient preference, plan of care, and health plan requirements

Ongoing Support

- Providing personalized support during major life events, such as a change in insurance status, travel, or relocation
- Exploring alternative infusion locations while patients travel, based on patient preference, plan of treatment, and health plan requirements
- Continuing collaboration with designated specialty pharmacy on therapy-related services as applicable

Community Connections

- Providing information about in-person and online meetings and events
- Connecting patients with the atypical-HUS community and advocacy groups
- Supporting patients who would like to get involved as patient ambassadors

ALEXION ACCESS NAVIGATOR

Alexion Access Navigator

Alexion Access Navigator is 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®
(ravulizumab-cwvz)
injection for intravenous use
300 mg/3 mL vial

ULTOMIRIS IS THE FIRST AND ONLY LONG-ACTING COMPLEMENT INHIBITOR FOR ATYPICAL-HUS

For adult and pediatric patients one month of age and older with atypical-HUS to inhibit complement-mediated TMA[a]

- ULTOMIRIS, built on the foundation of eculizumab, has an ~4x longer half-life
- ULTOMIRIS resulted in complete TMA response in the majority of adult (54% [30/56; CI: 40-67%]) and pediatric (71% [10/14; CI: 42-92%]) patients with atypical-HUS by 26 weeks in 2 clinical studies
- Improvements in kidney function, including reduced requirement for dialysis in a majority of adult and pediatric patients requiring dialysis at study entry, were observed in both studies
- ULTOMIRIS is administered based on weight and is infused once every 4 or 8 weeks, depending on body weight, in the maintenance phase

[a]Not indicated for STEC-HUS.
CI=confidence interval; defined as 95%; STEC-HUS=Shiga toxin–producing *E coli* hemolytic uremic syndrome; TMA=thrombotic microangiopathy.

The most frequent adverse reactions reported in ≥20% of patients treated with ULTOMIRIS were upper respiratory tract infection, diarrhea, nausea, vomiting, headache, hypertension, and pyrexia

References: 1. ULTOMIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. **2.** Laurence J. *Clin Adv Hematol Oncol.* 2016;14(11)(suppl 11):2-15. **3.** Asif A, et al. *J Nephrol*. 2017;30(3):347-362. **4.** Jamme M, et al. *PLoS One*. 2017;12(5):e0177894. **5.** Azoulay E, et al. *Chest*. 2017;152(2):424-434. **6.** Goodship THJ, et al. *Kidney Int*. 2017;91(3):539-551. **7.** Data on file [ALXN1210-aHUS-311CSR]. **8.** Data on file [ALXN1210-aHUS-312CSR]. **9.** SOLIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. **10.** Sheridan D, et al. *PLoS One*. 2018;13(4):e0195909. **11.** Noris M, Remuzzi G. *N Engl J Med*. 2009;361(17):1676-1687. **12.** Fremeaux-Bacchi V, et al. *Clin J Am Soc Nephrol*. 2013;8(4):554-562. **13.** National Heart, Lung, and Blood Institute. Thrombocytopenia. https://www.nhlbi.nih.gov/health-topics/thrombocytopenia. Accessed May 20, 2019. **14.** Gauer RL, Braun MM. *Am Fam Physician*. 2012;85(6):612-622. **15.** Dhaliwal G, et al. *Am Fam Physician*. 2004;69(11):2599-2606. **16.** Rahman M, et al. *Am Fam Physician*. 2012;86(7):631-639.

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

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)*].

ALEXION®
AstraZeneca Rare Disease