



# CODING AND BILLING GUIDE FOR THE USE OF ULTOMIRIS

## In Atypical Hemolytic Uremic Syndrome (Atypical-HUS)

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

#### 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).

#### 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)*].

Please see additional Important Safety Information on pages [1](#) and [12-13](#) and accompanying full [Prescribing Information](#) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

## Purpose of This Guide

Alexion Pharmaceuticals, Inc. has developed the ULTOMIRIS Coding and Billing Guide to provide objective and publicly available coding and billing information.

This document is provided for informational purposes only and is not legal advice or official guidance from payers. It is not intended to increase or maximize reimbursement by any payer. Alexion does not warrant, promise, guarantee, or make any statement that the use of this information will result in coverage or payment for ULTOMIRIS or that any payment received will cover providers' costs. Alexion is not responsible for any action providers take in billing for, or appealing, ULTOMIRIS claims.

Hospitals and physicians are responsible for compliance with Medicare and other payer rules and requirements and for the information submitted with all claims and appeals. Before any claims or appeals are submitted, hospitals and physicians should review official payer instructions and requirements, should confirm the accuracy of their coding or billing practices with these payers, and should use independent judgment when selecting codes that most appropriately describe the services or supplies provided to a patient.

Please visit [www.ULTOMIRIS.com](http://www.ULTOMIRIS.com) for additional information, or call 1-888-765-4747 to speak with the Alexion OneSource™ Team.

**Please see additional Important Safety Information on pages [1](#) and [12-13](#) and accompanying full [Prescribing Information](#) for ULTOMIRIS, including **Boxed WARNING** regarding serious and life-threatening or fatal meningococcal infections.**

# Coding for ULTOMIRIS® (ravulizumab-cwvz) in Atypical-HUS

## Diagnosis Coding

The following *International Classification of Diseases, 10th Revision, Clinical Modification* (ICD-10-CM) diagnosis code may be appropriate to describe patients diagnosed with atypical-HUS:

ICD-10-CM Diagnosis Code <sup>1</sup>	D59.39	D59.32
Code Descriptor	<b>Other hemolytic-uremic syndrome</b> <ul style="list-style-type: none"> <li>Atypical (nongenetic) hemolytic uremic syndrome</li> <li>Secondary hemolytic-uremic syndrome</li> </ul>	<b>Hereditary hemolytic-uremic syndrome</b> <ul style="list-style-type: none"> <li>Atypical hemolytic uremic syndrome with an identified genetic cause</li> </ul>
Appropriate Use	Assign this code when medical record documentation supports that atypical hemolytic uremic syndrome is not further specified as due to a genetic cause	Assign this code when medical record documentation supports that atypical hemolytic uremic syndrome is due to a genetic cause
Coding Instructional Notes <sup>1</sup>	<p><b>Code first</b>, if applicable, any associated:</p> <ul style="list-style-type: none"> <li>COVID-19 (U07.1)</li> <li>complications of kidney transplant (T86.1-)</li> <li>complications of heart transplant (T86.2-)</li> <li>complications of liver transplant (T86.4-)</li> </ul> <p><b>Code also</b>, if applicable, any associated condition, such as:</p> <ul style="list-style-type: none"> <li>hypertensive emergency (I16.1)</li> <li>malignant neoplasm (C00-C96)</li> <li>systemic lupus erythematosus (M32.-)</li> </ul> <p><b>Use additional code</b>, if applicable, for adverse effect to identify drug (T36-T50 with fifth or sixth character 5)</p>	<p><b>Code also</b>, if applicable:</p> <ul style="list-style-type: none"> <li>defects in the complement system (D84.1)</li> <li>methylmalonic acidemia (E71.120)</li> </ul>



**Coding Tip: Coding atypical-HUS to the highest level of specificity requires 5 characters. Use only valid codes based on medical record documentation to avoid claims processing delays.**

Please see additional Important Safety Information on pages [1](#) and [12-13](#) and accompanying full [Prescribing Information](#) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

## Drug Coding

The following drug-specific Healthcare Common Procedure Coding System (HCPCS) billing code can be reported on ULTOMIRIS® (ravulizumab-cwvz) medical claims forms to payers:

HCPCS Code <sup>2*</sup>	Code Descriptor
J1303	Injection, ravulizumab-cwvz, 10 mg

\*Applies to all available ULTOMIRIS vials/National Drug Codes (NDCs).

The following HCPCS modifiers may be required for ULTOMIRIS, as applicable:

Modifier <sup>2</sup>	Description	Commercial Requirement	Medicare Requirement
JZ	Zero drug amount discarded/not administered to any patient	Varies by payer	Y
JG	Drug or biological acquired with 340B drug pricing program discount, reported for informational purposes	N	Y
RE	Furnished in full compliance with FDA-mandated risk evaluation and mitigation strategy (REMS)	Y	Y
TB	Drug or biological acquired with 340B drug pricing program discount, reported for informational purposes for select entities	N	Y

Some payers, including Medicaid, require drugs like ULTOMIRIS to be billed on medical claims with the product's NDC in addition to the HCPCS code. Payers typically require healthcare professionals to use the Health Insurance Portability and Accountability Act (HIPAA)-compliant, 11-digit NDC format<sup>3</sup>:

11-Digit NDC <sup>4</sup>	Code Descriptor	Strength
25682-0025-01	ULTOMIRIS for intravenous use, single-dose vial	300 mg/3 mL
25682-0028-01	ULTOMIRIS for intravenous use, single-dose vial	1100 mg/11 mL

Please note that payers have different guidance for placement of the NDC on medical claims. Typically, the 11-digit NDC is reported without any dashes or other punctuation.

Some payers may also require a unit of measure (UoM) qualifier. For ULTOMIRIS, the unit of measure qualifier is mL (milliliter).

Check payer requirements for reporting the NDC and UoM on claims.

Please see additional Important Safety Information on pages [1](#) and [12-13](#) and accompanying full [Prescribing Information](#) for ULTOMIRIS, including **Boxed WARNING** regarding serious and life-threatening or fatal meningococcal infections.

## Drug Administration Services

Payers may offer separate coverage and reimbursement for drug administration services. The following are possible ICD, 10th Revision, Procedure Coding System (ICD-10-PCS) procedure codes to report the administration of ULTOMIRIS® (ravulizumab-cwvz) in inpatient settings:

ICD-10-PCS <sup>5</sup>	Code Descriptor
3E033GR	Introduction of other therapeutic monoclonal antibody into peripheral vein, percutaneous approach
3E043GR	Introduction of other therapeutic monoclonal antibody into central vein, percutaneous approach

The following Current Procedural Terminology (CPT®) codes may be appropriate to report administration of ULTOMIRIS in physician office and hospital outpatient facilities:

CPT Code <sup>6</sup>	Code Descriptor
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to one hour
+ 96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (list separately in addition to primary procedure)
96413 <sup>a</sup>	Chemotherapy administration, intravenous infusion technique, up to one hour, single or initial substance/drug
+ 96415 <sup>a</sup>	Chemotherapy administration, intravenous infusion technique; each additional hour (list separately in addition to primary procedure)

a. Billing highly complex administration codes (96413 and 96415) requires the provider in the medical record to document the complexity beyond what is required for therapeutic infusions (96365 and 96366).<sup>7</sup>

## Diagnosis Coding

For an encounter strictly for the vaccination, the diagnosis code for prophylactic vaccination is assigned along with the diagnosis code for aHUS and any other conditions the patient may have.

ICD-10-CM Diagnosis Code <sup>1</sup>	Code Descriptor
Z23	Encounter for immunization

Please see additional Important Safety Information on pages [1](#) and [12-13](#) and accompanying full [Prescribing Information](#) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

# Coding for Meningococcal Vaccination

## Vaccine Coding

CPT Code <sup>6</sup>	Code Descriptor
90619	Meningococcal conjugate vaccine, serogroups A, C, W, Y, quadrivalent, tetanus toxoid carrier (MenACWY-TT), for intramuscular use
90620	Meningococcal recombinant protein and outer membrane vesicle vaccine, serogroup B (MenB-4C), 2 dose schedule, for intramuscular use
90621	Meningococcal recombinant lipoprotein vaccine, serogroup B (MenB-FHbp), 2 or 3 dose schedule, for intramuscular use
90733	Meningococcal polysaccharide vaccine, serogroups A, C, Y, W-135, quadrivalent (MPSV4), for subcutaneous use
90734	Meningococcal conjugate vaccine, serogroups A, C, W, Y, quadrivalent, diphtheria toxoid carrier (MenACWY-D) or CRM197 carrier (MenACWY-CRM), for intramuscular use
90749	Unlisted vaccine/toxoid

## Vaccine Administration Coding

CPT Code <sup>6</sup>	Code Descriptor
90471	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); 1 vaccine (single or combination vaccine/toxoid)
+ 90472	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); each additional vaccine (single or combination vaccine/toxoid) (List separately in addition to code for primary procedure)

Please see additional Important Safety Information on pages [1](#) and [12-13](#) and accompanying full [Prescribing Information](#) for ULTOMIRIS, including **Boxed WARNING** regarding serious and life-threatening or fatal meningococcal infections.

# Claim Forms

## Sample CMS-1500: Physician Office

For an example of a completed CMS-1500 form, go to [page 8](#).

**Box 21 Diagnosis:** Enter the appropriate diagnosis code; eg,  
 – ICD-10-CM D59.39 for other hemolytic uremic syndrome.

*Note: Other diagnosis codes may apply.*

**Box 23 Prior Authorization:**  
 Enter the prior authorization number as obtained prior to services rendered.

21. DIAGNOSIS OR NATURE OF ILLNESS OR INJURY Relate A-L to service line below (24E) ICD Ind.										22. RESUBMISSION CODE <input type="checkbox"/> YES <input type="checkbox"/> NO		ORIGINAL REF. NO.	
A. _____ B. _____ C. _____ D. _____ E. _____ F. _____ G. _____ H. _____ I. _____ J. _____ K. _____										23. PRIOR AUTHORIZATION NUMBER			
24. A. DATE(S) OF SERVICE			B. PLACE OF SERVICE	C. EMG	D. PROCEDURES, SERVICES, OR SUPPLIES (Explain Unusual Circumstances)			E. DIAGNOSIS POINTER	F. \$ CHARGES	G. DAYS OR UNITS	H. EPSDT Family Plan	I. ID. QUAL.	J. RENDERING PROVIDER ID. #
From	To				CPT/HCPCS	MODIFIER							
MM	DD	YY	MM	DD	YY								
1												NPI	
2												NPI	
3												NPI	
4												NPI	

**Box 24A Date(s) of Service:**  
 Enter the NDC number(s) in the shaded area and the month, day, and year in the white space below.

**Box 24E Diagnosis Pointer:** Enter the letter (A-L) that corresponds to the diagnosis in box 21.

**Box 24G Days or Units:**  
 Enter the appropriate number of units of service; eg, ULTOMIRIS® (ravulizumab-cwvz) 300 mg is reported with “30” units.

**Box 24D Procedures/Services/Supplies:**  
 Enter the appropriate CPT/HCPCS codes and modifiers, eg,  
 – Drug: **J1303** Injection, ravulizumab-cwvz per 10 mg  
 – Applicable modifiers:  
 • **JZ** Zero drug amount discarded/not administered to any patient  
 • **RE** Furnished in full compliance with FDA-mandated risk evaluation and mitigation strategy (REMS)  
 – Administration: **96365** for IV infusion

*Note: Some payers may provide specific guidance.*

Please see additional Important Safety Information on pages [1](#) and [12-13](#) and accompanying full [Prescribing Information](#) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

## Sample CMS-1500: Physician Office

### Example claim form for an ULTOMIRIS® (ravulizumab-cwvz) IV infusion:

To achieve an ULTOMIRIS maintenance dose of 3600 mg for a patient ≥100 kg, the following vial combination was used:

- 3 single-dose 1100 mg/11 mL vials (NDC 25682-0028-01)
- 1 single-dose 300 mg/3 mL vial (NDC 25682-0025-01)

17. NAME OF REFERRING PROVIDER OR OTHER SOURCE										17a.		18. HOSPITALIZATION DATES RELATED TO CURRENT SERVICES																	
										17b. NPI		FROM		TO															
19. ADDITIONAL CLAIM INFORMATION (Designated by NUCC)														20. OUTSIDE LAB? \$ CHARGES															
														<input type="checkbox"/> YES <input type="checkbox"/> NO															
21. DIAGNOSIS OR NATURE OF ILLNESS OR INJURY Relate A-L to service line below (24E) ICD Ind.												22. RESUBMISSION CODE		ORIGINAL REF. NO.															
A. <b>D59.39</b>														23. PRIOR AUTHORIZATION NUMBER															
B. _____																													
C. _____																													
D. _____																													
E. _____																													
F. _____																													
G. _____																													
H. _____																													
I. _____																													
J. _____																													
K. _____																													
L. _____																													
24. A. DATE(S) OF SERVICE										B. PLACE OF SERVICE		C. EMG		D. PROCEDURES, SERVICES, OR SUPPLIES (Explain Unusual Circumstances) CPT/HCPCS MODIFIER				E. DIAGNOSIS POINTER		F. \$ CHARGES		G. DAYS OR UNITS		H. EPSDT Family Plan		I. ID. QUAL.		J. RENDERING PROVIDER ID. #	
MM DD YY MM DD YY 11														J1303 JZ RE				A		XXX XX 360		NPI							
MM DD YY MM DD YY 11														96365				A		XXX XX 1		NPI							

#### Box 24A (Shaded Area):

The "N4" qualifier is required before the NDC; do not include dashes.

- Some payers may also require a Unit of Measure (UoM) for each NDC; eg,
- N425682002501 ML3
  - N425682002801 ML33

*Note: Double check payer requirements and format for reporting the UoM.*

#### Box 24D Procedures/ Services/Supplies:

- Enter the appropriate CPT/HCPCS codes and modifiers, eg,
- Drug: **J1303** Injection, ravulizumab-cwvz per 10 mg
  - Applicable modifiers:
    - **JZ** Zero drug amount discarded/not administered to any patient
    - **RE** Furnished in full compliance with FDA-mandated risk evaluation and mitigation strategy (REMS)
  - Administration: **96365** for IV infusion

*Note: Some payers may provide specific guidance.*

#### Box 24E Diagnosis Pointer:

Enter the letter corresponding to the diagnosis code in box 21.

**Box 24G Days or Units:** Given the HCPCS code is the same for both vials, applying the 10 mg billing unit for J1303 to the total administered dose of 3600 mg results in 360 billing units.

Please see additional Important Safety Information on pages [1](#) and [12-13](#) and accompanying full [Prescribing Information](#) for ULTOMIRIS, including **Boxed WARNING** regarding serious and life-threatening or fatal meningococcal infections.



## Sample CMS-1450: Hospital Clinic or Facility

For an example of a completed CMS-1450 form, go to [page 10](#).

**Fields 42-43:** Enter the appropriate revenue code and description corresponding to the HCPCS code in field 44; eg,

- 0636 for drugs requiring detailed coding
- 0510 for clinic, general

*Note: Other revenue codes may apply.*

**Field 46:** Enter the appropriate number of units of service; eg, ULTOMIRIS® (ravulizumab-cwvz) 300 mg is reported with “30” units.

42 REV. CD.	43 DESCRIPTION	44 HCPCS / RATE / HIPPS CODE	45 SERV. DATE	46 SERV. UNITS	7 TOTAL CHARGES	48 NON-COVERED CHARGES
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						
16						
17						
18						
19						
20						
21						
22						
PAGE ____ OF ____		CREATION DATE		TOTALS		
50 PAYER NAME		51 HEALTH PLAN ID	52 REL INFO	53 ASSO BEN	54 PRIOR PAYMENTS	55 EST. AMOUNT DUE
A						56 NPI
B						57 OTHER
C						PRV ID
58 IN						NO.
A						
B						
C						
63 TR						
A						
B						
C						
66 DX						68
A						
B						
C						
69 ADMIT DX		70 PATIENT REASON DX	a. OTHER PROCEDURE CODE	b. OTHER PROCEDURE DATE	71 PPS CODE	72 ECI
74 PRINCIPAL PROCEDURE CODE		75	76 ATTENDING NPI		QUAL	73

**Field 44:** Enter the appropriate CPT/HCPCS codes and modifiers, eg,

- Drug: **J1303** for ULTOMIRIS (ravulizumab-cwvz) per 10 mg
- Applicable modifiers:
  - **JZ** Zero drug amount discarded/not administered to any patient
  - **RE** Furnished in full compliance with FDA-mandated risk evaluation and mitigation strategy (REMS)
- Administration: **96365** for IV infusion

*Note: Some payers may provide specific guidance.*

**Fields 67 and 67A-67Q:** Enter the appropriate diagnosis code; eg,

- ICD-10-CM: D59.39 for other hemolytic-uremic syndrome

*Note: Other diagnosis codes may apply.*

Please see additional Important Safety Information on pages [1](#) and [12-13](#) and accompanying full [Prescribing Information](#) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

## Sample CMS-1450: Hospital Clinic or Facility

### Example claim form for an ULTOMIRIS® (ravulizumab-cwvz) IV infusion:

To achieve an ULTOMIRIS maintenance dose of 3600 mg for a patient ≥100 kg, the following vial combination was used:

- 3 single-dose 1100 mg/11 mL vials (NDC 25682-0028-01)
- 1 single-dose 300 mg/3 mL vial (NDC 25682-0025-01)

42 REV. CD.	43 DESCRIPTION	44 HCPCS / RATE / HIPPS CODE	45 SERV. DATE	46 SERV. UNITS	47 TOTAL CHARGES	48 NON-COVERED CHARGES
0636	N425682002501 ML3, N425682002801 ML33	J1303 JZ RE	MM DD YY	360	XXX XX	
0510	IV infusion, initial, up to 1 hour	96365	MM DD YY	1	XXX XX	

  

**Field 43 Description:**  
The “N4” qualifier is required before the NDC; do not include dashes.  
Some payers may require a Unit of Measure (UoM) for each NDC; eg,  
– N425682002501 ML3  
– N425682002801 ML33  
*Note: Double check payer requirements and format for reporting the UoM.*

**Field 44:** Enter the appropriate CPT/ HCPCS codes and modifiers, eg,  
– Drug: **J1303** for ULTOMIRIS (ravulizumab-cwvz) per 10 mg  
– Applicable modifiers:  
• **JZ** Zero drug amount discarded/ not administered to any patient  
• **RE** Furnished in full compliance with FDA-mandated risk evaluation and mitigation strategy (REMS)  
– Administration: **96365** for IV infusion  
*Note: Some payers may provide specific guidance.*

**Field 46:** Given the HCPCS code is the same for both vials, applying the 10 mg billing unit for J1303 to the total administered dose of 3600 mg results in 360 billing units.

  

PAGE _____ OF _____		T. AMOUNT DUE		56 NPI	
50 PAYER NAME		51		57 OTHER PRV ID	
58 INSURED'S NAME		59 P REL 60 INSURED'S UNIQUE ID		61 GROUP NAME 62 INSURANCE GROUP NO.	
63 TREATMENT AUTHC					
66 DX					
67 A B C D E F G H					
69 ADMIT DX 70 PATIENT REASON DX 71 PPS CODE 72 ECI 73					
74 PRINCIPAL PROCEDURE CODE		a. OTHER PROCEDURE CODE		b. OTHER PROCEDURE CODE	
75		76 ATTENDING NPI		QUAL	

Please see additional Important Safety Information on pages [1](#) and [12-13](#) and accompanying full [Prescribing Information](#) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.



# ALEXION ACCESS NAVIGATOR

Alexion Access Navigator is a dedicated resource website for US Healthcare Professionals and their offices that contains downloadable access and reimbursement materials for ULTOMIRIS® (ravulizumab-cwvz).

Online: <https://alexionaccessnavigator.com>

## OneSource™ Offers Patient Support

Contact OneSource™:

Phone:  
1-888-765-4747

Online:  
<https://alexiononesource.com>

## References

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Please see additional Important Safety Information on pages **1** and **12-13** and accompanying full **Prescribing Information** for ULTOMIRIS, including **Boxed WARNING** regarding serious and life-threatening or fatal meningococcal infections.

## SELECT IMPORTANT SAFETY INFORMATION for ULTOMIRIS® (ravulizumab-cwvz) (cont'd)

### 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.

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

#### 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 on pages **1** and **12-13** and accompanying full **Prescribing Information** for ULTOMIRIS, including **Boxed WARNING** regarding serious and life-threatening or fatal meningococcal infections.

## SELECT IMPORTANT SAFETY INFORMATION for ULTOMIRIS® (ravulizumab-cwvz) (cont'd)

### WARNINGS AND PRECAUTIONS (cont'd)

#### Monitoring Disease Manifestations after ULTOMIRIS Discontinuation

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

#### Thromboembolic Event Management

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

#### Infusion-Related Reactions

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  $\geq 20\%$ ) were upper respiratory tract infection, diarrhea, nausea, vomiting, headache, hypertension and pyrexia. Serious adverse reactions were reported in 42 (57%) patients with aHUS receiving ULTOMIRIS. The most frequent serious adverse reactions reported in more than 2 patients (2.7%) treated with ULTOMIRIS were hypertension, pneumonia and abdominal pain.

Adverse reactions reported in  $\geq 20\%$  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](http://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](http://www.fda.gov/medwatch).**

**Please see accompanying full [Prescribing Information](#) for ULTOMIRIS, including **Boxed WARNING** regarding serious and life-threatening or fatal meningococcal infections.**