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



Have questions?
Talk to your atypical-HUS representative

How long should I treat my patient with atypical-HUS?

1 Define the treatment expectations with your patient with atypical-HUS

2 Treat your patient to potentially achieve the treatment expectations

3 Evaluate treatment continuation with your patient

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]

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)*].

HUS=hemolytic uremic syndrome.

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 the Patient Information and Instructions for Use in the accompanying full Prescribing Information (UltomirisHCP.com/PI) for ULTOMIRIS (ravulizumab-cwvz), including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections, or scan the QR code.



Actor portrayal

Have questions?

Talk to your atypical-HUS representative

Business card holder

HUS=hemolytic uremic syndrome.

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*.

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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What can you potentially expect to see in your patients with atypical-HUS treated with ULTOMIRIS®?*

- Complete TMA response[1-4†]
- Normalization of hematologic (platelet count and LDH) and improvement in renal (SCr) parameters[1-4‡]
- Possibility of dialysis discontinuation[1-4§‖]
- Improvement in renal function (eGFR)[1-4§¶]

*Based on data from Phase 3, single-arm, global clinical trials evaluating the efficacy and safety of ULTOMIRIS in complement inhibitor–naïve adult patients (N=58) and in complement inhibitor–naïve pediatric patients (aged <18 years) (N=24) with atypical-HUS over an initial 26-week evaluation period, followed by a 4.5-year extension period.[1-4]

†Primary endpoint. Complete TMA response was defined as normalization of hematologic parameters (platelet count and LDH) and ≥25% improvement in SCr from baseline during the 26-week initial evaluation period. Patients had to meet all criteria at 2 separate assessments obtained ≥4 weeks (28 days) apart and for any measurement in-between.[1]

‡Components of the primary endpoint—complete TMA response.[1]

§Secondary endpoint.[1]

‖Six of 27 (22%) adult patients who were off dialysis at baseline were on dialysis by Week 26.[1] Four of 20 (20%) adult patients who were available at the Year 2 visit had initiated dialysis.[5] All the pediatric patients for whom data were available (6/7) who received dialysis at baseline had discontinued dialysis by Year 2.[4-6]

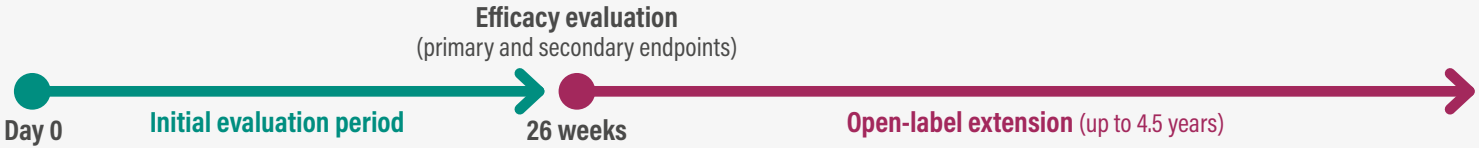
¶At 26 weeks, 2 adult patients experienced a worsening of eGFR category despite treatment with ULTOMIRIS.[2]

eGFR=estimated glomerular filtration rate; HUS=hemolytic uremic syndrome; LDH=lactate dehydrogenase; SCr=serum creatinine; TMA=thrombotic microangiopathy.

Please see additional Important Safety Information throughout and the Patient Information and Instructions for Use in the accompanying full Prescribing Information (UltomirisHCP.com/PI) for ULTOMIRIS (ravulizumab-cwvz), including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections or scan the QR code on Page 1.

ULTOMIRIS® was studied in critically ill* adult patients in the 311 study[1,2]

Study 311: Phase 3, 26-week, open-label, single-arm study of complement inhibitor–naïve adult patients (≥18 years old and ≥40 kg; N=56)[1,2]



Clinical trial criteria

Select inclusion criteria[1]:

- Platelet count ≤150 × 10^9/L
- Evidence of hemolysis such as an elevation in serum LDH
- SCr above the ULN or required dialysis

Select exclusion criteria:

- Patients with TMA due to ADAMTS13 deficiency, STEC-HUS, or genetic defect in cobalamin C metabolism[1]
- Patients receiving prior PE/PI for ≥28 days before screening[2]
- Patients on chronic dialysis[2†]

Efficacy evaluation[1]

Primary endpoint: complete TMA response (at 26 weeks), which comprised of[‡]:

Hematologic parameters

- Platelet count normalization (≥150 × 10^9/L)[2]
- Serum LDH normalization (≤246 U/L)[2]

Renal parameters

- ≥25% improvement in SCr from baseline

Secondary endpoints[1,2]:

- Time to complete TMA response
- Dialysis requirement
- Change in eGFR
- eGFR category stage change
- Change in hematologic variables (platelets, LDH, and hemoglobin)

*Defined as receiving ICU-level care.[6]
†Defined as dialysis on a regular basis for ESKD.[2]
‡Patients had to meet all criteria at 2 separate assessments obtained at least 4 weeks (28 days) apart and for any measurement in between.[1]

ADAMTS13=a disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13; eGFR=estimated glomerular filtration rate; ESKD=end-stage kidney disease; ICU=intensive care unit; LDH=lactate dehydrogenase; PE=plasma exchange; PI=plasma infusion; SCr=serum creatinine; STEC-HUS=Shiga toxin–producing *Escherichia coli* hemolytic uremic syndrome; TMA=thrombotic microangiopathy; ULN=upper limit of normal.

Please see additional Important Safety Information throughout and the Patient Information and Instructions for Use in the accompanying full Prescribing Information (UltomirisHCP.com/PI) for ULTOMIRIS (ravulizumab-cwvz), including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections or scan the QR code on Page 1.

Adult patients in the 311 study met the following endpoints through primary evaluation and 2 years[1]

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

		Week 26[1,2]	Year 1[6,7]	Year 2[4]
		Primary evaluation		
Primary endpoint				
Complete TMA response*		54% (n=30/56) 95% CI: 40%-67%	61% (n=34/56) 95% CI: 47%-74%	61% (n=34/56) 95% CI: 47%-74%
Hematologic parameters	Platelet count normalization	84% (n=47/56)	86% (n=48/56)	86% (n=48/56)
	LDH normalization	77% (n=43/56)	84% (n=47/56)	88% (n=49/56)
Renal parameters	≥25% improvement in SCr	59% (n=33/56)	63% (n=35/56)	63% (n=35/56)
Select secondary endpoints				
Renal parameters	Patients who discontinued dialysis†	59% (n=17/29)	70% (n=16/23)‡	67% (n=12/18)†
	Change in eGFR from baseline (median)†	29 mL/min/1.73 m²	23 mL/min/1.73 m²	35 mL/min/1.73 m²

†Six of 27 (22%) adult patients who were off dialysis at baseline were on dialysis by Week 26.[1] Four of 20 (20%) adult patients who were available at the Year 2 visit had initiated dialysis.[5] At 26 weeks, 2 adult patients experienced a worsening of eGFR category despite treatment with ULTOMIRIS®.[2]

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]

*Complete TMA response was defined as normalization of hematologic parameters (platelet count and LDH) and ≥25% improvement in SCr 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 for any measurement in between.[1]

‡Denominator represents the number of patients available at each visit.

CI=confidence interval; eGFR=estimated glomerular filtration rate; HUS=hemolytic uremic syndrome; LDH=lactate dehydrogenase; SCr=serum creatinine; TMA=thrombotic microangiopathy.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont'd)

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.

Safety profile of ULTOMIRIS® in adult patients with atypical-HUS[1]

Adverse reactions reported in ≥10% of ULTOMIRIS-treated adult patients with atypical-HUS at 26 weeks*

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 patients in the initial evaluation were headache, diarrhea, nausea, vomiting, upper respiratory tract infection, hypertension, and pyrexia[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 2 patients and intracranial hemorrhage in 1 patient. The fourth patient, who was excluded from the trial after a diagnosis of STEC-HUS, died due to pretreatment cerebral arterial thrombosis.[1]

*Graded per CTCAE v5.0.[1]

†Grouped term includes nasopharyngitis, pharyngitis, upper respiratory tract infection, rhinitis, viral upper respiratory tract infection, rhinovirus infection, viral pharyngitis, rhinorrhea, and oropharyngeal pain.[1]

‡Grouped term includes gastroenteritis, gastrointestinal infection, enterocolitis infection, infectious colitis, and enterocolitis.[1]

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

Long-term safety profile of ULTOMIRIS® in adult patients with atypical-HUS[4]

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Most common adverse events reported in ≥15% of ULTOMIRIS-treated adult patients with atypical-HUS through a 2-year follow-up[5]

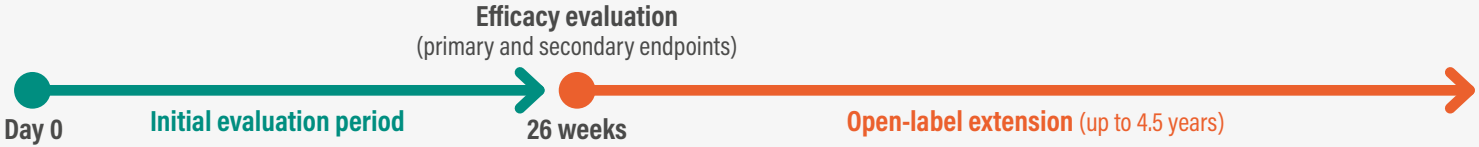
No unexpected safety signals were observed between 26-week and 2-year data[1,4]

Adverse event	n (%) (n=58)
Headache	23 (40)
Diarrhea	20 (35)
Nausea	17 (29)
Vomiting	17 (29)
Arthralgia	16 (28)
Hypertension	14 (24)
Dyspnea	12 (21)
Pyrexia	12 (21)
Urinary tract infection	11 (19)
Anemia	10 (17)
Cough	10 (17)
Peripheral edema	10 (17)
Constipation	9 (16)
Fatigue	9 (16)
Nasopharyngitis	9 (16)

HUS=hemolytic uremic syndrome.

ULTOMIRIS® was studied in critically ill* pediatric patients in the 312 study[1,3]

Study 312: Phase 3, 26-week, open-label, single-arm study of complement inhibitor–naïve pediatric patients (<18 years old; N=20)[1,3,4]



Clinical trial criteria

Select inclusion criteria[1]:

- Platelet count ≤150 × 10^9/L
- Evidence of hemolysis such as an elevation in serum LDH
- SCr ≥97.5% or required dialysis

Select exclusion criteria:

- Patients with TMA due to ADAMTS13 deficiency, STEC-HUS, or genetic defect in cobalamin C metabolism[1]
- Patients receiving prior PE/PI for ≥28 days before screening[3]
- Patients on chronic dialysis[3†]

Efficacy evaluation[1]

Primary endpoint: complete TMA response (at 26 weeks), which comprised of[‡]:

Hematologic parameters

- Platelet count normalization (≥150 × 10^9/L)[3]
- Serum LDH normalization (<ULN)[1,6]

Renal parameters

- ≥25% improvement in SCr from baseline

Secondary endpoints[1,3]:

- Time to complete TMA response
- Dialysis requirement
- Change in eGFR
- eGFR category stage change
- Change in hematologic variables (platelets, LDH, and hemoglobin)

*Defined as receiving ICU-level care.[4]
†Defined as dialysis on a regular basis for ESKD.[3]
‡Patients had to meet all criteria at 2 separate assessments obtained at least 4 weeks (28 days) apart and for any measurement in between.[1]

ADAMTS13=a disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13; eGFR=estimated glomerular filtration rate; ESKD=end-stage kidney disease; ICU=intensive care unit; LDH=lactate dehydrogenase; PE=plasma exchange; PI=plasma infusion; SCr=serum creatinine; STEC-HUS=Shiga toxin–producing *Escherichia coli* hemolytic uremic syndrome; TMA=thrombotic microangiopathy; ULN=upper limit of normal.

Please see additional Important Safety Information throughout and the Patient Information and Instructions for Use in the accompanying full Prescribing Information (UltomirisHCP.com/PI) for ULTOMIRIS (ravulizumab-cwvz), including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections or scan the QR code on Page 1.

Pediatric patients in the 312 study met the following endpoints through primary evaluation and 2 years[4]

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

		Week 26[3,4,6]	Year 1[3,6]	Year 2[4,6]
		Primary evaluation		
Primary endpoint				
Complete TMA response*†		75% (n=15/20) 95% CI: 51%-91%	90% (n=18/20) 95% CI: 68%-99%	90% (n=18/20) 95% CI: 68%-99%
Hematologic parameters	Platelet count normalization	95% (n=19/20) 95% CI: 75%-99.9%	95% (n=19/20) 95% CI: 75%-99.9%	95% (n=19/20) 95% CI: 75%-99.9%
	LDH normalization	90% (n=18/20) 95% CI: 68%-99%	95% (n=19/20) 95% CI: 75%-99.9%	95% (n=19/20) 95% CI: 75%-99.9%
Renal parameters	≥25% improvement in SCr	80% (n=16/20) 95% CI: 56%-94%	90% (n=18/20) 95% CI: 68%-99%	90% (n=18/20) 95% CI: 68%-99%
Select secondary endpoints				
Renal parameters	Patients who discontinued dialysis	83% (n=5/6)	100% (n=6/6)	100% (n=6/6)
	Change in eGFR from baseline (median)	80 mL/min/1.73 m²	94 mL/min/1.73 m²	83 mL/min/1.73 m²

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]

*Complete TMA response was defined as normalization of hematologic parameters (platelet count and LDH) and ≥25% improvement in SCr 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 for any measurement in between.[1]

†The initial interim analysis included in the US PI at the time of approval included 14 pediatric patients with atypical-HUS. The data presented are based on the analysis published by Dixon et al. in 2024 (and Data on File) at 26 weeks through 2 years, which included 20 patients.[4-6]

CI=confidence interval; eGFR=estimated glomerular filtration rate; HUS=hemolytic uremic syndrome; LDH=lactate dehydrogenase; SCr=serum creatinine; TMA=thrombotic microangiopathy.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont'd)

ULTOMIRIS and SOLIRIS REMS (cont'd)

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.

Safety profile of ULTOMIRIS® in C5 inhibitor–naïve patients with atypical-HUS[1]

Adverse reactions reported in ≥10% of ULTOMIRIS-treated adult patients with atypical-HUS at 26 weeks*

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)

*Safety data were based on 26-week interim analysis.
†Graded per CTCAE v5.0.
‡Grouped term includes nasopharyngitis, pharyngitis, upper respiratory tract infection, rhinitis, viral upper respiratory tract infection, rhinovirus infection, viral pharyngitis, rhinorrhea, and oropharyngeal pain.
C5=complement component 5; CTCAE=Common Terminology Criteria for Adverse Events; HUS=hemolytic uremic syndrome.

Long-term safety profile of ULTOMIRIS® in C5 inhibitor–naïve patients with atypical-HUS up to 2 years[5]

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Most common adverse events reported in ≥15% of C5 inhibitor–naïve pediatric patients (N=24)*

No unexpected safety signals were observed between 26-week and 2-year data[1,5]

Adverse event	n (%) (n=24)
Pyrexia	13 (54)
Diarrhea	8 (33)
Vomiting	8 (33)
Headache	7 (29)
Nasopharyngitis	7 (29)
Abdominal pain	6 (25)
Hypertension	6 (25)
Constipation	5 (21)
Contusion	5 (21)
Cough	5 (21)
Myalgia	4 (17)
Nausea	4 (17)
Rash	4 (17)
Rhinorrhea	4 (17)
Upper respiratory tract infection	4 (17)

*The initial interim safety analysis included in the US Prescribing Information at the time of approval included 16 pediatric patients with atypical-HUS. The data presented are based on the safety analysis published by Dixon et al. in 2024 through 2 years, which included 24 patients.[4,5]
C5=complement component 5; HUS=hemolytic uremic syndrome.

Assess your patients for the following risk factors associated with atypical-HUS recurrence

Exposure to triggers

Certain triggers can activate the complement pathway and lead to atypical-HUS.

Examples of triggers include kidney transplant, malignant hypertension, and autoimmune disorders.[8]

Identified genetic mutation



- Some mutations in complement genes have been associated with a higher risk of atypical-HUS recurrence[9-14]
- *CFH* mutations might have a higher risk of atypical-HUS recurrence[14,15]
- Pathogenic *MCP* variant may lead to a lower risk of relapse in case of kidney transplantation[14]

History of renal transplant



- Patients with atypical-HUS with a history of kidney transplantation and certain genetic mutations may be at increased risk of recurrence[14,16,17]

CFH=complement factor H; *CFI*=complement factor I; ESKD=end-stage kidney disease; HUS=hemolytic uremic syndrome; *MCP*=membrane cofactor protein.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont'd)

Other Infections

Serious infections with *Neisseria* species (other than *Neisseria meningitidis*), including disseminated gonococcal infections, have been reported.

ULTOMIRIS blocks terminal complement activation; therefore, patients may have increased susceptibility to infections, especially with encapsulated bacteria, such as infections caused by *Neisseria meningitidis* but also *Streptococcus pneumoniae*, *Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*. Children treated with ULTOMIRIS may be at increased risk of developing serious infections due to *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib). Administer vaccinations for the prevention of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) infections according to ACIP recommendations. Patients receiving ULTOMIRIS are at increased risk for infections due to these organisms, even if they develop antibodies following vaccination.

Consider genetic testing in your patients to assess the risk of atypical-HUS recurrence[14,15]

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Approximately

45%-70%

of patients with atypical-HUS have an identified genetic mutation[18-22]

Genetic testing is not definitive for an atypical-HUS diagnosis.[8]

Patients with *DGKE* mutations do not appear to benefit from C5 inhibition therapy.[14,23]

Clinical outcomes of adult and pediatric patients with atypical-HUS carrying identified genetic mutations[16,17]*

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

Table adapted from Goodship THJ, et al. 2017 and Loirat C, et al. 2011.

*Clinical outcomes of patients with atypical-HUS who were not treated with C5 inhibitors.[24]

C3=complement component 3; C5=complement component 5; *CFB*=complement factor B; *CFH*=complement factor H; *CFI*=complement factor I; *DGKE*=diacylglycerol kinase epsilon; ESKD=end-stage kidney disease; FH=factor H; HUS=hemolytic uremic syndrome; *MCP*=membrane cofactor protein; *THBD*=thrombomodulin.

SELECT IMPORTANT SAFETY INFORMATION

Monitoring Disease Manifestations after ULTOMIRIS Discontinuation

Treatment Discontinuation for aHUS

ULTOMIRIS treatment of aHUS should be a minimum duration of 6 months. Due to heterogeneous nature of aHUS events and patient-specific risk factors, treatment duration beyond the initial 6 months should be individualized. There are no specific data on ULTOMIRIS discontinuation. After discontinuing treatment with ULTOMIRIS, patients should be monitored for clinical symptoms and laboratory signs of TMA complications for at least 12 months. TMA complications post-discontinuation can be identified if any of the following is observed: Clinical symptoms of TMA include changes in mental status, seizures, angina, dyspnea, thrombosis or increasing blood pressure. In addition, at least two of the following laboratory signs observed concurrently and results should be confirmed by a second measurement 28 days apart with no interruption: a decrease in platelet count of 25% or more as compared to either baseline or to peak platelet count during ULTOMIRIS treatment; an increase in serum creatinine of 25% or more as compared to baseline or to nadir during ULTOMIRIS treatment; or, an increase in serum LDH of 25% or more as compared to baseline or to nadir during ULTOMIRIS treatment. If TMA complications occur after discontinuation, consider reinitiation of ULTOMIRIS treatment or appropriate organ-specific supportive measures.

Please see additional Important Safety Information throughout and the Patient Information and Instructions for Use in the accompanying full Prescribing Information (UltomirisHCP.com/PI) for ULTOMIRIS (ravulizumab-cwvz), including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections or scan the QR code on Page 1.

Carefully monitor your patient for TMA recurrence if discontinuing ULTOMIRIS® therapy[1]

Monitor patients for a minimum of 12 months

The ULTOMIRIS label specifies that:

- 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
- Patients should be monitored for a minimum of 12 months after discontinuing ULTOMIRIS

Per US Prescribing Information, there are no specific data on ULTOMIRIS discontinuation in atypical-HUS.[1]

Monitor for the following:

Laboratory tests[1]

TMA indicated by ≥2 of the following laboratory signs observed concurrently (results should be confirmed by a second measurement 28 days apart):

≥25%

Decrease in platelet count

compared with baseline or the peak platelet count during ULTOMIRIS treatment

≥25%

Increase in serum LDH

compared with baseline or the lowest recorded value during ULTOMIRIS treatment

≥25%

Increase in SCr

compared with baseline or the lowest recorded value during ULTOMIRIS treatment

Clinical symptoms of TMA[1]

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

HUS=hemolytic uremic syndrome; LDH=lactate dehydrogenase; SCr=serum creatinine; TMA=thrombotic microangiopathy.

Please see additional Important Safety Information throughout and the Patient Information and Instructions for Use in the accompanying full Prescribing Information (UltomirisHCP.com/PI) for ULTOMIRIS (ravulizumab-cwvz), including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections or scan the QR code on Page 1.

If TMA complications occur after ULTOMIRIS discontinuation, consider reinitiation of ULTOMIRIS treatment or appropriate supportive measures[1]

TMA=thrombotic microangiopathy.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont'd)

Thromboembolic Event Management

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

Infusion-Related Reactions

Administration of ULTOMIRIS may result in systemic infusion-related reactions, including anaphylaxis and hypersensitivity reactions. In clinical trials, infusion-related reactions occurred in approximately 1 to 7% of patients, including lower back pain, abdominal pain, muscle spasms, drop or elevation in blood pressure, rigors, limb discomfort, drug hypersensitivity (allergic reaction), and dysgeusia (bad taste). These reactions did not require discontinuation of ULTOMIRIS. If signs of cardiovascular instability or respiratory compromise occur, interrupt ULTOMIRIS and institute appropriate supportive measures.

ADVERSE REACTIONS

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.

DRUG INTERACTIONS

Plasma Exchange, Plasmapheresis, and Intravenous Immunoglobulins

Concomitant use of ULTOMIRIS with plasma exchange (PE), plasmapheresis (PP), or intravenous immunoglobulin (IVIg) treatment can reduce serum ravulizumab concentrations and requires a supplemental dose of ULTOMIRIS.

Neonatal Fc Receptor Blockers

Concomitant use of ULTOMIRIS with neonatal Fc receptor (FcRn) blockers (e.g., efgartigimod) may lower systemic exposures and reduce effectiveness of ULTOMIRIS. Closely monitor for reduced effectiveness of ULTOMIRIS.

USE IN SPECIFIC POPULATIONS

Pregnancy Exposure Registry

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

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.

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


Actor portrayal

Individualize treatment plan for each patient to achieve the optimal outcome

1. Define treatment expectations with your patient
2. Treat your patient to potentially achieve the treatment expectations
3. Assess individual risk factors to determine the risk of atypical-HUS recurrence
4. Consider restarting therapy or appropriate supportive measures in your patients who are exhibiting signs of atypical-HUS recurrence

Have questions?
Talk to your atypical-HUS representative

HUS=hemolytic uremic syndrome.

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