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

Access and Reimbursement Guide

ALEXION®
AstraZeneca Rare Disease

Please see Important Safety Information on pages 2 and 37-40 and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

US/ALL/0399 V4 05/2023

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

INDICATIONS

Paroxysmal Nocturnal Hemoglobinuria (PNH)
ULTOMIRIS is indicated for the treatment of adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH).

Atypical Hemolytic Uremic Syndrome (aHUS)
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).

Generalized Myasthenia Gravis (gMG)
ULTOMIRIS is indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.

Neuromyelitis Optica Spectrum Disorder
ULTOMIRIS is indicated for the treatment of adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin 4 (AQP4) antibody-positive.

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)*].

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ABOUT THIS GUIDE

Alexion is committed to providing access and reimbursement education and support to physicians, physician offices, and infusion centers that administer ULTOMIRIS® (ravulizumab-cwvz). We have developed this guide to provide the information to help you understand the administrative aspects of the ULTOMIRIS access and reimbursement process, including benefits investigations, site of care considerations, prior authorizations (PAs), reauthorizations, coding and claims filing, ordering, product acquisition, and navigating denials and appeals.

The ULTOMIRIS Access and Reimbursement Guide is intended for educational purposes only and does not represent legal or billing advice.

Alexion Field Reimbursement Managers (FRMs) and OneSource™ provide support to practices administering ULTOMIRIS and to patients receiving ULTOMIRIS regarding the access and reimbursement process.

Explore Alexion Access Navigator

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.

Online: https://alexionaccessnavigator.com

Support for your practice:

Alexion's Field Reimbursement Managers (FRMs) are available to provide important education to healthcare professionals and their staff pertaining to:

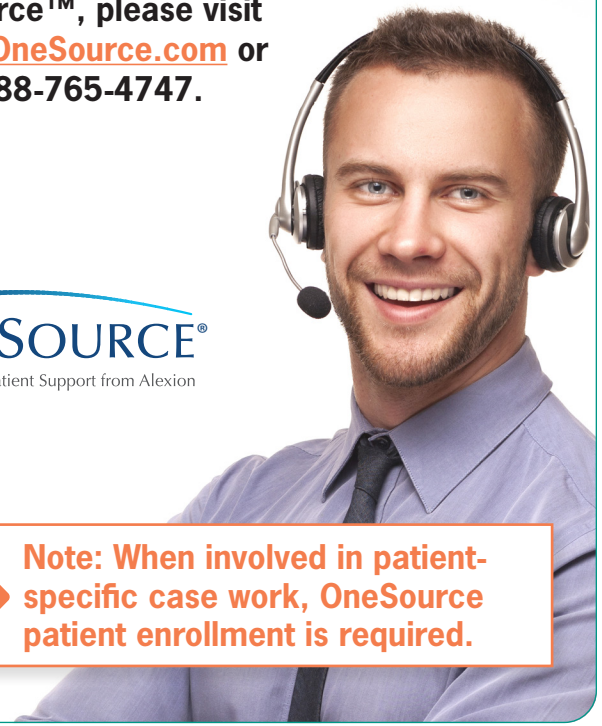
1. Access and reimbursement education
2. Coding, billing, and appropriate claims submission support
3. Prior authorization (PA) and appeal assistance
4. Product acquisition education for buy-and-bill and specialty pharmacy
5. Site of care identification and support
6. Options for accessing ULTOMIRIS® (ravulizumab-cwvz)
7. Common errors in PA or claims submission process that may lead to denials and delays in time to treatment

Support for your patients:

OneSource™ can provide information about options for accessing treatment, regardless of your patients' insurance. In addition, our team can provide information to those who are insured, underinsured, or may need help identifying external funding resources for out-of-pocket costs or coverage gaps.

For more information on OneSource™, please visit AlexionOneSource.com or call 1-888-765-4747.

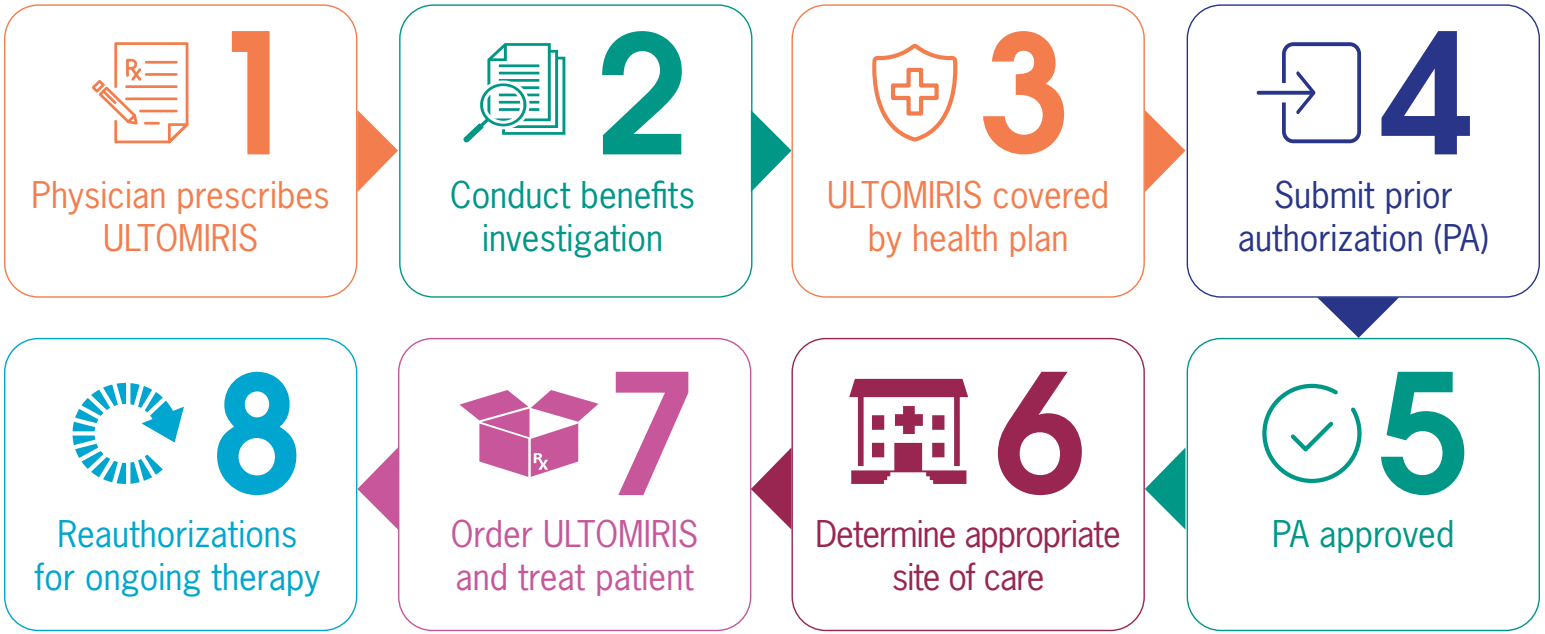
ONESOURCE®
Personalized Patient Support from Alexion



Note: When involved in patient-specific case work, OneSource patient enrollment is required.

PROCESS OVERVIEW TO ACCESS ULTOMIRIS® (ravulizumab-cwvz)

The diagram below provides a general overview of the access process to start patients on ULTOMIRIS. Once the decision to prescribe ULTOMIRIS has been made, your patient is encouraged to enroll in OneSource™, and the Alexion OneSource™ CoPay program if they are eligible. Forms for enrollment in these programs are available at AlexionOneSource.com.



The next step in getting the patient started is conducting a benefits investigation.

Benefits Investigation

ULTOMIRIS® (ravulizumab-cwvz) is administered as an infusion, and health plans often manage ULTOMIRIS under the medical benefit.[1] Once the decision to prescribe ULTOMIRIS has been made, your office will need to conduct a benefits investigation. Health plans can have different requirements,[2] so it is important to complete a benefits investigation to understand the key clinical and coverage criteria that apply to each patient given their unique plan. Once a patient is enrolled, OneSource™ can conduct a co-benefits investigation as well.

The benefits investigation will provide you with information that will answer key questions regarding a patient's health plan coverage and requirements,[3] such as:

- Prior authorization (PA) requirements and specific documentation that must be submitted to obtain approval[a]
- Reauthorization criteria and timeframe for continuation of therapy
- Site of care policies and guidelines and related reimbursement considerations
- Health plan product acquisition requirements or guidelines[b]
- An outline of a patient's financial obligations[c]

Note: It is the responsibility of the provider to complete the benefits investigation.

a. For example, letter of medical necessity or prescriber information. **b.** For example, a requirement to administer as buy-and-bill or if the product can be obtained through a designated specialty pharmacy. **c.** Including copay or coinsurance, annual out-of-pocket maximum, lifetime maximum, and annual benefit cap.

Benefits Investigation[3] (cont.)

Prior Authorization (PA) and required documentation

Does the patient need approval from the payer before receiving ULTOMIRIS® (ravulizumab-cwvz) treatment, in order for it to be covered?

Does the payer require specific documentation (eg, Letter of Medical Necessity, prescribing information, FDA approval letter, pricing sheet, or clinical reprint) before approving?

Site of care considerations

Does the payer require a specific site of care? The payer may also have preferred networks for sites of care so you need to check the payer's policy.

Medical exception

If the payer does not cover ULTOMIRIS or if it denies coverage, then your office can seek a medical exception.

Each payer has a different policy for handling medical exceptions.

Acquisition requirements

Does the payer require your office to acquire ULTOMIRIS from a designated specialty pharmacy?

Coding and claims submission details

When submitting a claim to the insurance company, your office will need to use the appropriate billing codes.

Patient financial responsibility

Depending on the patient's payer, the copay and deductible may vary.

Co-Benefits Investigation

OneSource™ can conduct a co-benefits investigation simultaneously for enrolled patients. The following information is needed for OneSource to conduct a co-benefits investigation:

Completed OneSource™ Enrollment form	Patient name	Health plan name and contact information
Subscriber information[a]	Contact person for follow-up at provider's office	Practice tax ID number

A co-benefits investigation occurs when OneSource conducts a benefits investigation at the same time that the healthcare provider's office is conducting one. It is important because OneSource cannot provide any assistance with insurance or other financial support to a patient without having completed this investigation. They can ensure that all requirements are understood and conveyed to the provider's office and/or facility. In addition, if a patient needs financial assistance, OneSource can refer them to appropriate programs. The co-benefits verification by OneSource can include:

- Identification of a patient's primary and any secondary insurance coverage
- Patient out-of-pocket costs
- Referral to appropriate financial assistance programs if needed
- Coordination of benefits
- Identification of payer coverage requirements and conveying that information to provider office

a. Member number, group number.

PRIOR AUTHORIZATIONS (PAs)

Health plans often require prior approval for a patient to receive ULTOMIRIS® (ravulizumab-cwvz). This is generally referred to as a PA, precertification, or coverage determination. PAs are very common for orphan drugs that treat rare diseases.[4]

In addition, health plans may require a reauthorization for continuation of therapy after a specified period of time.[3] Information about reauthorization timing and requirements can be found in the medical policy or on the PA form.

Providers can contact their FRM for additional educational support about the PA and reauthorization process.

Prior Authorization (PA) Steps[3]

1 Review the patient's health plan coverage requirements.

Alexion has created Physician Quick Reference Guides in the Healthcare Provider (HCP) Starter Kits for atypical-HUS, PNH, gMG, and NMOSD that contain indication-specific checklists to start patients on ULTOMIRIS® (ravulizumab-cwvz).

Note: Many health plans have a specific PA form that must be used. The form will indicate what specific requirements and documentation are needed for the PA.

2 Ensure that the information on the PA request is accurate and complete with all the requested information attached.

One of the most common reasons for denials is missing or incomplete information, so be sure to follow the health plan's instructions for PA submission.

3 Include all required supplemental documentation specified by the patient's health plan, such as relevant clinical studies or a letter of medical necessity.

Alexion has created sample letters of medical necessity, which can be found in the HCP Starter Kits for atypical-HUS, PNH, gMG, and NMOSD.

Submit the PA request through the appropriate health plan process and provide contact information for your office where required.

4 Check the PA status.

Once the PA has been submitted, your office and/or OneSource™ can check the PA status with the health plan as response time will vary by health plan.

PA Approval

After receiving PA approval, review the health plan's policy on site of care to determine if there are requirements or guidelines for product acquisition, such as using a specific specialty pharmacy.

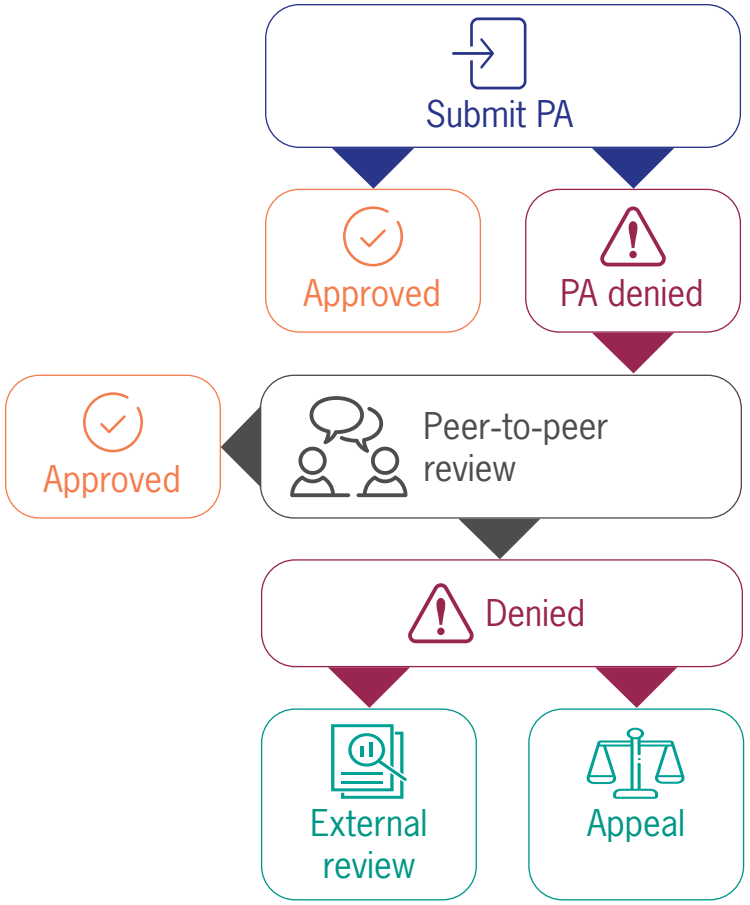
At this time, you should review the results of the benefits investigation to see if and when reauthorization is needed and what is required to submit and obtain reauthorization. This may include specific tests and documented improvements.

APPEALS AND DENIALS PROCESS[3]

If a prior authorization (PA) is denied, determine the reason and the best course of action. Each health plan has specific timeframes and appeal options. Review the summary of benefits for the denial reason and contact the health plan to obtain its appeals process. Please also contact your FRM for support in developing the best strategy to approach denials.

1 Determine the Reason for the Denial

Review the denial letter as well as the summary of benefits to determine the specific denial reason. Often, a denial is given due to missing or incomplete information. Some common reasons for denials include using the incorrect CPT/HCPCS code, entering the incorrect number of units billed, or the original claim was missing the PA number. You may be able to provide the missing documentation or correct the information to resubmit within the specified timeframe.



Process continued on next page.

APPEALS AND DENIALS PROCESS (cont.)

2 Consider a Peer-to-Peer Review

If the reason for denial is misalignment with the clinical policy, you may want to consider a peer-to-peer review as a next step before submitting a formal appeal. For this type of review, the prescribing physician may contact the health plan to discuss the clinical rationale with the physician in charge of the determination or a medical director with a similar specialty.[5]

If the peer-to-peer discussion does not resolve the denial, the prescribing physician may submit an appeal.

3 Appeal Preparation and Submission Process

An appeal is a request to the patient's health plan to reverse its decision and approve the infused specialty drug. Review the health plan's appeal process and timelines to determine:

- The specific form to be filled out for an appeal
- The health plan's preferred method of appeal (eg, phone, written, etc)
- Which documentation should be included (eg, appeal letter, original claims, etc)
- If an expedited review is available and appropriate for a patient's situation

Expedited Review: In urgent situations, you or your patient may request an external review at the same time as an internal review to speed up the process. An expedited appeal may be granted if your patient is currently receiving or prescribed treatment and you believe a delay would risk their life, affect their ability to regain maximum function, or subject them to severe pain. The request for an expedited appeal may be made verbally, and the health plan must make a decision within a specified timeframe.

APPEALS AND DENIALS PROCESS[3] (cont.)

4 Follow up

Follow up with the health plan to confirm that the appeal was received and to check on the decision.

5 External Review

If the internal appeals process is exhausted, inform your patient that they can ask for an external review by independent, accredited medical professionals. External reviewers do not receive any financial incentives to perform the review, and a patient's health plan is required by law to accept the reviewer's decision. The health plan's original denial letter should describe how to request an external review.

To request an external review, your patient must file a written request within the plan's specified timeframe. External review decisions are made as soon as possible, but generally take no longer than 60 days from receipt of request.

6 Another Option: Secondary Health Plan

If your patient has additional coverage that is secondary health plan coverage, you can submit to a patient's secondary health plan for coverage after attempts with the primary health plan have been exhausted. It is suggested that you use a sample letter of medical necessity (see page 11 for more information on the letter of medical necessity) for support to build the request for coverage.

Compile the required documents and submit the appeal as per the instructions of the health plan.

Contact your Alexion FRM to help provide the best strategy to approach denials.

SITE OF CARE CONSIDERATIONS

After receiving prior authorization (PA) approval, review the health plan's policy on site of care to determine if there are requirements or guidelines for product acquisition, such as using a specific specialty pharmacy.[6]

To avoid delays in initiating treatment, refer patients to a site of care that is covered under their payer network.

- Provider's Office
- Hospital Outpatient Infusion Center
- Stand-Alone Infusion Center
- Home Infusion

If an infusion center is responsible for product acquisition, it should also conduct a benefits investigation. If the patient is able to receive home infusion through their health plan, the provider must ensure that the home infusion vendor is covered (or in the preferred network) by the patient's health plan.

If a patient is enrolled in OneSource™, a benefit co-investigation will also include the health plan's policy about site of care for review.

Determine Product Acquisition Options

Based on a patient's coverage, the infusion provider will either purchase ULTOMIRIS® (ravulizumab-cwvz) as a buy-and-bill product through an approved Alexion distributor or obtain ULTOMIRIS through the payer's network of preferred specialty pharmacies.[7]

Buy-and-Bill Option:

- The process is called "buy-and-bill" because the health plan is covering the infusion through the medical benefit, and a medical claim is submitted after the provider has purchased and administered the drug
- For provider-administered outpatient drugs, a healthcare provider first purchases ULTOMIRIS through an authorized distributor, stores it, administers ULTOMIRIS to a patient, and then submits a claim for reimbursement
- For the buy-and-bill option, it is important to ensure that the billing and coding for ULTOMIRIS is correct to secure reimbursement. Alexion has billing and coding guides for each indication (see page 22)

Specialty Pharmacy Provider Option:

- For this option, the infusion provider does not purchase or seek reimbursement for ULTOMIRIS
- ULTOMIRIS is dispensed to the patient by a specialty pharmacy that is indicated by the health plan and is then drop-shipped directly to the infusion office specifically for that patient
- The infusion provider holds the patient-specific ULTOMIRIS until the patient arrives for treatment and administers ULTOMIRIS to that patient
- The specialty pharmacy will file a claim with the health plan for reimbursement of ULTOMIRIS and the provider is able to file a claim for ULTOMIRIS administration services only

ORDERING PROCESS

1 REMS certification

ULTOMIRIS® (ravulizumab-cwvz) is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS), which can be viewed online at www.UltSolREMS.com. Providers who prescribe ULTOMIRIS must be certified.

A prescriber, clinical pharmacist, registered nurse, or physician assistant can complete this process and will need a prescriber's National Provider Identifier (NPI) number for the REMS requirements.

Certification consists of reviewing REMS educational materials and enrollment in ULTOMIRIS and SOLIRIS REMS. Information about the ULTOMIRIS and SOLIRIS REMS program can be viewed online at www.UltSolREMS.com.

The purpose of the ULTOMIRIS and SOLIRIS REMS is to mitigate the occurrence and morbidity associated with meningococcal infections by informing healthcare providers and patients about the:

- Increased risk of meningococcal infections with ULTOMIRIS
- Early signs of invasive meningococcal infections
- Need for immediate medical evaluation of signs and symptoms consistent with possible meningococcal infections.

ORDERING PROCESS (cont.)

2 Order

Each patient must be registered directly with Alexion to obtain ULTOMIRIS® (ravulizumab-cwvz). To register a patient with Alexion, your office can contact the Alexion Customer Operations Center at 1-888-765-4747 Monday through Friday from 8:30 AM to 5:00 PM ET. A representative is available 24/7 for emergent needs.

Alexion requests the following information to order ULTOMIRIS and coordinate shipments for individual patient treatments:

a. Patient initials
b. Patient birth year
c. Diagnosis (indication)
d. Prescriber name
e. Prescriber NPI

To comply with REMS requirements, Alexion must have the prescriber name and NPI prior to shipping the product.

Once the infusion provider has verified the patient's insurance information, they can place an order for ULTOMIRIS, either through an authorized specialty distributor (for a buy-and-bill patient) or through a specialty pharmacy as specified by the patient's health plan.

For accounts that are ordering for the first time, call the Customer Operations Team at Alexion to set up a new account. Note that Alexion will need a purchase order from the specialty distributor or pharmacy to set up a new account. Your office can contact the Alexion Customer Operations Center at 1-888-765-4747 Monday through Friday from 8:30 AM to 5:00 PM ET. A representative is available 24/7 for emergent needs.

The Customer Operations Team will verify that the ordering physician is REMS-certified and can answer any additional questions about the ordering process.

3 Drug Shipment

ULTOMIRIS will be directly shipped from Alexion. The site or provider will receive a confirmation number from the Customer Operations Team once ULTOMIRIS has been ordered. Once the drug has shipped, the FedEx tracking number will be sent in an email with the shipping confirmation.

Approved Alexion Distributors

ASD Healthcare (AmerisourceBergen)
800.746.6273
asd.customerservice@asdhealthcare.com

BioCareSD
800.304.3064
BioCareAccSetup@biocaresd.com

Cardinal Health
800.218.5688
Multi-Specialty-Priority@cardinalhealth.com

CuraScriptSD (Express Scripts)
877.5999.7748
Customer.Service@curascript.com

McKesson Plasma & Biologics
877.625.2566
mpborders@mckesson.com

McKesson Specialty Health
855.477.9800
msh.providers@McKesson.com

Metro Medical (Cardinal Health)
800.768.2002
customerservice@metromedical.com

Oncology Supply (AmerisourceBergen)
800.633.7555
custserv@oncologysupply.com

You can contact an Alexion Customer Operations Representative from the US Patient Supply Group at:

1-888-765-4747

Monday–Friday
8:30 AM to 5:00 PM ET

A representative is available 24/7 for emergent needs.

Each account will have a dedicated representative from this team to help with this process.

Note: Some payers require product acquisition from a payer-designated specialty pharmacy. Please check payer requirements.

ALEXION OneSource™ COPAY PROGRAM[a]

COMMERCIALLY INSURED

The Alexion OneSource™ CoPay Program helps patients pay for eligible out-of-pocket medication and infusion costs.

ALL OTHERS

The Program is not valid for costs eligible to be reimbursed, in whole or in part, by government insurance programs, including Medicaid, Medicare (including Medicare Part D), Medicare Advantage Plans, Medigap, Veterans Affairs, Department of Defense or TRICARE, or other federal or state programs (including any state prescription drug assistance programs). Patients residing in Massachusetts, Minnesota, or Rhode Island are eligible for assistance with medication costs but are not eligible for assistance with infusion costs.

ONESOURCE®
Personalized Patient Support from Alexion

Program eligibility

- Patient enrolled in OneSource™
- Patient with commercial insurance who has a valid prescription for a US Food and Drug Administration–approved indication for ULTOMIRIS® (ravulizumab-cwvz)[8]
- Patients must reside and receive treatment with a Qualifying Alexion Product in the United States or its territories

Have a question? Received an invoice? Contact OneSource:

AlexionOneSource.com

1-888-765-4747

a. The Alexion OneSource™ CoPay Program covers copayments, deductibles, and co-insurance costs.

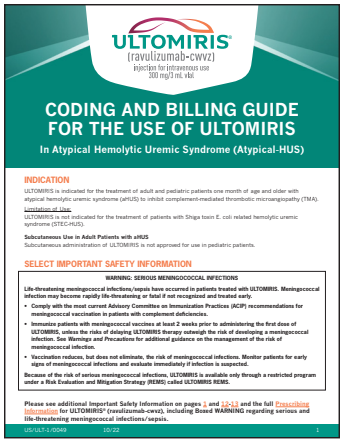
CODING AND BILLING GUIDES

Alexion Pharmaceuticals, Inc. has developed Coding and Billing Guides to provide objective and publicly available coding and billing information for its infused specialty drugs. These guides provide the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) diagnostic codes, Medicare Severity-Diagnosis Related Group (MS-DRG) codes, Healthcare Common Procedure Coding System (HCPCS) codes for infusion, National Drug Code (NDC) number for each dose, and the ICD-10-CM and Current Procedural Terminology (CPT) codes for drug administration services. The diseases that are indicated for use of ULTOMIRIS® (ravulizumab-cwvz) have their own Billing and Coding Guides with codes specific for each indication. The coding guide for meningococcal vaccination is included as the vaccination may be required for prescribing ULTOMIRIS.

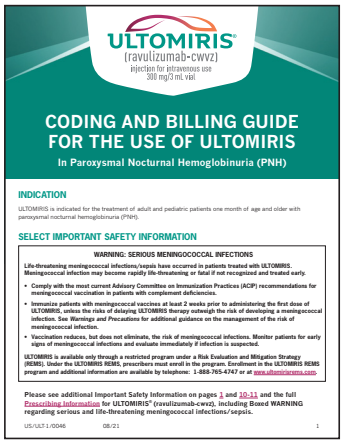
Hospitals and physicians are responsible for compliance with Medicare and other health plan rules and requirements and for the information submitted with all claims and appeals. Before any claims or appeals are submitted, hospitals and physicians should review official health plan instructions and requirements,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

The following pages contain a summary of the relevant codes for each indication. For the full Coding and Billing Guide or to receive additional information, please contact your Alexion FRM.

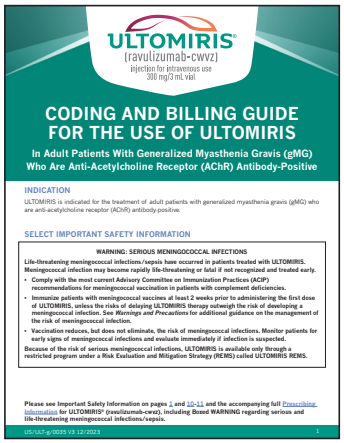
CODING AND BILLING GUIDES (cont.)



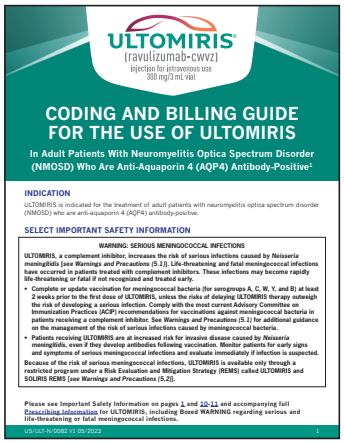
Atypical Hemolytic Uremic Syndrome (aHUS)



Paroxysmal Nocturnal Hemoglobinuria (PNH)



Generalized Myasthenia Gravis (gMG)



Neuromyelitis Optica Spectrum Disorder (NMOSD)

This document is provided for informational purposes only and is not legal advice or official guidance from health plans. It is not intended to increase or maximize reimbursement by any health plan. Alexion does not warrant, promise, guarantee, or make any statement that the use of this information will result in coverage or payment for ULTOMIRIS® (ravulizumab-cwvz), 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.

Coding for ULTOMIRIS® (ravulizumab-cwvz) in aHUS

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. At this time, there is no ICD-10-CM diagnosis code that specifically describes atypical-HUS:

ICD-10-CM Diagnosis Code[9]	D59.39	D59.32
Code Descriptor	**Other hemolytic-uremic syndrome** • Atypical (nongenetic) hemolytic uremic syndrome • Secondary hemolytic-uremic syndrome	**Hereditary hemolytic-uremic syndrome** • Atypical hemolytic uremic syndrome with an identified genetic cause
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[9]	**Code first**, if applicable, any associated: • COVID-19 (U07.1) • complications of kidney transplant (T86.1-) • complications of heart transplant (T86.2-) • complications of liver transplant (T86.4-) **Code also**, if applicable, any associated condition, such as: • hypertensive emergency (I16.1) • malignant neoplasm (C00-C96) • systemic lupus erythematosus (M32.-) **Use additional code**, if applicable, for adverse effect to identify drug (T36-T50 with fifth or sixth character 5)	**Code also**, if applicable: • defects in the complement system (D84.1) • methylmalonic acidemia (E71.120)

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.

Coding for ULTOMIRIS® (ravulizumab-cwvz) in aHUS (cont.)

Drug Coding

The following drug-specific Healthcare Common Procedure Coding System (HCPCS) billing code can be reported on medical claims forms to payers, effective October 1, 2019:

HCPCS Code[10,a]	Code Descriptor
J1303	Injection, ravulizumab-cwvz, 10 mg

Beginning January 1, 2023, the following HCPCS modifiers may be required for ULTOMIRIS, as applicable:

Modifier[10]	Description	Commercial Requirement	Medicare Requirement
JZ[b]	Zero drug amount discarded/not administered to any patient	Varies by payer	Y
JG[b]	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[b]	Drug or biological acquired with 340B drug pricing program discount, reported for informational purposes for select entities	N	Y

IMPORTANT NOTE: CMS will start auditing claims for "JZ" modifiers on July 1, 2023. CMS will start **rejecting claims** without "JW" or "JZ" modifiers on October 1, 2023. "JG" and "TB" are required on Medicare claims no later than January 1, 2024.

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[13]:

11-Digit NDC[8]	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.

Note: Other modifiers may apply to HCPCS coding.

a. Applies to all available ULTOMIRIS vials/National Drug Codes (NDCs). **b.** Modifier "JZ" is effective for claims with dates of service (DOS) on and after January 1, 2023. CMS will start auditing claims for "JZ" modifiers on claims with single/multisource single-dose packaged drugs on outpatient claims starting DOS July 1, 2023 and start rejecting claims without these modifiers effective October 1, 2023.[11] **c.** 340B entities paid under the Medicare Outpatient Prospective Payment System (OPPS) are required to report either modifier "JG" or "TB" on OPPS claims beginning January 1, 2023. No later than January 1, 2024, 340B modifiers, "JG" or "TB" are required on Medicare claims for separately payable Part B–covered drugs and biologicals that are acquired through the discount program for all 340B-covered entities, including hospital-based and non–hospital-based entities.[12]

Coding for ULTOMIRIS® (ravulizumab-cwvz) in aHUS (cont.)

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 in inpatient settings:

ICD-10-PCS[14]	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[15]	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	Chemotherapy administration, intravenous infusion technique, up to one hour, single or initial substance/drug
+ 96415	Chemotherapy administration, intravenous infusion technique; each additional hour (list separately in addition to primary procedure)

Coding for ULTOMIRIS® (ravulizumab-cwvz) in PNH

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 PNH:

ICD-10-CM Diagnosis Code[9]	Code Descriptor
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]

Drug Coding

The following drug-specific Healthcare Common Procedure Coding System (HCPCS) billing code can be reported on medical claims forms to payers, effective October 1, 2019:

HCPCS Code[10]	Code Descriptor
J1303	Injection, ravulizumab-cwvz, 10 mg

Beginning January 1, 2023, the following HCPCS modifiers may be required for ULTOMIRIS, as applicable:

Modifier[10]	Description	Commercial Requirement	Medicare Requirement
JZ[a]	Zero drug amount discarded/not administered to any patient	Varies by payer	Y
JG[b]	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[b]	Drug or biological acquired with 340B drug pricing program discount, reported for informational purposes for select entities	N	Y

IMPORTANT NOTE: CMS will start auditing claims for "JZ" modifiers on July 1, 2023. CMS will start **rejecting claims** without "JW" or "JZ" modifiers on October 1, 2023. "JG" and "TB" are required on Medicare claims no later than January 1, 2024.

Note: Other modifiers may apply to HCPCS coding.

a. Modifier "JZ" is effective for claims with dates of service (DOS) on and after January 1, 2023. CMS will start auditing claims for "JZ" modifiers on claims with single/multisource single-dose packaged drugs on outpatient claims starting DOS July 1, 2023 and start rejecting claims without these modifiers effective October 1, 2023.[11] **b.** 340B entities paid under the Medicare Outpatient Prospective Payment System (OPPS) are required to report either modifier "JG" or "TB" on OPPS claims beginning January 1, 2023. No later than January 1, 2024, 340B modifiers, "JG" or "TB" are required on Medicare claims for separately payable Part B–covered drugs and biologicals that are acquired through the discount program for all 340B-covered entities, including hospital-based and non–hospital-based entities.[12]

Coding for ULTOMIRIS® (ravulizumab-cwvz) in PNH (cont.)

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[13]:

NDC[8]	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.

Drug Administration Services

Payers may offer separate coverage and reimbursement for drug administration services. The following Current Procedural Terminology (CPT®) codes may be appropriate to report administration of ULTOMIRIS in physician office and hospital outpatient facilities:

CPT[15]	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	Chemotherapy administration, intravenous infusion technique, up to one hour, single or initial substance/drug
+ 96415	Chemotherapy administration, intravenous infusion technique; each additional hour (list separately in addition to primary procedure)

Coding for ULTOMIRIS® (ravulizumab-cwvz) in Adult Patients With Anti-AChR Antibody-Positive gMG

Diagnosis Coding

The following International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes may be appropriate to describe adult patients diagnosed with gMG who are anti-AChR antibody-positive:

ICD-10-CM Diagnosis Code[9]	Code Descriptor
G70.00	Myasthenia gravis without (acute) exacerbation
G70.01	Myasthenia gravis with (acute) exacerbation

Drug Coding

The following Healthcare Common Procedure Coding System (HCPCS) billing code can be reported on medical claim forms to payers:

HCPCS Code[10,a]	Code Descriptor
J1303	Injection, ravulizumab-cwvz, 10 mg

Beginning January 1, 2023, the following HCPCS modifiers may be required for ULTOMIRIS, as applicable:

Modifier[10]	Description	Commercial Requirement	Medicare Requirement
JZ[b]	Zero drug amount discarded/not administered to any patient	Varies by payer	Y
JG[c]	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[c]	Drug or biological acquired with 340B drug pricing program discount, reported for informational purposes for select entities	N	Y

IMPORTANT NOTE: CMS will start auditing claims for "JZ" modifiers on July 1, 2023. CMS will start **rejecting claims** without "JW" or "JZ" modifiers on October 1, 2023. "JG" and "TB" are required on Medicare claims no later than January 1, 2024.

Note: Other modifiers may apply to HCPCS coding.

a. Applies to all available ULTOMIRIS vials/National Drug Codes (NDCs). **b.** Modifier "JZ" is effective for claims with dates of service (DOS) on and after January 1, 2023. CMS will start auditing claims for "JZ" modifiers on claims with single/multisource single-dose packaged drugs on outpatient claims starting DOS July 1, 2023 and start rejecting claims without these modifiers effective October 1, 2023.[11] **c.** 340B entities paid under the Medicare Outpatient Prospective Payment System (OPPS) are required to report either modifier "JG" or "TB" on OPPS claims beginning January 1, 2023. No later than January 1, 2024, 340B modifiers, "JG" or "TB" are required on Medicare claims for separately payable Part B–covered drugs and biologicals that are acquired through the discount program for all 340B-covered entities, including hospital-based and non–hospital-based entities.[12]

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Coding for ULTOMIRIS® (ravulizumab-cwvz) in Adult Patients With Anti-AChR Antibody-Positive gMG (cont.)

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[13]:

11-Digit NDC[8,13]	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.[10]

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 in inpatient settings:

ICD-10-PCS[14]	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 offices and hospital outpatient facilities. Individual payer policies should be reviewed for reporting requirements.

CPT Code[15]	Code Descriptor
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis; 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[a]	Chemotherapy administration, intravenous infusion technique, up to one hour, single or initial substance/drug
+ 96415[a]	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).[16]

Coding for ULTOMIRIS® (ravulizumab-cwvz) in Adult Patients With Anti-AQP4 Antibody-Positive NMOSD

Diagnosis Coding

The following International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes may be appropriate to describe adult patients diagnosed with NMOSD who are anti-AQP4 antibody-positive:

ICD-10-CM Diagnosis Code[9]	Code Descriptor
G36.0	Neuromyelitis optica [Devic]

Drug Coding

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

HCPCS Code[10,a]	Code Descriptor
J1303	Injection, ravulizumab-cwvz, 10 mg

Beginning January 1, 2023, the following HCPCS modifiers may be required for ULTOMIRIS, as applicable:

Modifier[10]	Description	Commercial Requirement	Medicare Requirement
JZ[b]	Zero drug amount discarded/not administered to any patient	Varies by payer	Y
JG[c]	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[c]	Drug or biological acquired with 340B drug pricing program discount, reported for informational purposes for select entities	N	Y

IMPORTANT NOTE: CMS will start auditing claims for "JZ" modifiers on July 1, 2023. CMS will start **rejecting claims** without "JW" or "JZ" modifiers on October 1, 2023. "JG" and "TB" are required on Medicare claims no later than January 1, 2024.

Note: Other modifiers may apply to HCPCS coding.

a. Applies to all available ULTOMIRIS vials/National Drug Codes (NDCs). **b.** Modifier "JZ" is effective for claims with dates of service (DOS) on and after January 1, 2023. CMS will start auditing claims for "JZ" modifiers on claims with single/multisource single-dose packaged drugs on outpatient claims starting DOS July 1, 2023 and start rejecting claims without these modifiers effective October 1, 2023.[11] **c.** 340B entities paid under the Medicare Outpatient Prospective Payment System (OPPS) are required to report either modifier "JG" or "TB" on OPPS claims beginning January 1, 2023. No later than January 1, 2024, 340B modifiers, "JG" or "TB" are required on Medicare claims for separately payable Part B–covered drugs and biologicals that are acquired through the discount program for all 340B-covered entities, including hospital-based and non–hospital-based entities.[12]

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Coding for ULTOMIRIS® (ravulizumab-cwvz) in Adult Patients With Anti-AQP4 Antibody-Positive NMOSD (cont.)

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[13]:

11-Digit NDC[8,13]	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.[10]

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.

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 in inpatient settings:

ICD-10-PCS[14]	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 offices and hospital outpatient facilities. Individual payer policies should be reviewed for reporting requirements.

CPT Code[15]	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[a]	Chemotherapy administration, intravenous infusion technique, up to one hour, single or initial substance/drug
+ 96415[a]	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).[16]

Coding for Meningococcal Vaccination

Meningococcal vaccines must be administered to all patients without a history of meningococcal vaccination at least 2 weeks prior to the initial dose of ULTOMIRIS® (ravulizumab-cwvz). Providers should review and comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.[8]

Diagnosis Coding

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

ICD-10-CM Diagnosis Code[9]	Code Descriptor
Z23	Encounter for immunization

Vaccine Coding

CPT Code[15]	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
90644	Meningococcal conjugate vaccine, serogroups C & Y and Haemophilus influenzae type b vaccine (Hib-MenCY), 4 dose schedule, when administered to children 6 weeks–18 months of age, 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

Coding for Meningococcal Vaccination

Vaccine Administration Coding

CPT Code[15]	Code Descriptor
90460	Immunization administration through 18 years of age via any route of administration, with counseling by physician or other qualified health care professional; first or only component of each vaccine or toxoid administered
+ 90461	Immunization administration through 18 years of age via any route of administration, with counseling by physician or other qualified health care professional; each additional vaccine or toxoid component administered (List separately in addition to code for primary procedure)
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)

REAUTHORIZATION

Many health plans may require a prior authorization (PA) renewal, or reauthorization after a specified period of time — this information is typically included in the medical policy and also the benefits investigation.[3] Continued coverage of ULTOMIRIS® (ravulizumab-cwvz) generally requires follow-up with the appropriate specialist and a positive clinical response from baseline for the appropriate indication.

Your Alexion FRM can provide education on payer-specific reauthorization criteria. OneSource™ will proactively reach out to patients enrolled in OneSource™ prior to the reauthorization date.

Please always refer to the specific health plan requirements for each patient.

OneSource™ PATIENT SUPPORT PROGRAM

OneSource is a complimentary, personalized patient support program offered by Alexion

Available for eligible enrolled patients with the following indications:

- Atypical hemolytic uremic syndrome (aHUS)
- Paroxysmal nocturnal hemoglobinuria (PNH)
- Generalized myasthenia gravis (gMG)
- Neuromyelitis optica spectrum disorder (NMOSD)

- Complimentary
- Voluntary
- For eligible patients
- Patient centric
- Professional support for your patients

More information and the online enrollment form are available at:

1-888-765-4747

AlexionOneSource.com

OneSource™ Services

EDUCATION

- Providing patients with educational and supporting materials related to their rare disease and/or Alexion therapy, such as brochures and website resources
- Safety education regarding Alexion therapies
- Vaccination support program information, as applicable
- Education and assistance coordinating 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

COMMUNITY CONNECTIONS

Staffed by Case Managers with:

- Advanced rare disease knowledge
- Health insurance expertise
- Information about community resources

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/provider preference and health plan requirements
- Continuing collaboration with designated specialty pharmacy on therapy-related services as applicable

SELECT IMPORTANT SAFETY INFORMATION for ULTOMIRIS® (ravulizumab-cwvz) (cont.)

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

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 or 1-888-765-4747.

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WARNINGS AND PRECAUTIONS (cont.)

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.

Monitoring Disease Manifestations after ULTOMIRIS Discontinuation

Treatment Discontinuation for PNH

After discontinuing treatment with ULTOMIRIS, closely monitor for signs and symptoms of hemolysis, identified by elevated LDH along with sudden decrease in PNH clone size or hemoglobin, or re-appearance of symptoms such as fatigue, hemoglobinuria, abdominal pain, shortness of breath (dyspnea), major adverse vascular event (including thrombosis), dysphagia, or erectile dysfunction. Monitor any patient who discontinues ULTOMIRIS for at least 16 weeks to detect hemolysis and other reactions. If signs and symptoms of hemolysis occur after discontinuation, including elevated LDH, consider restarting treatment with ULTOMIRIS.

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.

Thromboembolic Event Management

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

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WARNINGS AND PRECAUTIONS (cont.)

Infusion-Related Reactions

Intravenous administration 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 treated with ULTOMIRIS. These events included lower back pain, drop in blood pressure, limb discomfort, drug hypersensitivity (allergic reaction), dysgeusia (bad taste), and drowsiness. These reactions did not require discontinuation of ULTOMIRIS. If signs of cardiovascular instability or respiratory compromise occur, interrupt ULTOMIRIS infusion and institute appropriate supportive measures.

ADVERSE REACTIONS

Adverse Reactions for PNH

Adverse reactions reported in ≥10% or more of patients with PNH were upper respiratory tract infection and headache. Serious adverse reactions were reported in 15 (6.8%) patients receiving ULTOMIRIS. The serious adverse reactions in patients treated with ULTOMIRIS included hyperthermia and pyrexia. No serious adverse reaction was reported in more than 1 patient treated with ULTOMIRIS. One fatal case of sepsis was identified in a patient treated with ULTOMIRIS. In clinical studies, clinically relevant adverse reactions in 1% of adult patients include infusion-related reactions.

Adverse reactions reported in ≥10% of pediatric patients treated with ULTOMIRIS who were treatment-naïve vs. Eculizumab-experienced was Anemia (20% vs. 25%), Abdominal pain (0% vs. 38%), Constipation (0% vs. 25%), Pyrexia (20% vs. 13%), Upper respiratory tract infection (20% vs. 75%), Pain in extremity (0% vs. 25%), Headache (20% vs. 25%).

Adverse Reactions for aHUS

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.

Adverse Reactions for gMG

Most common adverse reactions in adult patients with gMG (incidence ≥10%) were diarrhea and upper respiratory tract infection. Serious adverse reactions were reported in 20 (23%) of patients treated with ULTOMIRIS and in 14 (16%) patients receiving placebo. The most frequent serious adverse reactions were infections reported in at least 8 (9%) patients treated with ULTOMIRIS and in 4 (4%) patients treated with placebo. Of these infections, one fatal case of COVID-19 pneumonia was identified in a patient treated with ULTOMIRIS and one case of infection led to discontinuation of ULTOMIRIS.

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SELECT IMPORTANT SAFETY INFORMATION for ULTOMIRIS® (ravulizumab-cwvz) (cont.)

ADVERSE REACTIONS (cont.)

Adverse Reactions for NMOSD

Most common adverse reactions in adult patients with NMOSD (incidence >10%) were COVID-19, headache, back pain, arthralgia, and urinary tract infection. Serious adverse reactions were reported in 8 (13.8%) patients with NMOSD receiving ULTOMIRIS.

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.

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 accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

REFERENCES

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