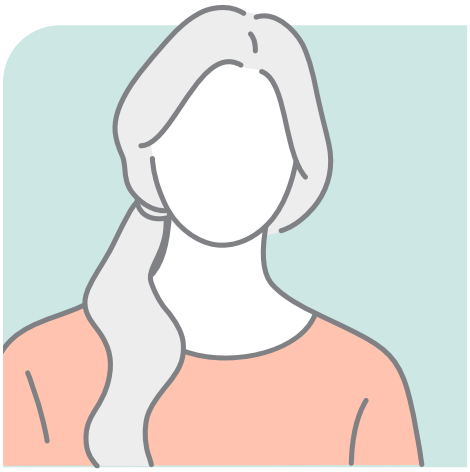
A female adult patient with an 11-year history of anti-AQP4 antibody-positive NMOSD who transitioned from rituximab therapy to ULTOMIRIS® (ravulizumab-cwvz)*



All information is current up to August 2025.
Any follow-up information is not currently available.
Contributed by Jon Poling, MD
Athens Neurological Associates, Athens, GA

***This case is based on a single patient with anti-AQP4 antibody-positive NMOSD and may not be fully representative of the overall patient population. To protect patient privacy, patient details have been modified.**

OVERVIEW OF PATIENT'S CASE

Caucasian female in her mid-20s, college-educated professional

- Managed her anti-AQP4 antibody-positive NMOSD for nearly 10 years with rituximab
- Discontinued rituximab following a series of infections
- HCP considered trying an FDA-approved treatment option and decided to initiate ULTOMIRIS

INDICATION

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)*].

Please see Important Safety Information on pages 1, 4, 6-7, and full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

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

A female adult patient with an 11-year history of anti-AQP4 antibody-positive NMOSD who transitioned from rituximab therapy to ULTOMIRIS® (ravulizumab-cwvz)*

Rituximab treatment

IVIg treatment

ULTOMIRIS treatment

2013

Diagnosed with NMOSD as a teenager

Hospitalized first for gastroenteritis and shortly after for ongoing nausea and vomiting and right hemiparesthesias

- MRI: right medullary T2 hyperintense lesion
- Diagnosed with area postrema syndrome
- Positive for CSF anti-AQP4 antibodies and serum anti-AQP4 antibodies
- Alternative diagnosis were excluded

1 MONTH LATER

- Diagnosed with NMOSD based on HCP's clinical evaluation
- Initiated treatment with high-dose steroids and IVIg with improvement
- One month later: VERs normal and c-spine MRI normal

2014

Experienced an exacerbation of NMOSD (as determined by HCP)

Hospitalized for malaise, extreme fatigue, and excessive sleeping

- MRI: new hypothalamic lesion, which was causing central neurogenic SIADH
- Treated with high-dose steroids, fluid restriction, and symptoms resolved

Initiated rituximab treatment

- No clinical or MRI disease activity was observed by HCP while on this treatment

2022-2023

Series of infections

Experienced several **UTIs**, **recurrent eye conjunctivitis**, and **a mild URI** (tested positive for **COVID-19**)

ER visit for left Bell's palsy

Experienced **mononucleosis**

2023

Discontinued rituximab

Hospitalized for **ear otitis media** with ruptured tympanic membrane and **malignant otitis externa** that escalated to **mastoiditis**, upper spinal **osteomyelitis**, and **transverse venous sinus septic thrombosis**, despite receiving antibiotics and steroids

- Urgent mastoidectomy was performed and received long course of IV antibiotics

6 MONTHS LATER

2024

ULTOMIRIS FDA approved for adults with anti-AQP4 antibody-positive NMOSD in March 2024

Meningococcal vaccinations received

- According to current ACIP recommendations for patients receiving complement inhibitors

Complete or update meningococcal vaccination at least 2 weeks prior to the first dose of ULTOMIRIS, unless the risks of delaying ULTOMIRIS outweigh the risks of developing a serious infection. Comply with the most current ACIP recommendations for meningococcal vaccination in patients receiving a complement inhibitor.[1]

INITIATED ULTOMIRIS

2025

Experienced Haemophilus influenzae (H flu) pneumonia

- Uncomplicated, walking pneumonia, that responded to oral antibiotics after positive mycoplasma test and clinical symptoms

NO RELAPSES SINCE STARTING ULTOMIRIS†

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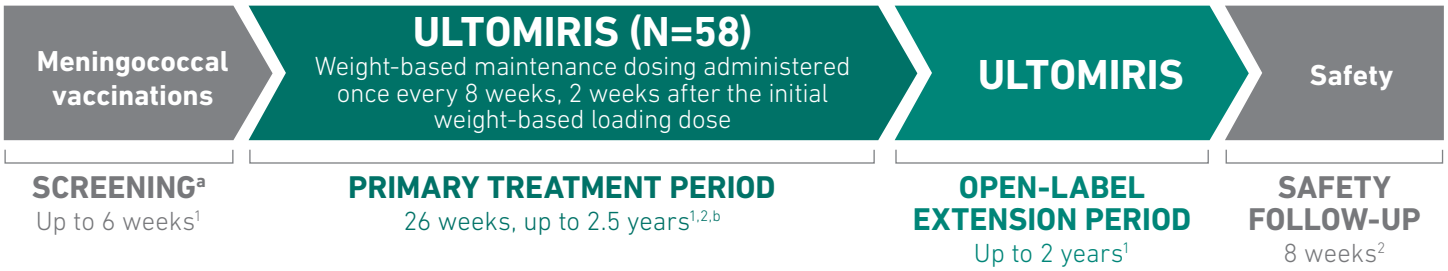
ULTOMIRIS Was Studied in CHAMPION-NMOSD, a Phase 3, Externally Placebo-Controlled, Open-Label Trial[1,2]

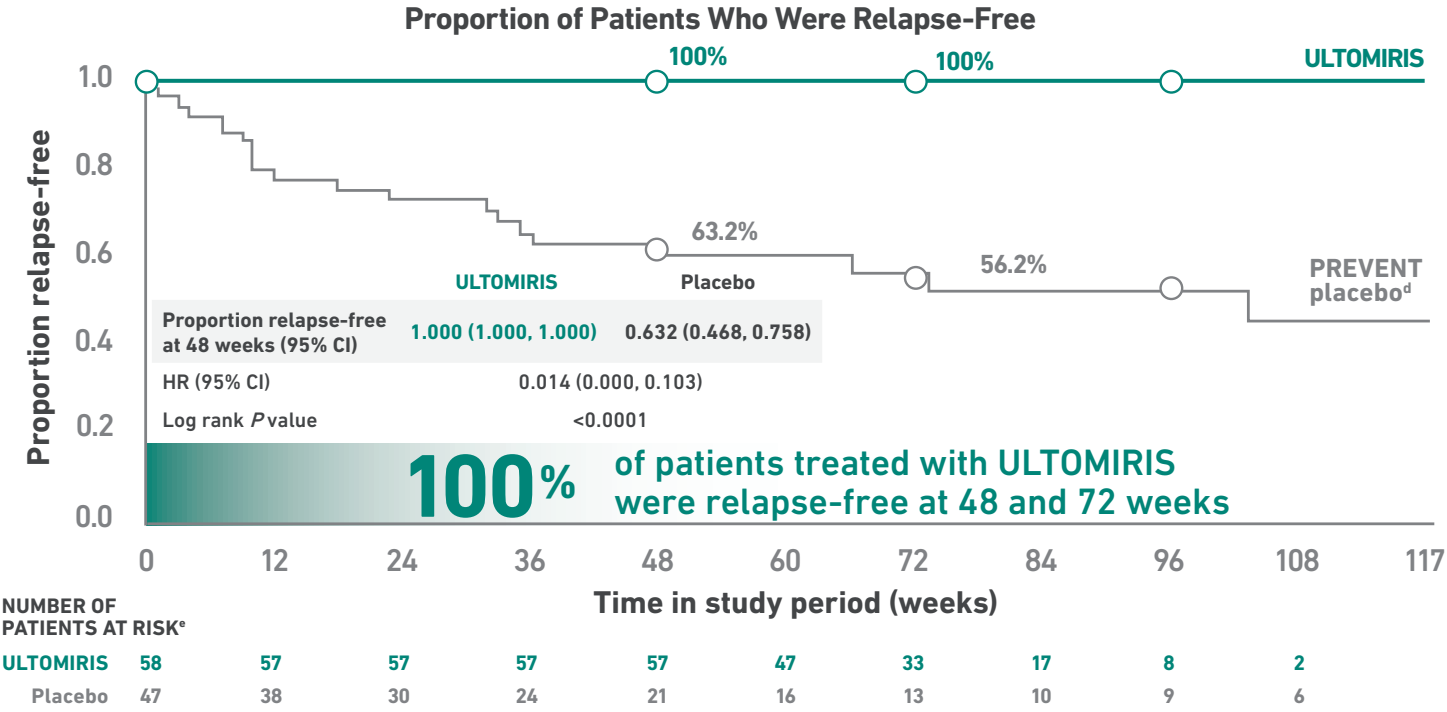
CHAMPION-NMOSD ENROLLED ADULTS WITH ANTI-AQP4 ANTIBODY-POSITIVE NMOSD[1]



- CHAMPION-NMOSD used an external placebo arm from the PREVENT study of eculizumab (n=47), another FDA-approved C5 complement inhibitor[2]
- PREVENT had a similar study design, patient population, and key endpoint–and the same adjudication committee[2]
- Patients who received rituximab within 3 months of screening were excluded from CHAMPION-NMOSD[2,c]
- Patients on selected ISTs (ie, corticosteroids, azathioprine, mycophenolate mofetil, methotrexate, and tacrolimus) were permitted to continue on therapy, with a requirement for stable dosing until they reached week 106 in the study[1]

ULTOMIRIS WAS SUPERIOR TO PLACEBO, BASED ON TIME TO FIRST ADJUDICATED ON-TRIAL RELAPSE (*P*<0.0001)[1]

ULTOMIRIS reduced the risk of relapse by 98.6% compared with placebo (HR=0.014; 95% CI: 0.000, 0.103)[1]



NUMBER OF PATIENTS AT RISK[e]

ULTOMIRIS	58	57	57	57	57	47	33	17	8	2
Placebo	47	38	30	24	21	16	13	10	9	6

[a]During the study, PE/PP or IVIg was allowed at the discretion of the treating physician for treatment of an on-trial relapse.[3] [b]The end of the primary treatment period could be triggered if 2 patients had an adjudicated on-trial relapse and all patients completed or discontinued prior to 26 weeks OR if there were <2 adjudicated on-trial relapses by the time all patients completed or discontinued prior to 50 weeks in the study.[2] [c]Concomitant use of rituximab with ULTOMIRIS was not permitted due to concerns about the potential impact on the efficacy of meningococcal vaccination and because concomitant treatment of a complement inhibitor may interfere with the MOA of rituximab (complement-dependent B-cell depletion).[2] [d]CHAMPION-NMOSD used an external placebo arm from the PREVENT study of eculizumab.[1] [e]Patients who did not experience an adjudicated on-trial relapse were censored at the end of the study period. If a patient in the placebo group (PREVENT) was followed for longer than any of the patients in the ULTOMIRIS arm, then that patient was censored at the longest ULTOMIRIS follow-up time.[1]

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CHAMPION-NMOSD Demonstrated Safety Data[1]

ADVERSE REACTIONS REPORTED IN ≥5% OF PATIENTS

Body System AR	ULTOMIRIS (n=58) n (%)
Blood and Lymphatic System Disorders	
Lymphadenopathy	3 (5)
Gastrointestinal Disorders	
Constipation	4 (7)
Vomiting	4 (7)
Diarrhea	3 (5)
Gastroesophageal reflux disease	3 (5)
General Disorders/Administration Site Reactions	
Pyrexia	5 (9)
Chills	3 (5)
Fatigue	3 (5)
Malaise	3 (5)
Non-cardiac chest pain	3 (5)
Vaccination site pain	3 (5)
Injury, Poisoning, and Procedural Complications	
Infusion-related reaction	4 (7)

Body System AR (cont'd)	ULTOMIRIS (n=58) n (%)
Infections and Infestations	
COVID-19	14 (24)
Urinary tract infection	6 (10)
Cystitis	5 (9)
Upper respiratory tract infection	5 (9)
Nasopharyngitis	3 (5)
Sinusitis	3 (5)
Musculoskeletal and Connective Tissue Disorders	
Back pain	7 (12)
Arthralgia	6 (10)
Myalgia	3 (5)
Nervous System Disorders	
Headache	14 (24)
Dizziness	4 (7)
Migraine	3 (5)
Respiratory, Thoracic, and Mediastinal Disorders	
Cough	3 (5)

Safety and efficacy of ULTOMIRIS were further studied in the long-term extension study[4]

SELECT IMPORTANT SAFETY INFORMATION (CONT'D)

CONTRAINDICATIONS

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

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Exploratory Analysis
Risk of Relapse in Patients With Prior Rituximab Use[2]

36.2% (21 of 58) of patients in CHAMPION-NMOSD had prior exposure to rituximab and at least 1 relapse in the 12 months prior to screening[a]

- In a prespecified exploratory analysis, 20 of the 21 patients treated with ULTOMIRIS were previously treated with rituximab in the year before screening (placebo, n=17)[b]

Zero relapses were seen in the CHAMPION-NMOSD study[c]

In patients with prior rituximab use, ULTOMIRIS reduced the risk of relapse by 93.7% compared with placebo

STUDY LIMITATION: Results or clinical outcomes should be interpreted with caution since this is a prespecified exploratory analysis.

In CHAMPION-NMOSD, the last rituximab dose permitted was >3 months prior to screening[2,5]

EXPERIENCE AMONG PATIENTS PREVIOUSLY ON RITUXIMAB

A post hoc analysis assessed safety outcomes in patients treated with ULTOMIRIS and eculizumab with previous exposure to rituximab within 1 year prior to enrolling in CHAMPION-NMOSD and PREVENT, respectively[5]

- Among the **154 patients** receiving complement inhibitors, **38 patients were exposed to rituximab** within the year prior to treatment[5]
- The mean (SD) time from the last rituximab dose to the first complement inhibitor dose was **6.5 (2.0) months**[5]
- The mean (SD) time from the last rituximab dose to the first meningococcal vaccination was **5.4 (2.0) months**[5]

There are currently no published guidelines on transitioning from rituximab to ULTOMIRIS in patients with NMOSD[6]

[a]Patients with prior exposure to rituximab may have been on additional concurrent therapies.
[b]One of the 21 patients exposed to rituximab was exposed >12 months prior to screening.[2]
[c]Observed during the primary treatment period, which ended when the last patient completed 50 weeks and represented a median study duration of 73.5 weeks (min 13.7, max 117.7).[2]

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SELECT IMPORTANT SAFETY INFORMATION (CONT'D)

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** 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.* Patients receiving ULTOMIRIS are at increased risk for infections due to these organisms, even if they develop antibodies following vaccination.

Thromboembolic Event Management

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

SELECT IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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 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.

USE IN SPECIFIC POPULATIONS

Pregnancy Exposure Registry

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

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

Abbreviations

ACIP, Advisory Committee on Immunization Practices; **AQP4,** aquaporin-4; **AR,** adverse reaction; **CD19,** cluster of differentiation 19; **CI,** confidence interval; **CN7,** cranial nerve 7; **COVID-19,** coronavirus disease 2019; **CSF,** cerebrospinal fluid; **c-spine,** cervical spine; **C5,** complement component 5; **ER,** emergency room; **FDA,** Food and Drug Administration; **GAD,** glutamic acid decarboxylase; **HCP,** healthcare professional; **HR,** hazard ratio; **IAC,** internal auditory canal; **ISTs,** immunosuppressive therapies; **IV,** intravenous; **IVIg,** intravenous immunoglobulin; **MOA,** mechanism of action; **MRI,** magnetic resonance imaging; **NMO,** neuromyelitis optica; **NMOSD,** neuromyelitis optica spectrum disorder; **PE,** plasma exchange; **PP,** plasmapheresis; **SD,** standard deviation; **SIADH,** syndrome of inappropriate antidiuretic hormone secretion; **T2,** transverse relaxation time; **URI,** upper respiratory tract infection; **UTI,** urinary tract infection; **VERs,** visual evoked responses; **WAC,** wholesale acquisition cost.

References

1. ULTOMIRIS. Prescribing Information. Alexion Pharmaceuticals, Inc. **2.** Pittock SJ, et al. *Ann Neurol*. 2023;93(6):1053-1068. **3.** Data on file. Alexion Pharmaceuticals, Inc. **4.** Pittock SJ, et al. Poster presented at: ACTRIMS Forum 2024; February 29-March 2, 2024; West Palm Beach, FL. **5.** Levy M, et al. Presented at: MSMilan 2023; October 11-13, 2023; Milan, Italy. **6.** Kümpfel T, et al. *J Neurol*. 2024;271(1):141-176. **7.** SOLIRIS. Prescribing Information. Alexion Pharmaceuticals, Inc. **8.** IBM Micromedex. Redbook. 2024. Accessed October 27th, 2025. https://www.micromedexsolutions.com

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

ULTOMIRIS Is an Accessible Option for Your Patients

BROAD ACCESS NATIONWIDE

Over 90% of lives **do not require step therapy**[7,a,b]

TREATMENT MADE AFFORDABLE; CARE MADE ACCESSIBLE

ULTOMIRIS reduces the annualized treatment cost by approximately 25% to 37% compared to eculizumab, based on WAC[1,7,8,c]

$0

As low as $0 out-of-pocket treatment costs for eligible patients[d]

Patients can choose to have their infusion at a hospital, at an independent infusion center, or at home.[e]

ALEXION ACCESS NAVIGATOR

Alexion Access Navigator is a dedicated resource website for US healthcare professionals and their offices, which contains downloadable access and reimbursement materials for ULTOMIRIS in NMOSD.

Resources include:

ULTOMIRIS NMOSD Sample Letter of Medical Necessity

- A template for responding to a request from a patient's insurance company to provide a letter of medical necessity when prescribing ULTOMIRIS in NMOSD

Field Reimbursement Managers

- Alexion Field Reimbursement Managers (FRMs) provide education and support to HCP offices to facilitate patient access to their prescribed Alexion medications

ULTOMIRIS NMOSD Coding & Billing Guide

- A guide that contains objective and factual coding, billing, and claims information to support access and appropriate reimbursement for ULTOMIRIS in NMOSD

For additional access resources, please visit: **https://alexionaccessnavigator.com/ultomiris/nmosd**

Why Consider ULTOMIRIS

ULTOMIRIS provides patients with:

Proven Efficacy
Reduced risk of relapse by 98.6% compared to an external placebo[1,f]

Immediate C5 Inhibition
Immediate, complete, and sustained C5 inhibition observed as early as <1 hour after the first infusion[1,g,h]

Freedom Between Doses
Once-every-8-week weight-based maintenance dosing, starting 2 weeks after loading dose, with just 6-7 infusions a year[1]

Demonstrated Results
Safety and efficacy data seen in over 700 patients across 4 indications[1,4,i]

[a]Refers to plans with commercial and Medicare policies in place. [b]Data as of November 2024. [c]Based on WAC as of January 2025 and calculations of annual product costs per patient for year 2+. [d]For eligible commercially insured patients. [e]In-home infusions may be available based on your patient's insurance and location.[1] [f]ULTOMIRIS was superior to placebo, based on time to first adjudicated on-trial relapse (primary endpoint; [HR=0.014; 95% CI: 0.000, 0.103], *P*<0.0001).[1] [g]Complete inhibition of serum-free C5 (concentration of <0.5 µg/mL) was observed by the end of the first ULTOMIRIS infusion and sustained throughout the entire 26-week treatment period in the majority (98.3%) of adult patients with anti-AQP4 antibody-positive NMOSD.[1] [h]The minimum infusion time for ULTOMIRIS maintenance doses ranges from 30 minutes to 1 hour, depending on body weight. Patients are monitored for at least 1 hour after infusions for signs or symptoms of an infusion-related reaction. If an adverse reaction occurs during the IV administration of ULTOMIRIS, the infusion may be slowed or stopped at the discretion of the physician.[1] [i]Safety data observed in all approved indications for ULTOMIRIS.[1,4]

US/ULT-N/0403 V1 11/2025
This message is intended for healthcare professionals in the United States only.

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ALEXION AstraZeneca Rare Disease

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