For your adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive[1]

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

Can ULTOMIRIS help with concomitant corticosteroid use in anti-AChR antibody-positive gMG patients?

Image is not of actual patient

INDICATION

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

SELECT IMPORTANT SAFETY INFORMATION FOR ULTOMIRIS (ravulizumab-cwvz)

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

INDICATION

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

SELECT IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab)

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)*].

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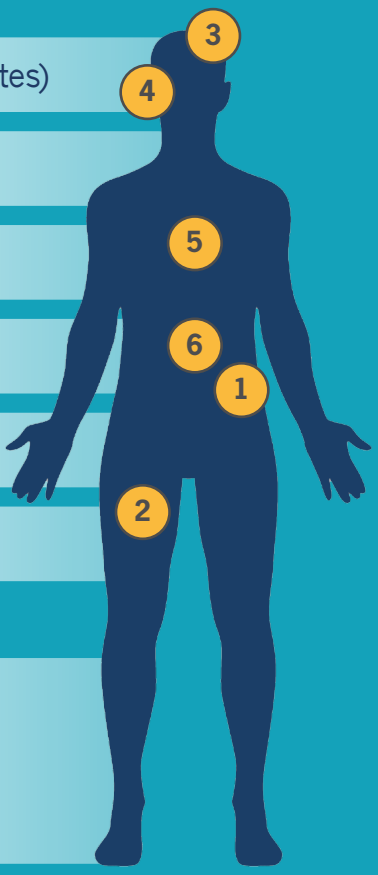
Long-term, high-dose corticosteroids are widely prescribed first-line for generalized myasthenia gravis (gMG), but they may have limitations[2-4]

Potential Limitations[3]

1. Metabolic conditions (weight gain, hyperglycemia, diabetes)
2. Osteoporosis
3. Neuropsychiatric issues
4. Ophthalmologic conditions
5. Cardiovascular issues (hypertension and arrhythmias)
6. Gastrointestinal issues



Additional Considerations[3]

- Electrolyte imbalances
- Increased risk of infection
- Myopathy

It is important to consider options that may allow you to reduce or eliminate corticosteroids from your patients' gMG treatment regimen.[5]

It can take over a year to reduce corticosteroids to a low dose (<5 mg/day) while keeping risk of relapse low[6,7,a]

Reduction to <5 mg/day or elimination of corticosteroids is often the **preferred course of treatment if nonsteroidal agents are available**[2,4,6]

Recommendations and guidelines now include **corticosteroid reduction as a measure of efficacy in some clinical trials**[8,9]

[a]Based on a retrospective study of 125 patients with myasthenia gravis conducted in China. The primary endpoint was occurrence of disease relapse after reducing or eliminating corticosteroids.[7]

Help appropriate patients with gMG by considering options that may allow you to reduce or eliminate corticosteroids[3,10]

Are conventional treatments such as corticosteroids working for your gMG patients?[a]

Madison

Age: 32
Profession: Social worker
Length of Disease: 8 months; treatment initiated upon diagnosis
Location: Cleveland, Ohio

Past medical history

- Madison has no significant medical history except for a diagnosis of anti-AChR antibody-positive gMG 8 months ago
- Madison has a family history of osteoporosis and diabetes mellitus

History of present illness

- Madison's disease progressed from oMG to gMG quickly, requiring a corticosteroid and IST for management
- MGFA class IIIa
- MG-ADL total score: 6
- Initially on low-dose steroids and IST; increased steroids to 80 mg per day, then reduced to 40 mg per day and unable to reduce further

Current medications

- Prednisone 40 mg once daily
- Azathioprine 150 mg once daily
- Pyridostigmine 60 mg four times daily

Current chief complaints

- Madison has an incomplete response to current therapies and is experiencing breakthrough symptoms of intermittent slurring of speech, increased shortness of breath upon exertion, and lower limb paresis
- Madison is continuing to experience gMG symptoms as well as weight gain and increased acne. She and her physician are considering adding ULTOMIRIS to her current treatment plan

[a]Patient case is fictitious and intended only for discussion about patient experiences. Patient case is not intended for diagnosis or treatment purposes.
AChR, acetylcholine receptor; gMG, generalized myasthenia gravis; IST, immunosuppressive therapy; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; oMG, ocular myasthenia gravis.

Evaluation of SOLIRIS up to 130 weeks included patients taking ISTs[10]

REGAIN study design

SOLIRIS was studied in REGAIN, a Phase 3, randomized, double-blind, placebo-controlled trial with an open-label extension (OLE). Patients were randomized to receive either SOLIRIS (n=62) or placebo (n=63) for 26 weeks and were subsequently allowed to enter the OLE period for up to 4 years.[11-13]

Approximately 90% of patients had MGFA class II or III generalized myasthenia gravis (gMG) with mild or moderate weakness at baseline[12]

98% of patients received >2 ISTs at REGAIN baseline and were required to maintain stable doses through the RCT until the OLE[11-13]

- 77% were taking prednisone[10]

Primary endpoint:

4.2-point improvement in mean MG-ADL total score from baseline to Week 26 among patients receiving SOLIRIS vs 2.3-point improvement in patients receiving placebo (*P*=0.006). In the study, the average baseline total score for people receiving SOLIRIS was 10.5; for people receiving placebo, it was 9.9.[11,12,a]

Adverse reactions:

The most frequently reported adverse reaction in the gMG placebo-controlled clinical trial (≥10%) was musculoskeletal pain.[11]

The REGAIN OLE trial continued collecting corticosteroid use data through Week 130[10]

[a]The MG-ADL is a categorical scale that assesses the impact on daily function of 8 signs or symptoms that are typically affected in gMG. Each item is assessed on a 4-point scale where a score of 0 represents normal function and a score of 3 represents loss of ability to perform that function. The total score ranges from 0 to 24, with the higher scores indicating more impairment.[1]

IST, immunosuppressive therapy; MG-ADL, Myasthenia Gravis Activities of Daily Living, MGFA, Myasthenia Gravis Foundation of America; RCT, randomized controlled trial.

SELECT IMPORTANT SAFETY INFORMATION for SOLIRIS

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*.

SOLIRIS was evaluated in a real-world setting, including patients taking prednisone[11,14]

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

ELEVATE retrospective analysis

ELEVATE, a retrospective observational analysis conducted in the US, used physician-reported electronic medical records data. Each patient (n=119) served as their own control. ELEVATE retrospectively observed patient outcomes before SOLIRIS initiation for up to 2 years and patient outcomes after SOLIRIS initiation for up to 2 years.[14]

In ELEVATE, approximately 60% of patients (n=69) were taking prednisone at the time of SOLIRIS initiation[14]

Real-world outcomes:

Improvement in MG-ADL total scores was observed by 3 months (2.6-point improvement) and was still observed through 24 months (3.2-point improvement). The mean MG-ADL total score before SOLIRIS initiation was 8.0.[14]

ELEVATE was a retrospective chart review, with data derived from routine clinical practice and assessments based on clinical judgment. As a retrospective analysis, ELEVATE was designed to assess associations and not causality.[14]

ELEVATE RETROSPECTIVE ANALYSIS LIMITATION: ELEVATE was a retrospective analysis; therefore, results and clinical outcomes should be interpreted with caution.

MG-ADL, Myasthenia Gravis Activities of Daily Living.

SELECT IMPORTANT SAFETY INFORMATION for SOLIRIS

WARNINGS AND PRECAUTIONS, (continued)

Serious Meningococcal Infections, (continued)

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.

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

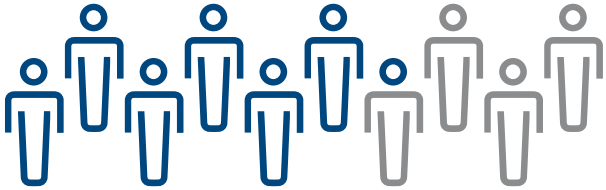
Alexion has been reporting on IST (including corticosteroid) reduction and discontinuation in both clinical trial and real-world settings[10,14]

In the REGAIN OLE trial, **71.8% (84 of 117) of patients decreased or discontinued their daily dose of 1 or more ISTs**[10,a]

43.6%
(51 of 117) discontinued at least one IST

63.2%
(74 of 117) decreased their daily dose of 1 IST

1.7% (2 of 117) decreased their daily dose of >1 IST



Of the patients who were taking prednisone at SOLIRIS initiation in the ELEVATE retrospective analysis (n=69), **77% reduced their dose or discontinued altogether**[14,b]

- **13% of patients discontinued prednisone** therapy altogether[14]

[a]**43.6% (51 of 117) of patients increased their daily dose of 1 IST. Three patients increased their dose of >1 IST. 31.6% (37 of 117) of patients started a new IST.[10]**

[b]**3% of patients increased their prednisone dosage and 20% of patients had their prednisone dose remain unchanged.[14]**

REGAIN OLE STUDY LIMITATION: Results should be interpreted with caution since the study was designed to evaluate safety and lacked a control group.

ELEVATE RETROSPECTIVE ANALYSIS LIMITATION: ELEVATE was a retrospective analysis; therefore, results and clinical outcomes should be interpreted with caution.

IST, immunosuppressive therapy.

SELECT IMPORTANT SAFETY INFORMATION for SOLIRIS

WARNINGS AND PRECAUTIONS, (continued)

ULTOMIRIS and SOLIRIS REMS, (continued)

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.

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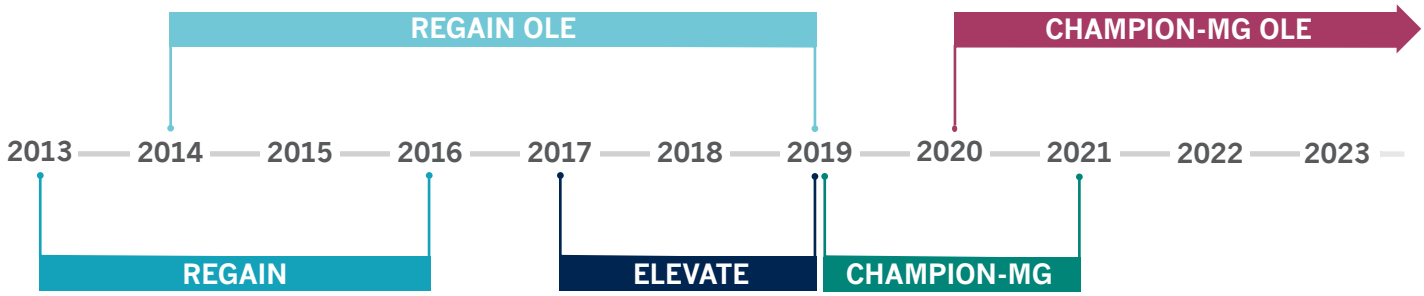
ULTOMIRIS® is advancing the 10-year legacy of C5 inhibition in gMG

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

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

ULTOMIRIS takes the legacy of C5 inhibition further by collecting steroid reduction data as patients remain on drug[12-18]



gMG, generalized myasthenia gravis; OLE, open-label extension.

SELECT IMPORTANT SAFETY INFORMATION for SOLIRIS

WARNINGS AND PRECAUTIONS, (continued)

ULTOMIRIS and SOLIRIS REMS, (continued)

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.

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*.

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SELECT IMPORTANT SAFETY INFORMATION for ULTOMIRIS

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

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IMPORTANT SAFETY INFORMATION FOR SOLIRIS®

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

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- **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.**
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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.

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WARNINGS AND PRECAUTIONS, (continued)

ULTOMIRIS and SOLIRIS REMS, (continued)

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

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

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

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.

CHAMPION-MG: The majority of patients were taking concomitant ISTs during this pivotal trial of ULTOMIRIS[18]

CHAMPION-MG was a Phase 3, randomized, double-blind, placebo-controlled trial with an OLE. Patients were randomized to receive either ULTOMIRIS (n=86) or placebo (n=89) for 26 weeks and were subsequently allowed to enter the OLE period for up to 4 years.[1,15,17]

90%
taking an IST at baseline[18]

In the CHAMPION-MG study, approximately **90% of patients were taking an immunosuppressive therapy (IST) at baseline** across both treatment arms[18]

At the time of ULTOMIRIS initiation, in the ULTOMIRIS arm, approximately 65% of patients were receiving prednisone/corticosteroid therapies[15]

- **The ISTs most commonly used (in ≥25% of total patients) at first dose of ULTOMIRIS in the ULTOMIRIS-treated arm were corticosteroids (65.1%) and mycophenolate mofetil (27.9%)**[15]

Patients were not given the opportunity to change dose or discontinue IST therapy until the OLE[17]

Adverse reactions reported in ≥5% and at greater frequency than placebo in ULTOMIRIS-treated patients[1]

Adverse Reactions	ULTOMIRIS (n=86), n (%)	Placebo (n=89), n (%)
GASTROINTESTINAL DISORDERS		
Diarrhea	13 (15)	11 (12)
Abdominal pain	5 (6)	0
INFECTIONS AND INFESTATIONS		
Upper respiratory tract infection	12 (14)	7 (8)
Urinary tract infection	5 (6)	4 (4)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS		
Back pain	7 (8)	5 (6)
NERVOUS SYSTEM DISORDERS		
Dizziness	8 (9)	3 (3)

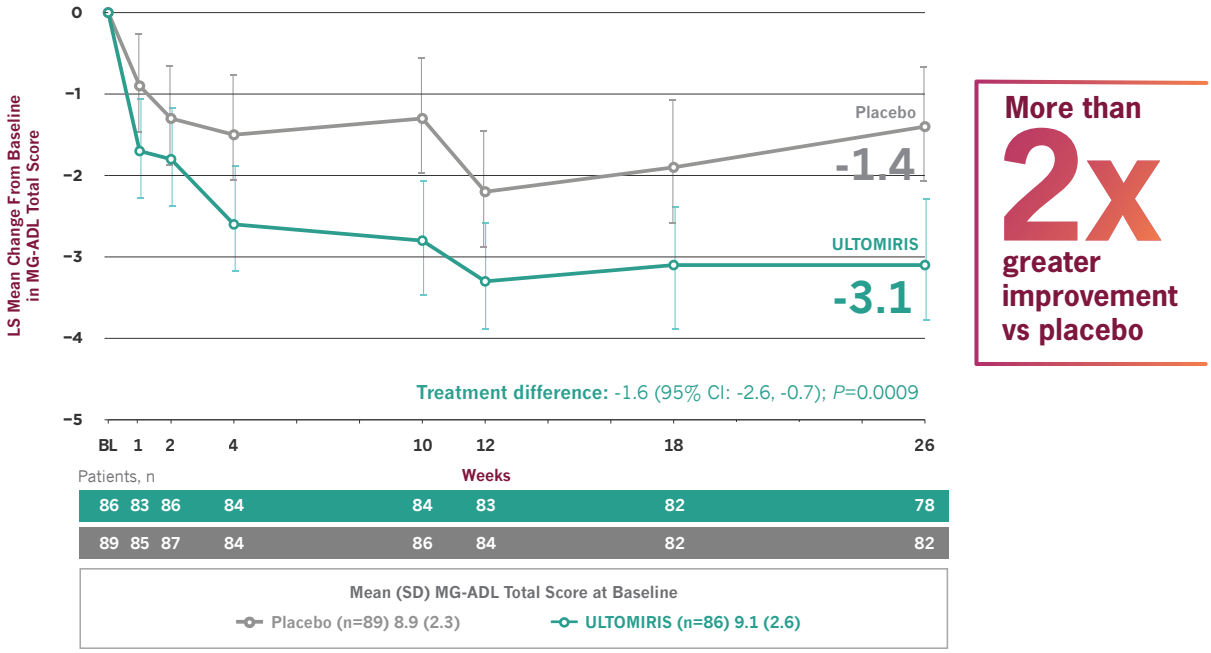
Proven to deliver improvement in activities of daily living at Week 26[1]

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

Among patients in the ULTOMIRIS treatment arm,

Improvements in MG-ADL total scores from baseline were observed within 1 week of treatment and were sustained through Week 26 of treatment.[1,17]

ULTOMIRIS demonstrated efficacy vs placebo at Week 26 (-3.1 vs -1.4, respectively [*P*=0.0009])[1,15]



More than 2x greater improvement vs placebo

CHAMPION-MG STUDY LIMITATIONS: Data shown are least-squares means and 95% confidence intervals (CIs), using a mixed model for repeated measures; 95% CIs were not adjusted for multiplicity.[1,15]

Time to response was part of the planned efficacy analysis, but the primary endpoint was at Week 26. Therefore, results should be interpreted with caution.[1,15]

Improvement in MG-ADL total score seen in CHAMPION-MG was observed through Week 60 in the OLE period[17]

- The OLE period began following Week 26, when all patients received ULTOMIRIS, and results were observed through Week 60[17]

CHAMPION-MG OLE STUDY LIMITATION: Results should be interpreted with caution since the study was designed to evaluate safety and lacked a control group.

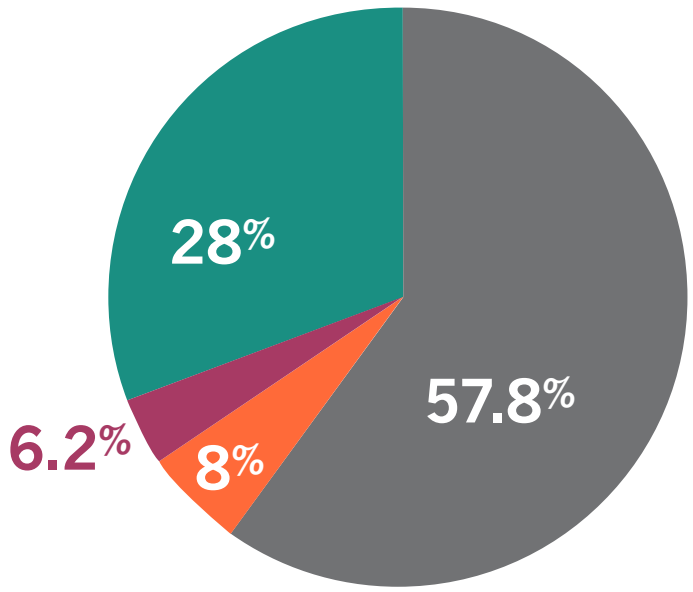
BL, baseline; LS, least squares; MG-ADL, Myasthenia Gravis Activities of Daily Living; OLE, open-label extension; SD, standard deviation.

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

ULTOMIRIS® is the first and only long-acting C5 inhibitor to report on corticosteroid use[1,17]

Advancing the legacy of complement inhibition, with corticosteroid use evaluated in patients receiving ULTOMIRIS in CHAMPION-MG OLE[17]

- In an interim analysis, 28% of patients reduced and 6.2% of patients stopped corticosteroid use after 34 weeks of the open-label extension (OLE) period (45 and 10 patients, respectively)[17,a-d]
- **Corticosteroid use continues to be examined in the ongoing OLE**[17]



- **Decreased corticosteroid use**
- **Increased corticosteroid use/ Added a corticosteroid**
- **Discontinued corticosteroids**
- **Corticosteroid use unchanged**

CHAMPION-MG OLE STUDY LIMITATION: Results should be interpreted with caution since the study was designed to evaluate safety and lacked a control group.

[a]Based on a prespecified interim analysis, N=161.[15]
[b]Dose changes were only allowed in the OLE period beginning after Week 26 of the RCP.[17]
[c]Data cutoff date of November 9, 2021.[15]
[d]Percentages based on all patients in the OLE, not just those on steroids.[15]

SELECT IMPORTANT SAFETY INFORMATION for ULTOMIRIS

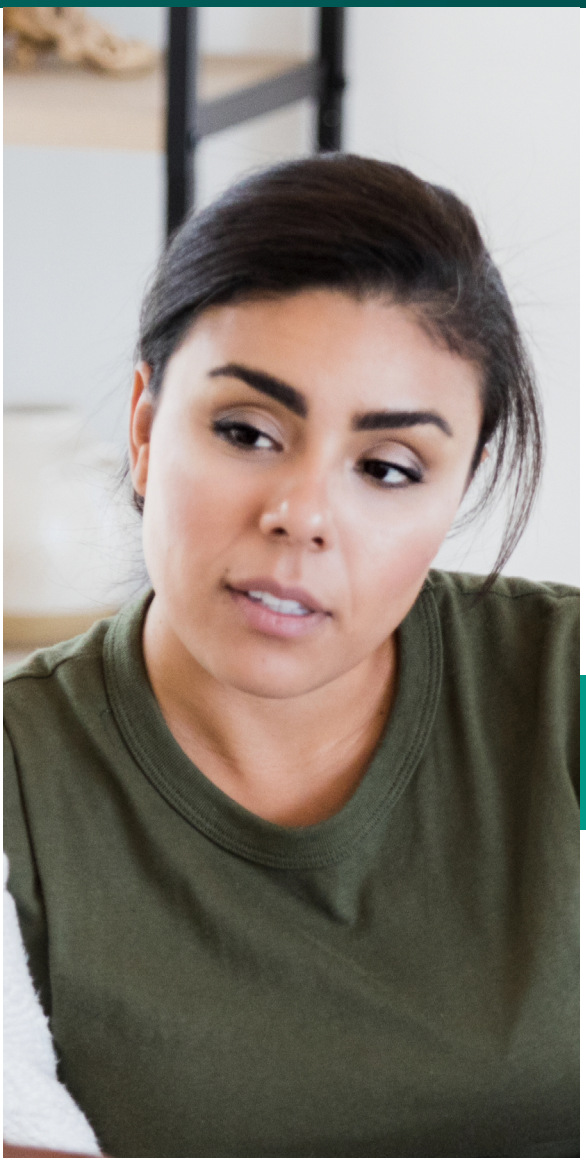
WARNINGS AND PRECAUTIONS, (continued)

Serious Meningococcal Infections, (continued)

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.

ULTOMIRIS may be an appropriate choice for Madison, a patient with gMG struggling with breakthrough symptoms[a]

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



Madison

Age: 32
Profession: Social worker
Length of Disease: 8 months; treatment initiated upon diagnosis
Location: Cleveland, Ohio

Current chief complaints

- Has an incomplete response to current therapies and is experiencing breakthrough symptoms of intermittent slurring of speech, increased shortness of breath upon exertion, and lower limb paresis

Madison and her physician are hoping to further decrease her dose of corticosteroids

[a]Patient case is fictitious and intended only for discussion about patient experiences. Patient case is not intended for diagnosis or treatment purposes.
gMG, generalized myasthenia gravis.

SELECT IMPORTANT SAFETY INFORMATION for ULTOMIRIS

WARNINGS AND PRECAUTIONS, (continued)

Serious Meningococcal Infections, (continued)

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.

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

IMPORTANT SAFETY INFORMATION FOR ULTOMIRIS®

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)*].

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

WARNINGS AND PRECAUTIONS, (continued)

Thromboembolic Event Management

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

Infusion-Related Reactions

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

ADVERSE REACTIONS

Most common adverse reactions in 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.

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.

ULTOMIRIS® is the first and only long-acting C5 inhibitor with data regarding corticosteroid use in gMG[1,19]

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

CHAMPION-MG

2x

More than 2x greater improvement in MG-ADL total score from baseline at Week 26 vs placebo (-3.1 vs -1.4, respectively [*P*=0.0009])[1,15,a]

Most common adverse reactions occurring in **≥10% of patients taking ULTOMIRIS** in CHAMPION-MG were diarrhea and upper respiratory tract infection[1]

CHAMPION-MG OLE

28% of patients decreased their daily dose of corticosteroids, with **6.2% discontinuing** corticosteroids altogether. Steroid-sparing data are still being collected past Week 60 of the CHAMPION-MG OLE trial[17,b-e]

8% initiated or increased use of corticosteroids in equal prominence

CHAMPION-MG OLE STUDY LIMITATION: Results should be interpreted with caution since the study was designed to evaluate safety and lacked a control group.

[a]Based on the MG-ADL, a categorical scale that assesses the impact on daily function of 8 signs or symptoms that are typically affected in gMG.[1]
[b]Based on an interim analysis, N=161.[15]
[c]Dose changes were only allowed in the OLE period beginning at Week 26.[17]
[d]Data cutoff date of November 9, 2021.[15]
[e]By Week 60, 8% of patients increased their daily dose of corticosteroids or added steroids to their treatment regimen. Percentage based on all patients in OLE, not just those on steroids.[17]

Consider prescribing ULTOMIRIS for your adult patients with gMG who may be concerned about their corticosteroid use

gMG, generalized myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; OLE, open-label extension.

1. ULTOMIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. **2.** Gilhus NE, et al. *Nat Rev Dis Primers.* 2019;5(1):30. **3.** Johnson S, et al. *Med Sci Monit.* 2021;27:e933296. **4.** Sanders DB, et al. *Neurology.* 2016;87(4):419-425. **5.** Hehir MK, et al. *Muscle Nerve.* 2020;61(6):767-772. **6.** Imai T, et al. *J Neurol Neurosurg Psychiatry.* 2018;89(5):513-517. **7.** Su S, et al. *Front Neurol.* 2022;13:816243. **8.** Benatar M, et al. *Muscle Nerve.* 2012;45(6):909-917. **9.** Kaminski HJ, et al. *Front Neurol.* 2022;13:886625. **10.** Nowak RJ, et al. *Front Neurol.* 2020;11:556104. **11.** SOLIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. **12.** Howard JF Jr, et al. *Lancet Neurol.* 2021;20(7):526-536. **13.** Muppidi S, et al. *Muscle Nerve.* 2019;60(1):14-24. **14.** Habib AA, et al. Poster presented at: the American Association of Neuromuscular & Electrodiagnostic Medicine Annual Myasthenia Gravis Foundation of American Scientific Session; September 21, 2022; Nashville, TN. **15.** Data on file. Alexion Pharmaceuticals, Inc. **16.** Safety and efficacy of eculizumab in refractory generalized myasthenia gravis (REGAIN study). ClinicalTrials.gov identifier: NCT01997229. Updated July 16, 2019. Accessed July 20, 2023. https://www.clinicaltrials.gov/study/NCT01997229 **17.** Meisel A, et al; CHAMPION MG Study Group. *J Neurol.* Published online April 27, 2023. doi:10.1007/s00415-023-11699-x **18.** Vu T, et al. *NEJM Evid.* 2022;1(5):I-22. **19.** Kulasekararaj AG, et al. *Blood.* 2019;133(6):540-549.

US/ULT-g/0509 V3 10/2024

ALEXION AstraZeneca Rare Disease

INDICATION

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

SELECT IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

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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.

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