# REAL-WORLD

## Meningococcal Infection Rates for ULTOMIRIS® (ravulizumab-cwvz) and SOLIRIS® (eculizumab)

ALEXION®
AstraZeneca Rare Disease

Explore the data from over 14 years of postmarketing experience for **ULTOMIRIS** and **SOLIRIS**[1,2]

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

### INDICATIONS AND 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 (NMOSD)**
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 additional Important Safety Information on pages 10-11 and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

SOLIRIS® (eculizumab) Injection for Intravenous Use 300 mg/30 mL vial

### INDICATIONS AND SELECT IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab)

#### INDICATIONS

**Paroxysmal Nocturnal Hemoglobinuria (PNH)**
SOLIRIS is indicated for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.

**Atypical Hemolytic Uremic Syndrome (aHUS)**
SOLIRIS is indicated for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

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

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

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

#### SELECT IMPORTANT SAFETY INFORMATION

**WARNING: SERIOUS MENINGOCOCCAL INFECTIONS**

**SOLIRIS, 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 SOLIRIS, unless the risks of delaying SOLIRIS 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 SOLIRIS 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, SOLIRIS 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)*].**

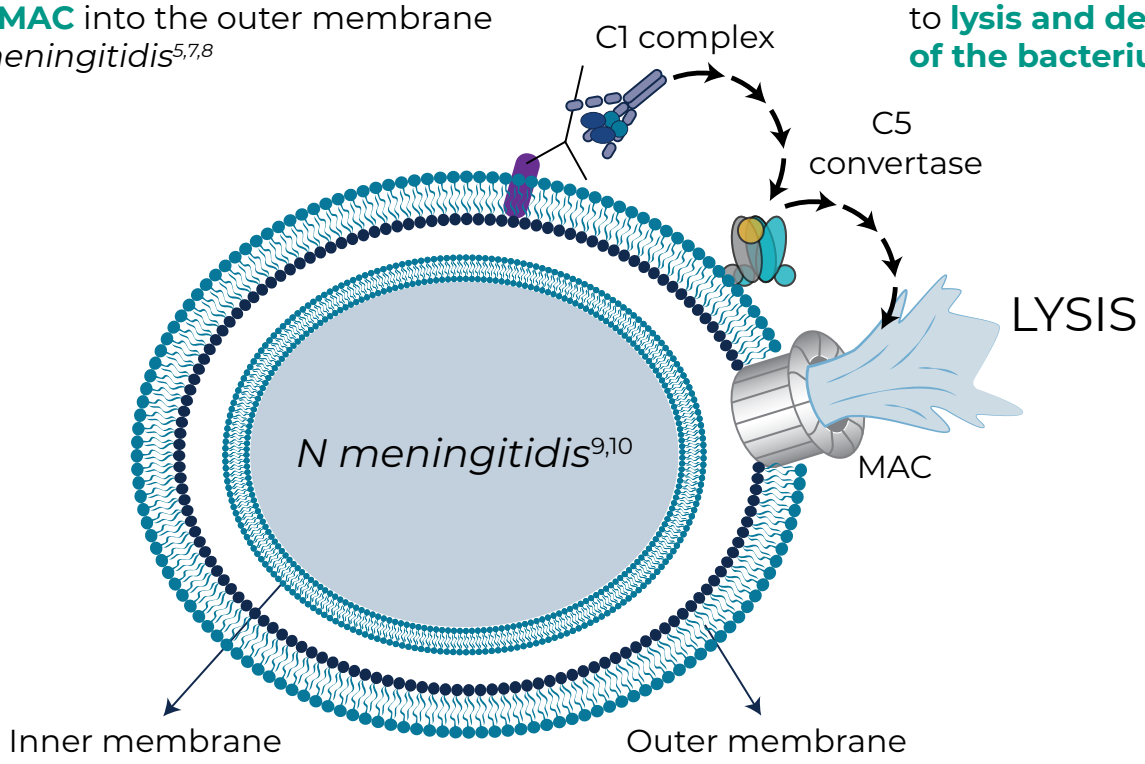
**Please see additional Important Safety Information on pages 11-12 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

# The Complement System Plays a Critical Role in Defense Against *N meningitidis*[3]

**Patients receiving complement inhibitors such as ULTOMIRIS (ravulizumab-cwvz) and SOLIRIS (eculizumab) are more susceptible to meningococcal infections because their complement system's defense against *N meningitidis* is compromised.**[4-6]

Bactericidal antibodies activate the classical pathway of the complement cascade, which leads to the insertion of the **MAC** into the outer membrane of *N meningitidis*[5,7,8]

**Insertion of the MAC** into the outer membrane of *N meningitidis* leads to **lysis and death of the bacterium**[8]




Vaccines **promote** bactericidal antibody development and can help **reduce the risk** of meningococcal disease.[11,12] Vaccination does not eliminate the risk of meningococcal infections, despite development of antibodies following vaccination.[13]

**Due to the risk of serious meningococcal infections, ULTOMIRIS and SOLIRIS are available only through a restricted program called ULTOMIRIS and SOLIRIS REMS. All prescribers and dispensing sites for ULTOMIRIS and SOLIRIS must be enrolled in this program. For more information on this program, please visit UltSolREMS.com**[13,14]

**MAC**, membrane attack complex; **REMS**, Risk Evaluation and Mitigation Strategy.

**Please see additional Important Safety Information on pages 10-11 and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

**Please see additional Important Safety Information on pages 11-12 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

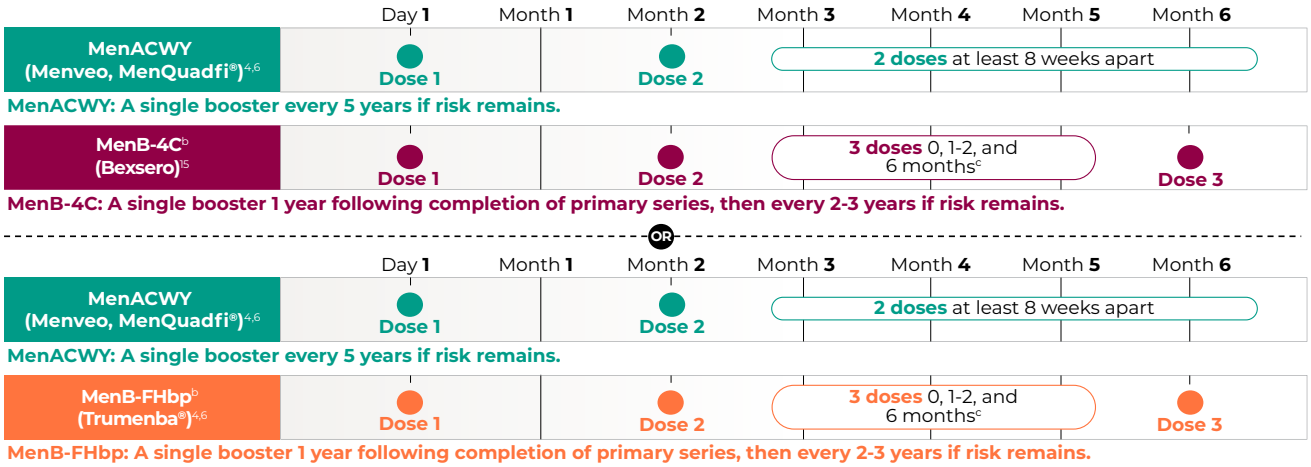
# Because patients on complement inhibitors are at a higher susceptibility for developing meningococcal infections, it is important they are vaccinated[4,6]

## Complete or update meningococcal vaccination (for serogroups A, C, W, Y and B) at least 2 weeks prior to administration of the first dose of ULTOMIRIS or SOLIRIS, per the current Advisory Committee on Immunization Practices (ACIP) recommendations for patients receiving a complement inhibitor.[13,14]

**1** ACIP recommends that persons using complement inhibitors should be vaccinated at least 2 weeks before complement inhibitor initiation unless the risks for delaying treatment outweigh the risks for developing meningococcal disease.[4]

**2** Revaccinate patients in accordance with ACIP recommendations considering the duration of therapy with **ULTOMIRIS** or **SOLIRIS**.[13,14,a]

**3** If urgent **ULTOMIRIS** or **SOLIRIS** therapy is indicated in a patient who is not up to date with meningococcal vaccines according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer meningococcal vaccines as soon as possible.[13]




***This list is not exhaustive and is intended to provide an example of most commonly prescribed meningococcal vaccines. The choice of vaccine brand deemed medically appropriate is the decision of the treating HCP.***

[a]Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information.[13]
[b]MenB vaccines are not interchangeable. Patients must receive the same product for all doses.[6]
[c]For additional information on clinical considerations, refer to the most current ACIP recommendation and CDC immunization schedule.[13]

**CDC**, Centers for Disease Control and Prevention; **HCP**, healthcare provider; **MenACWY**, meningococcal serogroups A, C, W, and Y; **MenB-4C**, multicomponent meningococcal serogroup B; **MenB-FHbp**, bivalent factor-H binding protein meningococcal serogroup B.

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**Please see additional Important Safety Information on pages 11-12 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

# Real-World Meningococcal Infection Rates Have Been Tracked Globally for Over 14 Years Outside of Clinical Studies[1,2]

The safety of **ULTOMIRIS** (ravulizumab-cwvz) and **SOLIRIS** (eculizumab) have been extensively studied:

**ULTOMIRIS** safety data have been evaluated across 4 rare, complement-mediated diseases, with over 5 years of postmarketing experience and 21,834 patient-years of exposure.[1,13]

**SOLIRIS** safety data have been evaluated across 4 rare, complement-mediated diseases, with over 16 years of postmarketing experience and 88,607 patient-years of exposure.[1,14]

Prior to data cutoff, **ULTOMIRIS** has been **approved** in **31 countries**[1]

Prior to data cutoff, **SOLIRIS** has been **approved** in **25 countries**[1]

## Real-world meningococcal infection rates were synthesized from the Alexion safety database[2]

**Data for ULTOMIRIS and SOLIRIS across approved indications were analyzed using the MedDRA High-Level Term "*Neisseria* infection," which included only *Neisseria meningitidis*-associated cases[2]**

- Cumulative and annual reporting rates were calculated per **100 patient-years**
- Data cutoff date for **SOLIRIS**: October 1, 2023
- Data cutoff date for **ULTOMIRIS**: December 31, 2023

**MedDRA**, Medical Dictionary for Regulatory Activities.

**Please see additional Important Safety Information on pages 10-11 and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

**Please see additional Important Safety Information on pages 11-12 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

# Real-world meningococcal infection rates for ULTOMIRIS and SOLIRIS were calculated per 100 patient-years (PY) to communicate the level of associated risk[2]

**PY** is calculated as the number of "cases" divided by the amount of "person(s)-time" at risk[16]

**For example, if the infection rate is 0.1 infections per 100 PY in the postmarketing years, this can be interpreted in the following ways:**[1]

## Patient-Years Example Calculation[1]

**0.1 case**

per 100 patients treated for 1 year

**1 case**

per 1,000 patients treated for 1 year

**10 cases**

per 10,000 patients treated for 1 year

Among **10,000 patients** exposed to product for one year, approximately **10 cases** could be expected.[1]

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# Global Real-World Analysis of *N meningitidis* Infection Rates in Patients on ULTOMIRIS (ravulizumab-cwvz) and SOLIRIS (eculizumab) Across Approved Indications[1,2]

Cumulative *N meningitidis* infection and associated mortality rates among patients with gMG, NMOSD, aHUS, and PNH treated with ULTOMIRIS or SOLIRIS[1,2]

| | | Number of *N meningitidis* infection | Number of *N meningitidis* fatalities | PY estimated exposure | *N meningitidis* infection rate (per 100 PY) | *N meningitidis* mortality rate (per 100 PY) |
|---|---|---|---|---|---|---|
| ULTOMIRIS[a] | Global Total (including US)[b,c] | 19 | 1 | 21,834 | 0.09 | 0.005 |
| | US Total[c] | 6 | 1 | 10,555 | 0.06 | 0.01 |
| | US gMG | 0 | 0 | 1,863 | 0 | 0 |
| | US NMOSD | n/a | n/a | n/a | n/a | n/a |
| SOLIRIS[d] | Global Total (including US)[e,f] | 186 | 21 | 88,607 | 0.21 | 0.02 |
| | US Total[f] | 41 | 3 | 34,484 | 0.12 | 0.01 |
| | US gMG | 4 | 0 | 9,181 | 0.04 | 0 |
| | US NMOSD | 2 | 0 | 1,988 | 0.10 | 0 |

***These data are from the Alexion safety database. Data may be missing or incomplete as it is limited to cases reported by prescribing clinicians. Results or clinical outcomes should be interpreted with caution.***

[a]ULTOMIRIS was approved for gMG in the US in April 2022. ULTOMIRIS was not approved for NMOSD in the US at data cutoff (approved March 2024). ULTOMIRIS data cutoff date: December 31, 2023. [b]The global total includes all global data of on-label use of ULTOMIRIS. It is included to provide a broader perspective on the risk of meningococcal infections. Per the methodology, the rest of the data included in this analysis is specific to US on-label utilization of ULTOMIRIS. [c]The total row includes all approved indications for ULTOMIRIS by data cutoff. [d]SOLIRIS data cutoff date: October 1, 2023. [e]The global total includes all global data of on-label use of SOLIRIS. It is included to provide a broader perspective on the risk of meningococcal infections. Per the methodology, the rest of the data included in this analysis is specific to US on-label utilization of SOLIRIS. [f]The total row includes all approved indications for SOLIRIS.

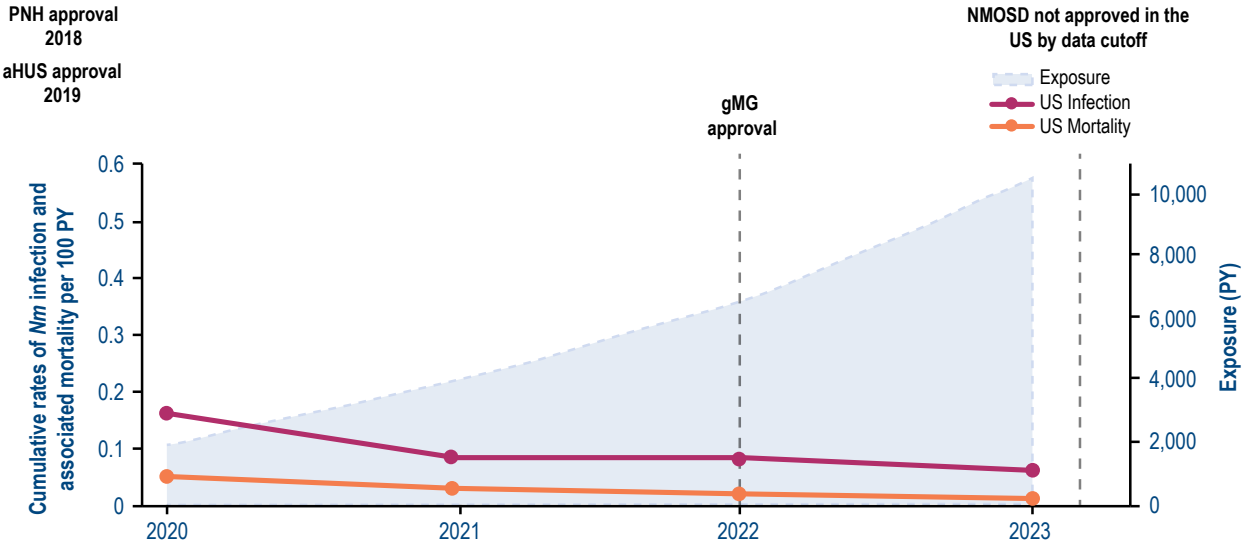
**aHUS**, atypical hemolytic uremic syndrome; **gMG**, generalized myasthenia gravis; **NMOSD,** neuromyelitis optica spectrum disorder; **PNH**, paroxysmal nocturnal hemoglobinuria; **PY**, patient-years; **US**, United States.

**Please see additional Important Safety Information on pages 10-11 and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

**Please see additional Important Safety Information on pages 11-12 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

# US Real-World Meningococcal Infection Rate for ULTOMIRIS (ravulizumab-cwvz)-Treated Patients Was 0.06 per 100 PY in 2023[1]

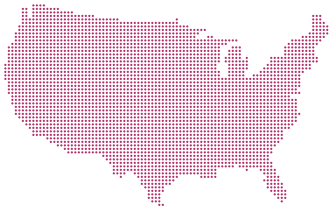
## Cumulative reported *Neisseria meningitidis* infection and associated mortality rates with ULTOMIRIS in the US[1]




| | 2020 | 2021 | 2022 | 2023 |
|---|---|---|---|---|
| *Nm* infection | 0.16 | 0.08 | 0.08 | 0.06 |
| Mortality | 0.05 | 0.03 | 0.02 | 0.01 |
| PY | 1,918.1 | 3,956.6 | 6,534 | 10,554.6 |

To minimize Weber Effect, the graph starts in 2020 when there was at least 1000 PY of ULTOMIRIS exposure

There have been **10,555 patient-years** of cumulative exposure to **ULTOMIRIS** in the US across all approved indications since 2019[1]



In 2023, the cumulative US *N meningitidis* infection rate in **ULTOMIRIS**-treated patients across all approved indications was **0.06 per 100 patient-years**[1]

Another way to say this is **6 meningococcal cases** in **10,000 ULTOMIRIS patients** in **1 year**[1]

All patients received appropriate vaccinations. **Vaccination does not eliminate the risk** of meningococcal infections, despite development of antibodies following vaccination.[13]

***These data are from the Alexion safety database. Data may be missing or incomplete as it is limited to cases reported by prescribing clinicians. Results or clinical outcomes should be interpreted with caution.***

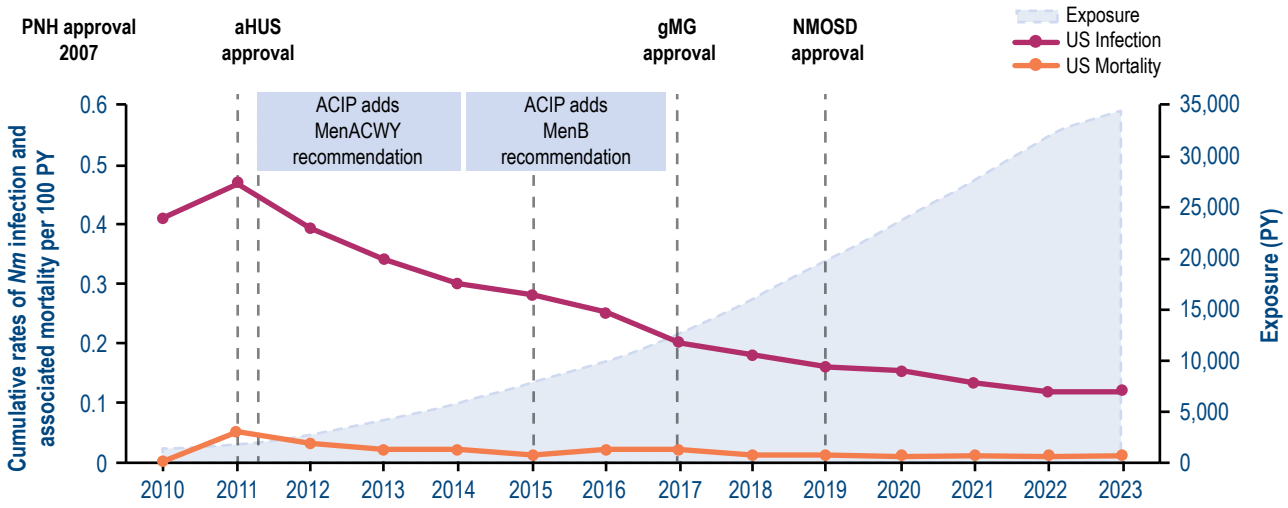
**aHUS**, atypical hemolytic uremic syndrome; **gMG**, generalized myasthenia gravis; ***Nm***, *Neisseria meningitidis*; **NMOSD**, neuromyelitis optica spectrum disorder; **PNH**, paroxysmal nocturnal hemoglobinuria; **PY**, patient-years; **US**, United States.

**Please see additional Important Safety Information on pages 10-11 and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

**Please see additional Important Safety Information on pages 11-12 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

# US Real-World Meningococcal Infection Rate for SOLIRIS (eculizumab)-Treated Patients Was 0.12 per 100 PY in 2023[2]

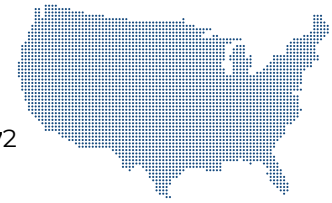
## Cumulative reported *Neisseria meningitidis* infection and associated mortality rates with SOLIRIS in the US[2]




| | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Nm* infection | 0.41 | 0.47 | 0.39 | 0.34 | 0.30 | 0.28 | 0.25 | 0.20 | 0.18 | 0.16 | 0.15 | 0.13 | 0.12 | 0.12 |
| Mortality | 0 | 0.05 | 0.03 | 0.02 | 0.02 | 0.01 | 0.02 | 0.02 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| PY | 1458 | 2122 | 3078 | 4356 | 5975 | 7945 | 10,237 | 12,811 | 15,975 | 19,790 | 21,857 | 28,029 | 31,941 | 34,484 |

To minimize Weber Effect, the graph starts in 2010 when there was at least 1000 PY of SOLIRIS exposure

There have been **34,484 patient-years** in this analysis of cumulative exposure to **SOLIRIS** in the US across all approved indications since 2007[2]



In 2023, the cumulative US *N meningitidis* infection rate in **SOLIRIS**-treated patients across all approved indications was **0.12 per 100 patient-years**[2]

Another way to say this is **12 meningococcal cases** in **10,000 SOLIRIS patients** in **1 year**[2]

All patients received appropriate vaccinations. **Vaccination does not eliminate the risk** of meningococcal infections, despite development of antibodies following vaccination.[14]

***These data are from the Alexion safety database. Data may be missing or incomplete as it is limited to cases reported by prescribing clinicians. Results or clinical outcomes should be interpreted with caution.***

**ACIP**, Advisory Committee on Immunization Practices; **aHUS**, atypical hemolytic uremic syndrome; **gMG,** generalized myasthenia gravis; **MenACWY**, meningococcal serogroups A, C, W, and Y; **MenB**, meningococcal serogroup B; ***Nm***, *Neisseria meningitidis*; **NMOSD**, neuromyelitis optica spectrum disorder; **PNH**, paroxysmal nocturnal hemoglobinuria; **PY**, patient-years; **US**, United States.

**Please see additional Important Safety Information on pages 10-11 and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

**Please see additional Important Safety Information on pages 11-12 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

# Alexion Maintains a Long-Standing Commitment to Providing Comprehensive Support to Help Your Patients and Your Practice

ONESOURCE®
Personalized Patient Support from Alexion

**OneSource™** is a comprehensive, complimentary, and personalized patient support program offered by Alexion to help with a variety of patient needs

**1-888-765-4747 | OneSource@alexion.com**

**EDUCATION**

**ONGOING SUPPORT**

**HEALTH INSURANCE NAVIGATION**

**COMMUNITY CONNECTIONS**

## OneSource can provide comprehensive vaccination support, including:

- Educating patients/caregivers about meningococcal vaccines
- Assisting patients in finding a local vaccination solution
- Providing VaxFirst, a complimentary program to help eligible patients access meningococcal vaccinations to ensure compliance with FDA-mandated REMS (Risk Evaluation and Mitigation Strategy) requirements and help reduce the risk of infections caused by *Neisseria meningitidis* which can increase a patient's susceptibility to serious, life-threatening, or fatal infections
- OneSource will help eligible patients find the appropriate vaccine options for each individual patient. Contact OneSource for more information at 1-888-765-4747

**Please see additional Important Safety Information on pages 10-11 and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

**Please see additional Important Safety Information on pages 11-12 and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

# SELECT IMPORTANT SAFETY INFORMATION FOR ULTOMIRIS® (ravulizumab-cwvz)

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

## 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 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.

**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.

**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

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 were 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%), and 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.

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.

## USE IN SPECIFIC POPULATIONS

Pregnancy Exposure Registry

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

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

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

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# SELECT IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab)

SOLIRIS® (eculizumab) Injection for Intravenous Use 300 mg/30 mL vial

## CONTRAINDICATIONS

- SOLIRIS is contraindicated for initiation in patients with unresolved serious *Neisseria meningitidis* infection.

## WARNINGS AND PRECAUTIONS

**Serious Meningococcal Infections**

SOLIRIS, 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 therapy with SOLIRIS. 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 SOLIRIS therapy is indicated in a patient who is not up to date with meningococcal vaccines according to ACIP recommendations, provide the patient with 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 SOLIRIS. The benefits and risks of treatment with SOLIRIS, 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 these signs and symptoms occur. Promptly treat known infections. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of SOLIRIS 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, SOLIRIS 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 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 SOLIRIS. 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 SOLIRIS. Patients must receive counseling about the need to receive meningococcal vaccines and to take antibiotics as directed, the signs and symptoms of meningococcal infection, and be instructed to carry the Patient Safety Card with them at all times during and for 3 months following SOLIRIS treatment.

Further information is available at www.UltSolREMS.com or 1-888-765-4747.

## WARNINGS AND PRECAUTIONS (cont'd)

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

SOLIRIS blocks terminal complement activation; therefore, patients may have increased susceptibility to infections, especially with encapsulated bacteria, such as infections with *Neisseria meningitidis* but also *Streptococcus pneumoniae, Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*. Additionally, *Aspergillus* infections have occurred in immunocompromised and neutropenic patients. Children treated with SOLIRIS 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 SOLIRIS are at increased risk for infections due to these organisms, even if they develop antibodies following vaccination.

**Monitoring Disease Manifestations After SOLIRIS Discontinuation**

Treatment Discontinuation for PNH
Monitor patients after discontinuing SOLIRIS for at least 8 weeks to detect hemolysis.

Treatment Discontinuation for aHUS
After discontinuing SOLIRIS, monitor patients with aHUS for signs and symptoms of thrombotic microangiopathy (TMA) complications for at least 12 weeks. In aHUS clinical trials, 18 patients (5 in the prospective studies) discontinued SOLIRIS treatment. TMA complications occurred following a missed dose in 5 patients, and SOLIRIS was reinitiated in 4 of these 5 patients.

Clinical signs and symptoms of TMA include changes in mental status, seizures, angina, dyspnea, or thrombosis. In addition, the following changes in laboratory parameters may identify a TMA complication: occurrence of 2, or repeated measurement of any one of the following: a decrease in platelet count by 25% or more compared to baseline or the peak platelet count during SOLIRIS treatment; an increase in serum creatinine by 25% or more compared to baseline or nadir during SOLIRIS treatment; or, an increase in serum LDH by 25% or more over baseline or nadir during SOLIRIS treatment.

If TMA complications occur after SOLIRIS discontinuation, consider reinstitution of SOLIRIS treatment, plasma therapy [plasmapheresis, plasma exchange, or fresh frozen plasma infusion (PE/PI)], or appropriate organ-specific supportive measures.

**Thrombosis Prevention and Management**
The effect of withdrawal of anticoagulant therapy during SOLIRIS treatment has not been established. Therefore, treatment with SOLIRIS should not alter anticoagulant management.

**Infusion-Related Reactions**
Administration of SOLIRIS may result in infusion-related reactions, including anaphylaxis or other hypersensitivity reactions. In clinical trials, no patients experienced an infusion-related reaction which required discontinuation of SOLIRIS. Interrupt SOLIRIS infusion and institute appropriate supportive measures if signs of cardiovascular instability or respiratory compromise occur.

## ADVERSE REACTIONS

Adverse Reactions for PNH
The most frequently reported adverse reactions in the PNH randomized trial (≥10% overall and greater than placebo) were: headache, nasopharyngitis, back pain, and nausea.

Adverse Reactions for aHUS
The most frequently reported adverse reactions in the aHUS single arm prospective trials (≥20%) were: headache, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, pyrexia.

Adverse Reactions for gMG
The most frequently reported adverse reaction in the gMG placebo-controlled clinical trial (≥10%) was: musculoskeletal pain.

Adverse Reactions for NMOSD
The most frequently reported adverse reactions in the NMOSD placebo-controlled trial (≥10%) were: upper respiratory infection, nasopharyngitis, diarrhea, back pain, dizziness, influenza, arthralgia, pharyngitis, and contusion.

## DRUG INTERACTIONS

Plasmapheresis, Plasma Exchange, or Fresh Frozen Plasma Infusion

Concomitant use of SOLIRIS with plasma exchange (PE), plasmapheresis (PP) or fresh frozen plasma infusion (PE/PI) treatment can reduce serum eculizumab concentrations and requires a supplemental dose of SOLIRIS.

Neonatal Fc Receptor Blockers

Concomitant use of SOLIRIS with neonatal Fc receptor (FcRn) blockers may lower systemic exposures and reduce effectiveness of SOLIRIS. Closely monitor for reduced effectiveness of SOLIRIS.

**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 SOLIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

**References: 1.** Data on file. Alexion Pharmaceuticals, Inc. **2.** Pandya S, et al. Presented at: AAN 2024 Summer Conference; July 19-20, 2024; Atlanta, GA. Abstract OP 076. **3.** Ram S, et al. *Clin Microbiol Rev*. 2010;23(4):740-780. **4.** Mbaeyi SA, et al. *MMWR Recomm Rep*. 2020;69(9):1-41. **5.** Uria MJ, et al. *J Exp Med*. 2008;205(6):1423-1434. **6.** Murthy N, et al. *Ann Intern Med*. 2023;176(3):367-380. **7.** Lo H, et al. *Lancet*. 2009;9(7):418-427. **8.** Drogari-Apiranthitou M, et al. *Infect Immun*. 2002;70(7):3752-3758. **9.** Doorduijn DJ, et al. *BioEssays*. 2019;41(10):1900074. **10.** Schneider MC, et al. *Trends Microbiol*. 2007;15(5):233-240. **11.** van Deuren M, et al. *Clin Microbiol Rev*. 2000;13(1):144-166. **12.** Feldman C, et al. *Pneumonia*. 2019;11(1):3. **13.** ULTOMIRIS. Prescribing Information. Alexion Pharmaceuticals, Inc. **14.** SOLIRIS. Prescribing Information. Alexion Pharmaceuticals, Inc. **15.** Recent Meeting Recommendations In: ACIP Recommendations. Updated October 2024. Accessed 29 October 2024. https://www.cdc.gov/acip/vaccine-recommendations/index.html **16.** Tenny S, et al. *StatPearls*. StatPearls Publishing; 2023.

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