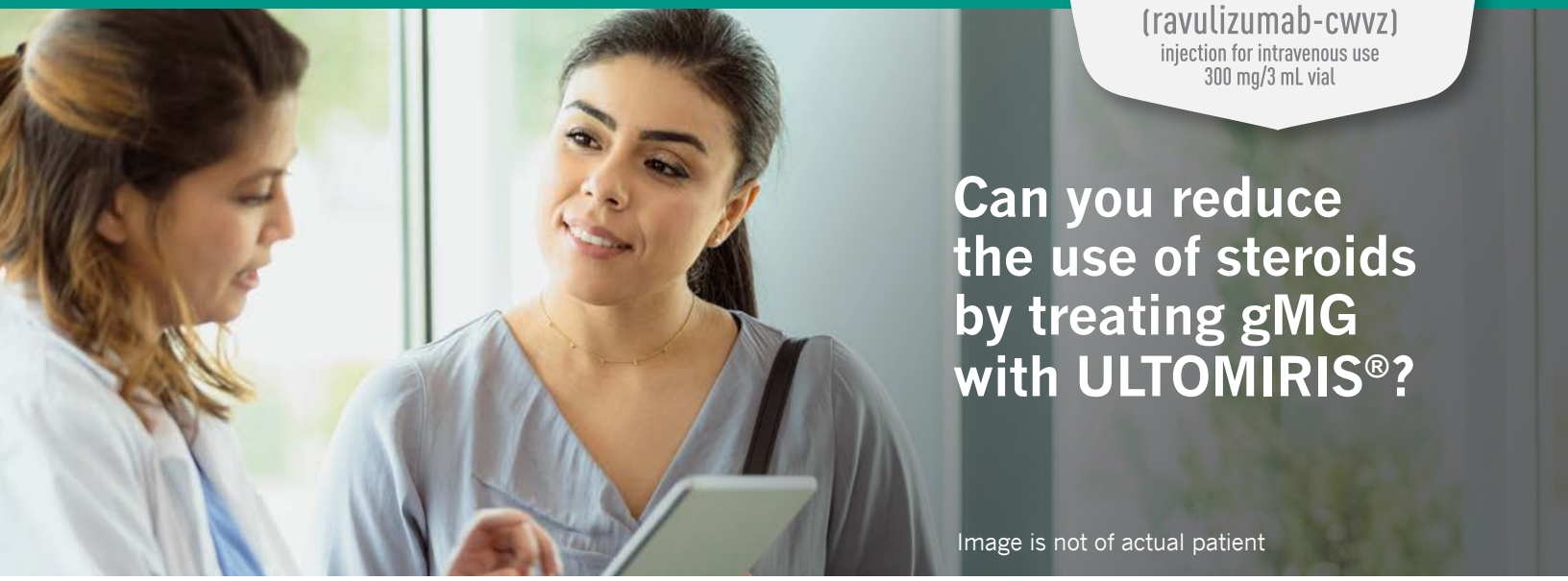
For your adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive[1]

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



Can you reduce the use of steroids by treating gMG with ULTOMIRIS®?

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

Life-threatening meningococcal infections/sepsis have occurred in patients treated with ULTOMIRIS. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.

- **Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.**
- **Immunize patients with meningococcal vaccines at least 2 weeks prior to administering the first dose of ULTOMIRIS, unless the risks of delaying ULTOMIRIS therapy outweigh the risk of developing a meningococcal infection. See *Warnings and Precautions* for additional guidance on the management of the risk of meningococcal infection.**
- **Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Monitor patients for early signs of 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 REMS.

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

INDICATION

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.

SELECT IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab)

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris and may become rapidly life-threatening or fatal if not recognized and treated early.

- **Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.**
- **Immunize patients with meningococcal vaccines at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection. (See *Serious Meningococcal Infections* for additional guidance on the management of the risk of meningococcal infection).**
- **Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Monitor patients for early signs of meningococcal infections and evaluate immediately if infection is suspected.**

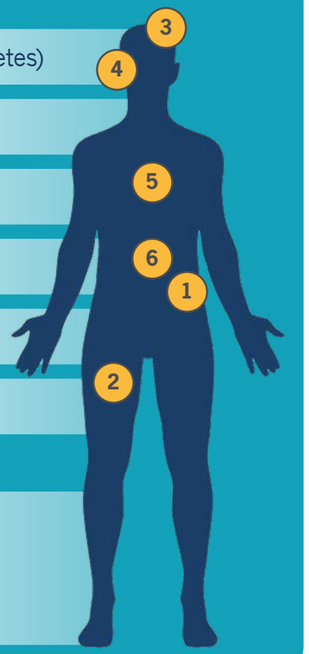
Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS, prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747) or at www.solirisrems.com.

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

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

Potential adverse reactions[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 systemic adverse events[3]

- Electrolyte imbalances
- Increased risk of infection
- Myopathy

Patients and HCPs share concerns about long-term exposure to immunosuppressive therapies (ISTs), including use of corticosteroids, but there is a fear of **risking a worsening of MG symptoms by reducing or discontinuing**[5]

It can take over a year to safely 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 avoid consequences of long-term corticosteroid use 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 corticosteroids and IST; increased corticosteroids to 80 mg per day due to incomplete response, then reduced to 40 mg per day due to corticosteroid-related adverse reactions but has been 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 experiencing corticosteroid-related adverse reactions including weight gain and increased acne
- Madison is concerned about the increased risk of comorbidities and serious adverse reactions associated with long-term corticosteroid use and ISTs

[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

- Patients with unresolved serious *Neisseria meningitidis* infection
- Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection

Warnings and Precautions

Serious Meningococcal Infections

Risk and Prevention

The use of Soliris increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis).

Vaccinate or revaccinate for meningococcal disease according to the most current ACIP recommendations for patients with complement deficiencies. Immunize patients without a history of meningococcal vaccination at least 2 weeks prior to receiving the first dose of Soliris. If Soliris must be initiated immediately in an unvaccinated patient, administer meningococcal vaccine(s) as soon as possible and provide 2 weeks of antibacterial drug prophylaxis. Discontinue Soliris in patients who are undergoing treatment for serious meningococcal infections.

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

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)

REMS

Prescribers must counsel patients about the risk of meningococcal infection, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccine(s).

Other Infections

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

Patients may have increased susceptibility to infections, especially with encapsulated bacteria. Additionally, *Aspergillus* infections have occurred in immunocompromised and neutropenic patients. Use caution when administering Soliris to patients with any systemic infection.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious 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]

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.

[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]

IST, immunosuppressive therapy.

SELECT IMPORTANT SAFETY INFORMATION for SOLIRIS

Warnings and Precautions, (continued)

Infusion-Related Reactions

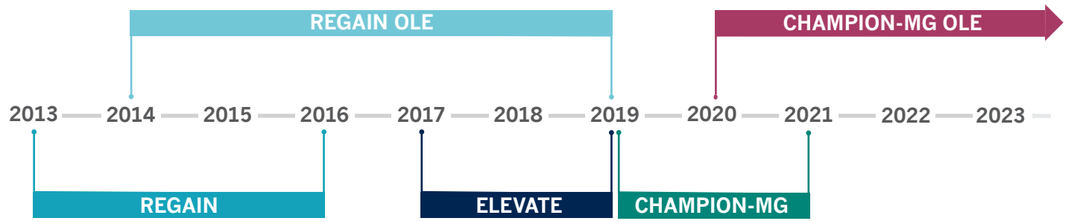
Administration of Soliris may result in infusion-related reactions, including anaphylaxis or other hypersensitivity reactions. Interrupt Soliris infusion and institute appropriate supportive measures if signs of cardiovascular instability or respiratory compromise occur.

Adverse Reactions

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

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

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

Contraindications

- Patients with unresolved serious *Neisseria meningitidis* infection
- Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection

Warnings and Precautions

Serious Meningococcal Infections

Risk and Prevention

The use of Soliris increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis).

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

SELECT IMPORTANT SAFETY INFORMATION for ULTOMIRIS

CONTRAINDICATIONS

- Patients with unresolved *Neisseria meningitidis* infection.
- Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying ULTOMIRIS treatment outweigh the risks of developing a meningococcal infection.

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

Life-threatening meningococcal infections have occurred in patients treated with ULTOMIRIS. The use of ULTOMIRIS increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis). Meningococcal disease due to any serogroup may occur.

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

INDICATION & IMPORTANT SAFETY INFORMATION FOR SOLIRIS®

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

INDICATION

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.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris and may become rapidly life-threatening or fatal if not recognized and treated early.

- **Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.**
- **Immunize patients with meningococcal vaccines at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection. (See *Serious Meningococcal Infections* for additional guidance on the management of the risk of meningococcal infection).**
- **Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Monitor patients for early signs of meningococcal infections and evaluate immediately if infection is suspected.**

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS, prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747) or at www.solirisrems.com.

Contraindications

- Patients with unresolved serious *Neisseria meningitidis* infection
- Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection

Warnings and Precautions

Serious Meningococcal Infections

Risk and Prevention

The use of Soliris increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis).

Vaccinate or revaccinate for meningococcal disease according to the most current ACIP recommendations for patients with complement deficiencies. Immunize patients without a history of meningococcal vaccination at least 2 weeks prior to receiving the first dose of Soliris. If Soliris must be initiated immediately in an unvaccinated patient, administer meningococcal vaccine(s) as soon as possible and provide 2 weeks of antibacterial drug prophylaxis. Discontinue Soliris in patients who are undergoing treatment for serious meningococcal infections.

Warnings and Precautions, (continued)

Serious Meningococcal Infections, (continued)

REMS

Prescribers must counsel patients about the risk of meningococcal infection, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccine(s).

Other Infections

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

Patients may have increased susceptibility to infections, especially with encapsulated bacteria. Additionally, *Aspergillus* infections have occurred in immunocompromised and neutropenic patients. Use caution when administering Soliris to patients with any systemic infection.

Infusion-Related Reactions

Administration of Soliris may result in infusion-related reactions, including anaphylaxis or other hypersensitivity reactions. 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%) is: musculoskeletal pain.

Please see accompanying full Prescribing Information for SOLIRIS, including Boxed WARNING regarding serious 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]

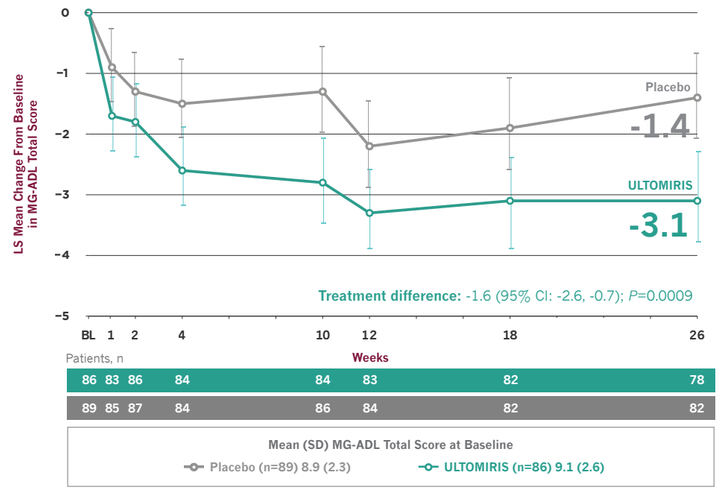
Adverse Reactions	ULTOMIRIS (n=86), n (%)	Placebo (n=89), n (%)
GASTROINTESTINAL DISORDERS		
Diarrhea	13 (15)	11 (12)
Abdominal pain	5 (6)	0
INFECTIONS AND INFESTATIONS		
Upper respiratory tract infection	12 (14)	7 (8)
Urinary tract infection	5 (6)	4 (4)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS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

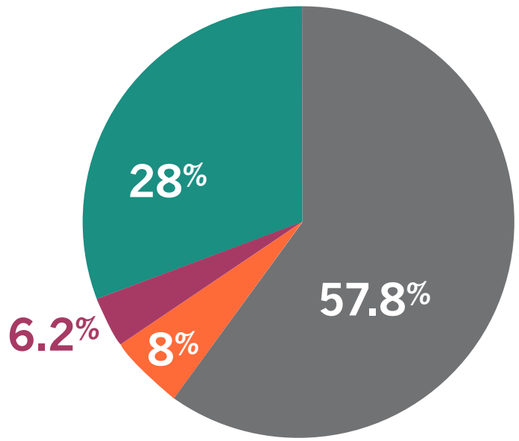
BL, baseline; LS, least squares; MG-ADL, Myasthenia Gravis Activities of Daily Living; OLE, open-label extension; SD, standard deviation.

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

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]



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

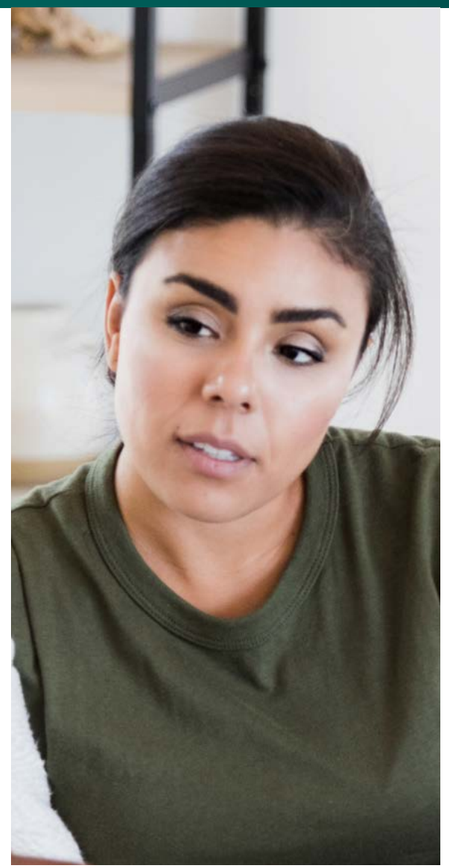
WARNINGS AND PRECAUTIONS, (continued)

Serious Meningococcal Infections, (continued)

Vaccinate or revaccinate for meningococcal disease according to the most current ACIP recommendations for patients with complement deficiencies. Immunize patients without history of meningococcal vaccination at least 2 weeks prior to the first dose of ULTOMIRIS. Patients who initiate ULTOMIRIS treatment less than 2 weeks after receiving meningococcal vaccine(s) must receive appropriate prophylactic antibiotics until 2 weeks after vaccination.

ULTOMIRIS may be an appropriate choice for Madison, a patient with gMG struggling with breakthrough symptoms and AEs from corticosteroids[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
- Is experiencing corticosteroid-related adverse events including weight gain and increased acne
- Is concerned about the increased risk of comorbidities and serious adverse events associated with long-term corticosteroid use and ISTs

[a]Patient case is fictitious and intended only for discussion about patient experiences. Patient case is not intended for diagnosis or treatment purposes.
AE, adverse event; gMG, generalized myasthenia gravis; IST, immunosuppressive therapy.

SELECT IMPORTANT SAFETY INFORMATION for ULTOMIRIS

WARNINGS AND PRECAUTIONS, (continued)

Serious Meningococcal Infections, (continued)

In clinical studies, 2 adult patients with gMG were treated with ULTOMIRIS less than 2 weeks after meningococcal vaccination. All of these patients received antibiotics for prophylaxis of meningococcal infection until at least 2 weeks after meningococcal vaccination. The benefits and risks of antibiotic prophylaxis for prevention of meningococcal infections in patients receiving ULTOMIRIS have not been established. Consider discontinuation of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection.

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

INDICATION & IMPORTANT SAFETY INFORMATION FOR ULTOMIRIS®

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

INDICATION

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

IMPORTANT SAFETY INFORMATION

WARNING:
SERIOUS MENINGOCOCCAL INFECTIONS

Life-threatening meningococcal infections/sepsis have occurred in patients treated with ULTOMIRIS. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.

- **Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.**
- **Immunize patients with meningococcal vaccines at least 2 weeks prior to administering the first dose of ULTOMIRIS, unless the risks of delaying ULTOMIRIS therapy outweigh the risk of developing a meningococcal infection. See *Warnings and Precautions* for additional guidance on the management of the risk of meningococcal infection.**
- **Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Monitor patients for early signs of 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 REMS.

CONTRAINDICATIONS

- Patients with unresolved *Neisseria meningitidis* infection.
- Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying ULTOMIRIS treatment outweigh the risks of developing a meningococcal infection.

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

Life-threatening meningococcal infections have occurred in patients treated with ULTOMIRIS. The use of ULTOMIRIS increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis). Meningococcal disease due to any serogroup may occur.

Vaccinate or revaccinate for meningococcal disease according to the most current ACIP recommendations for patients with complement deficiencies. Immunize patients without history of meningococcal vaccination at least 2 weeks prior to the first dose of ULTOMIRIS. Patients who initiate ULTOMIRIS treatment less than 2 weeks after receiving meningococcal vaccine(s) must receive appropriate prophylactic antibiotics until 2 weeks after vaccination.

In clinical studies, 2 adult patients with gMG were treated with ULTOMIRIS less than 2 weeks after meningococcal vaccination. All of these patients received antibiotics for prophylaxis of meningococcal infection until at least 2 weeks after meningococcal vaccination. The benefits and risks of antibiotic prophylaxis for prevention of meningococcal infections in patients receiving ULTOMIRIS have not been established. Consider discontinuation of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection.

ULTOMIRIS REMS

Due to the risk of meningococcal infections, ULTOMIRIS is available only through a restricted program under a REMS called ULTOMIRIS REMS.

Under the ULTOMIRIS REMS, prescribers must enroll in the program. Prescribers must counsel patients about the risk of meningococcal infection/sepsis, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccines.

Additional information on the REMS requirements is available at www.ultomirisrems.com or 1-888-765-4747.

WARNINGS AND PRECAUTIONS, (continued)

Other Infections

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*. If ULTOMIRIS is administered to patients with active systemic infections, monitor closely for worsening infection.

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

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

ADVERSE REACTIONS

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.

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

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]

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.

ALEXION AstraZeneca Rare Disease

US/ULT-g/0509 V1 09/2023

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

Life-threatening meningococcal infections/sepsis have occurred in patients treated with ULTOMIRIS. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.

- **Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.**
- **Immunize patients with meningococcal vaccines at least 2 weeks prior to administering the first dose of ULTOMIRIS, unless the risks of delaying ULTOMIRIS therapy outweigh the risk of developing a meningococcal infection. See *Warnings and Precautions* for additional guidance on the management of the risk of meningococcal infection.**
- **Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Monitor patients for early signs of 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 REMS.

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