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

Control the symptom journey ahead[1-4,a]

[a]Based on the MG-ADL, Myasthenia Gravis Activities of Daily Living, a categorical scale that assesses the impact on daily function of 8 signs or symptoms that are typically affected in gMG.[1]

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

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.

Corticosteroids are a widely prescribed first-line immunotherapy, but come with risks[5-7]

These risks come with long-term use. It's important to consider dose reduction and discontinuation when treating with corticosteroids.[5,6]

Adverse events associated with long-term corticosteroid use include[6]

1 Metabolic conditions (weight gain, hyperglycemia, diabetes)

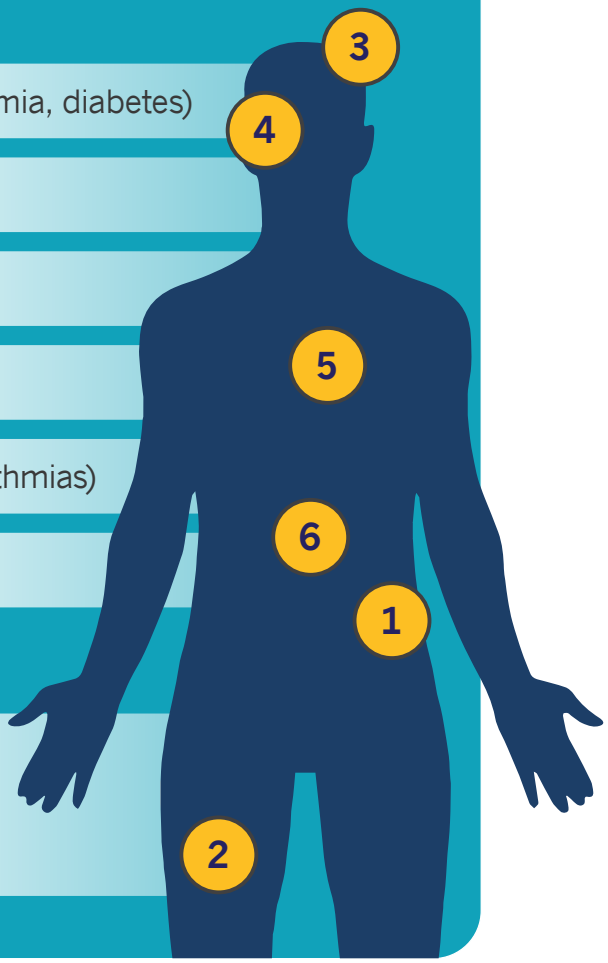
2 Osteoporosis

3 Neuropsychiatric symptoms

4 Ophthalmologic conditions

5 Cardiovascular issues (hypertension and arrhythmias)

6 Gastrointestinal issues



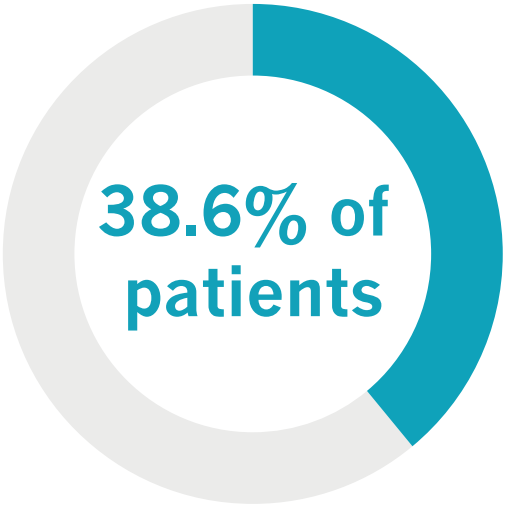
Additional systemic adverse events[6]

- Electrolyte imbalances
- Increased risk of infection
- Myopathy

Are conventional treatments such as corticosteroids working for your patients?

The consequences of incomplete symptom control and the risks inherent with long-term, high-dose steroids interfere with patients' treatment goals[8,9]

Even with the combination of corticosteroids and ISTs, not all patients experience an improvement in symptoms[10]



may experience MG-related hospitalizations, most striking within the first 2 years of disease onset.[8,a]

Under the threat of breakthrough symptoms, your patients with gMG need symptom control **as early as possible.**[8,9]

[a]This retrospective longitudinal cohort study evaluated 1149 adult patients with gMG living in England, using data recorded from 1997 to 2016.[8]

gMG, generalized myasthenia gravis; IST, immunosuppressive therapy; MG, myasthenia gravis.

In gMG, the complement cascade causes damage at the NMJ[11-13]

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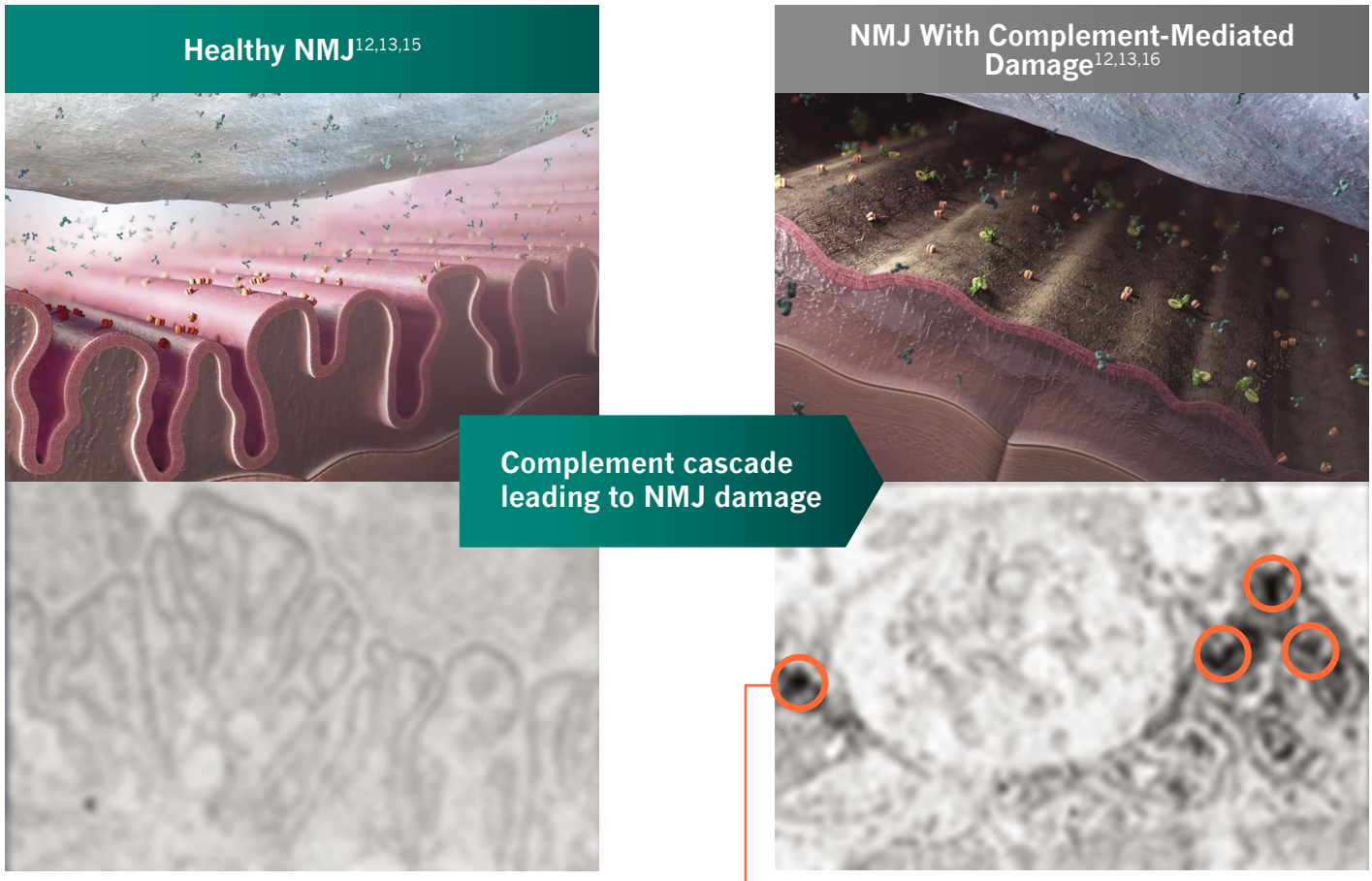
Alteration of folds in the muscle membrane reduces the efficiency of neuromuscular transmission[14]



Typical folds in the muscle membrane

Simplified membrane morphology

Circled areas indicate deposition of C9 (MAC component).

gMG, generalized myasthenia gravis; MAC, membrane attack complex; NMJ, neuromuscular junction.

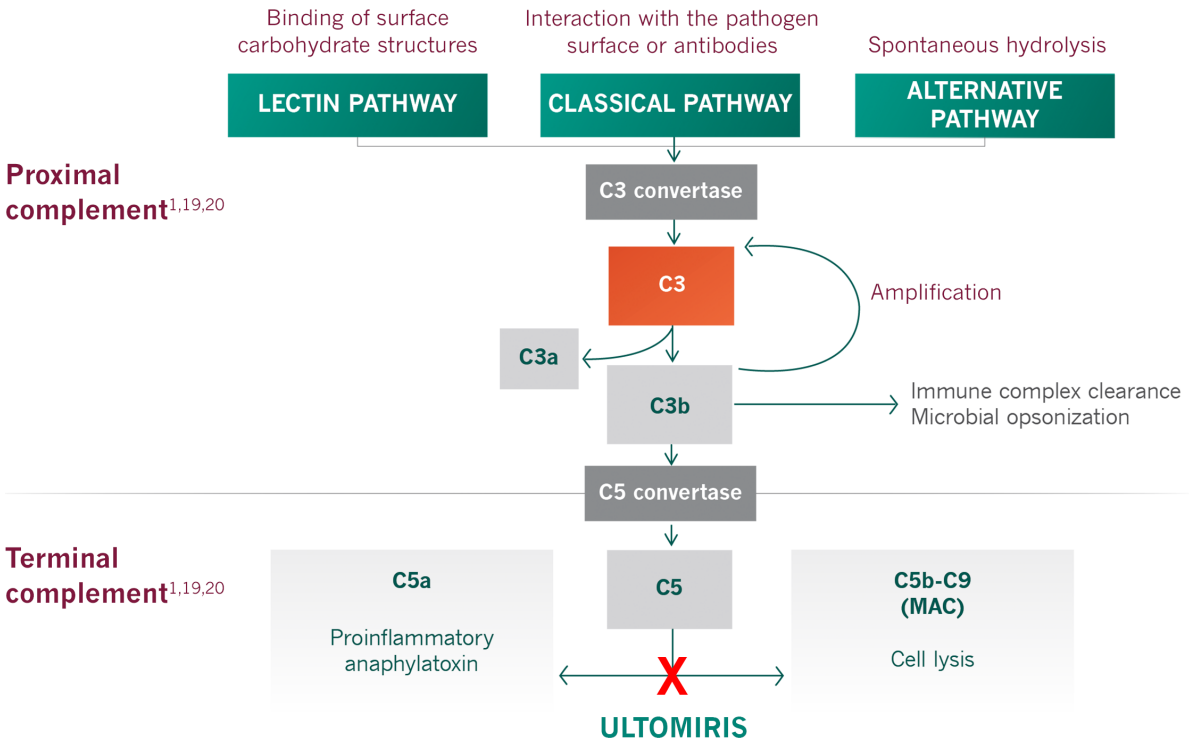
Left image: Reprinted from *Mayo Clin Proc*, 52(5), Engel AG, et al. 267-280. © 2009, with permission from Elsevier.
Right image: Sahashi K, et al. *J Neuropathol Exp Neurol*. 1980;39(2):160-172. © 1980 by permission of Oxford University Press.

SELECT IMPORTANT SAFETY INFORMATION, (continued)

CONTRAINDICATIONS

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

ULTOMIRIS® inhibits the complement protein C5—a key driver of damage to the NMJ in gMG[1,14]



The precise mechanism by which ULTOMIRIS exerts its therapeutic effect in gMG patients is not known.[1]

gMG, generalized myasthenia gravis; MAC, membrane attack complex; NMJ, neuromuscular junction.

SELECT IMPORTANT SAFETY INFORMATION, (continued)

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.

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.

Studied in one of the longest randomized clinical trials of a gMG treatment, in a broad population of patients[4,21,22]

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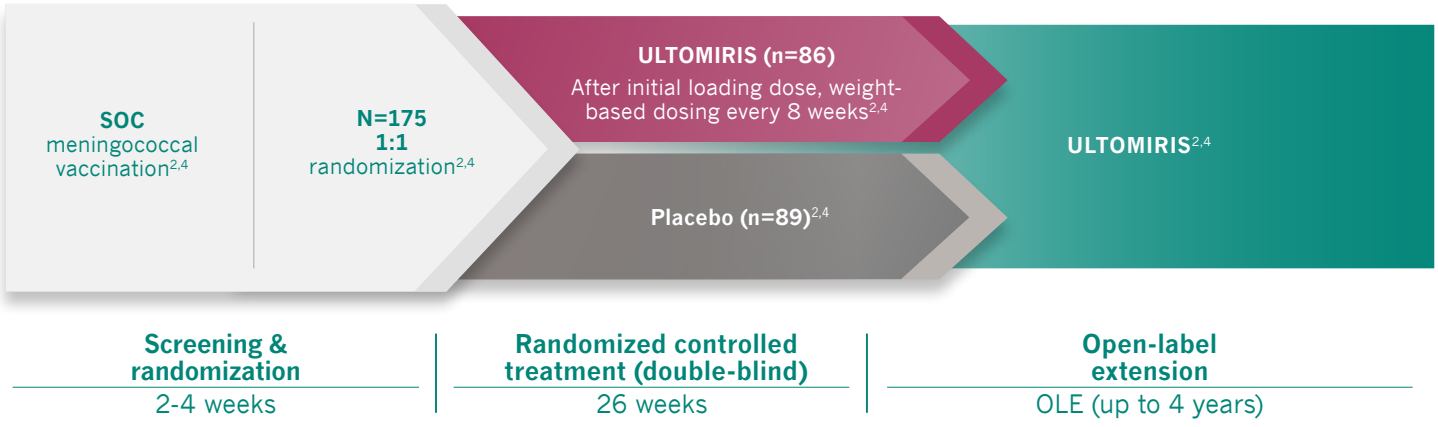
CHAMPION-MG was a randomized, double-blind, placebo-controlled trial with an open-label extension (OLE)

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.[1,2,4]



More than 90% of patients had MGFA class II or III gMG with mild or moderate weakness at baseline[1,21]

Key Inclusion Criteria[2]

Patients enrolled in this trial had to have:

- An MGFA clinical classification of class II through IV
- gMG (diagnosed for at least 6 months) with a positive serologic test for anti-AChR antibodies
- MG-ADL total score ≥6
- Vaccinations against meningococcal infections

Patients on concomitant ISTs were required to be on stable doses throughout the primary treatment period.

AChR, acetylcholine receptor; gMG, generalized myasthenia gravis; IST, immunosuppressive therapy; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; SOC, standard of care.

SELECT IMPORTANT SAFETY INFORMATION, (continued)
WARNINGS AND PRECAUTIONS, (continued)
Serious Meningococcal Infections, (continued)

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.

Baseline characteristics of patients in the CHAMPION-MG study[1,2]

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CHAMPION-MG baseline characteristics[1,2]

Baseline Characteristics	ULTOMIRIS (n=86)	Placebo (n=89)
Mean age at first infusion (years)	**58**	**53**
Mean age at gMG diagnosis (years)	**49**	**44**
Mean time from diagnosis to study participation (years [range])	**10** (0.5-39.5)	**10** (0.5-36.1)
Sex, male (%)	**49**	**49**
Sex, female (%)	**51**	**51**
Race, White (%)	**78**	**69**
Race, Asian (%)	**17**	**18**
Race, Black or African American (%)	**2**	**5**
Race, not reported (%)	**2**	**6**
Mean baseline weight, kg (lb)	**92** (201.9)	**91** (200.4)

Key Exclusion Criteria[2]

Patients were excluded from this trial if they had:

- Any active or untreated thymoma or history of thymic carcinoma or thymic malignancy
- History of thymectomy, thymomectomy, or any thymic surgery within 12 months prior to screening
- Clinical features consistent with myasthenic crisis/exacerbation or clinical deterioration at the time of the screening visit or at any time prior to randomization
- Therapies that were used within the following timeframes:
  -IVIg or PE within 4 weeks prior to randomization (Day 1)
  -Rituximab within 6 months prior to screening
  -Any previous treatment with complement inhibitors

gMG, generalized myasthenia gravis; IVIg, intravenous immunoglobulin; PE, plasma exchange.

SELECT IMPORTANT SAFETY INFORMATION, (continued)
WARNINGS AND PRECAUTIONS, (continued)
Serious Meningococcal Infections, (continued)

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.

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.

The majority of symptomatic patients were already being treated with an IST[21]

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In the randomized, double-blind, placebo-controlled CHAMPION-MG trial, approximately 90% of patients were taking an IST at baseline across both treatment arms[1,2,21]

- 47% of patients were taking 2 or more ISTs[2]

43% of patients received IVIg in the 2 years prior to trial screening[2]

Over 80% of patients were receiving acetylcholinesterase inhibitors, 70% were receiving corticosteroids, and 68% were receiving non-steroidal immunosuppressants at study entry[1]

Patients on concomitant medications to treat gMG were permitted to continue on therapy at stable doses throughout the course of the study, and those medications could be adjusted as necessary during the open-label extension (OLE).[2]

gMG, generalized myasthenia gravis; IST, immunosuppressive therapy; IVIg, intravenous immunoglobulin.

SELECT IMPORTANT SAFETY INFORMATION, (continued)
WARNINGS AND PRECAUTIONS, (continued)
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.

Multiple measures of gMG were studied in CHAMPION-MG[1,2]

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Primary endpoint[1]

- Change from baseline to Week 26 in the **Myasthenia Gravis Activities of Daily Living** (MG-ADL) total score[a]

Secondary endpoints[b,c]

- Change from baseline to Week 26 in the **Quantitative Myasthenia Gravis** (QMG) total score[1,d]
- The proportion of patients with **improvements of at least 5 points** in their **QMG** total score[1]
- Change in **revised Myasthenia Gravis Quality of Life 15-item scale** (MG-QoL15r)[2]
- Change in **Neurological Quality of Life** (Neuro-QoL) **Fatigue** assessment[2]
- The proportion of patients with **improvements of at least 3 points** in their **MG-ADL** total score[1]

[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]

[b]Hierarchical testing proceeded from the first to the fifth endpoint, and if statistical significance was not achieved (*P*-value >0.05), then subsequent endpoints were not considered statistically significant.[2]

[c]All secondary endpoints are at Week 26.[1]

[d]The QMG is a 13-item categorical scale assessing muscle weakness. Each item is assessed on a 4-point scale where a score of 0 represents no weakness and a score of 3 represents severe weakness. The total score ranges from 0 to 39, where higher scores indicate more severe impairment.[1]

gMG, generalized myasthenia gravis.

SELECT IMPORTANT SAFETY INFORMATION, (continued)
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 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.

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.

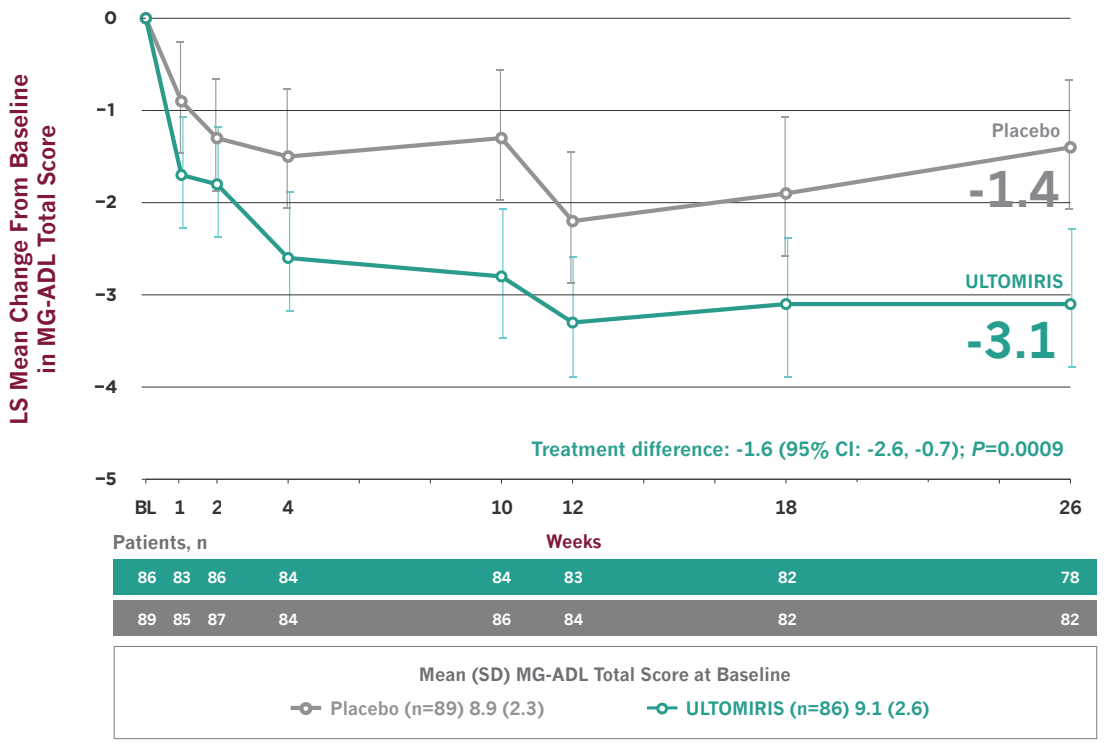
Proven to deliver improvement in activities of daily living[1,4]

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]

ULTOMIRIS demonstrated efficacy vs placebo at Week 26 (-3.1 vs -1.4, respectively [*P*=0.0009])[1,2]



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.[1,2]

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.

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

SELECT IMPORTANT SAFETY INFORMATION, (continued)

WARNINGS AND PRECAUTIONS, (continued)

Other Infections

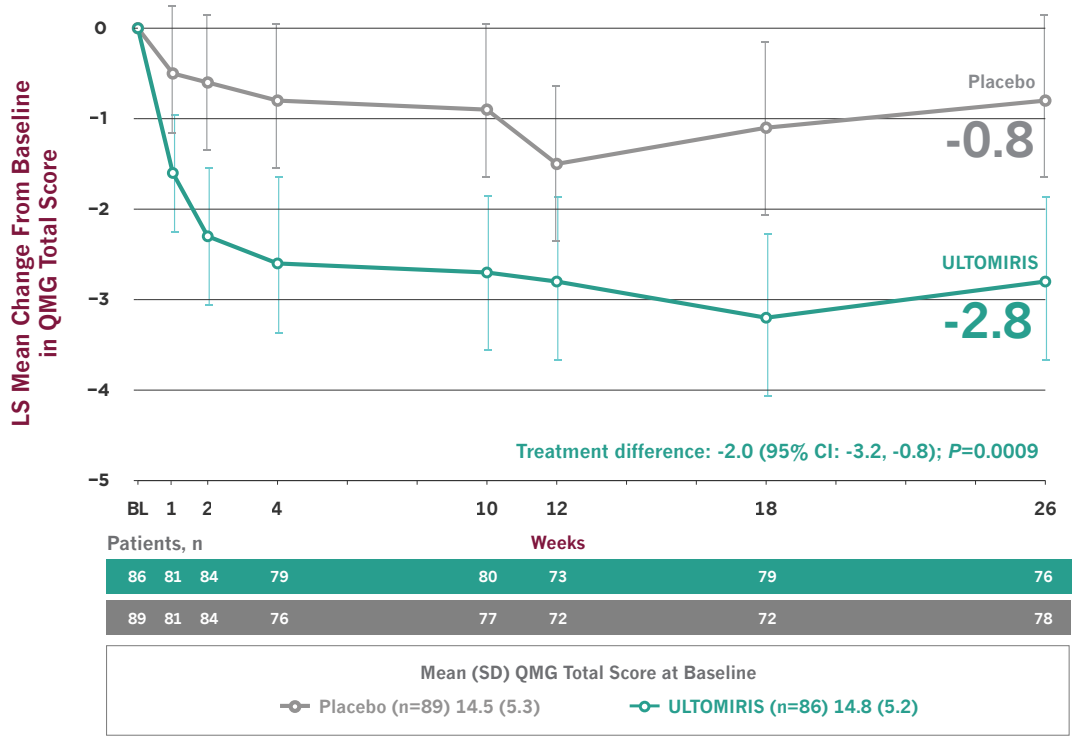
Serious infections with *Neisseria* species (other than *Neisseria meningitidis*), including disseminated gonococcal infections, have been reported.

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.

Improvement in muscle strength demonstrated by QMG total score from baseline through Week 26[1,2]

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

Improvement was shown in the key secondary endpoint, patients' QMG total score through Week 26 (-2.8 points for ULTOMIRIS® vs -0.8 points for placebo [*P*=0.0009])[1,2]



3.5x greater improvement vs placebo[1]

Improvements in QMG scores were seen across the ocular, bulbar, and limb domain scores from baseline to Week 26.[2]

- **CHAMPION-MG STUDY LIMITATION:** Change from baseline in QMG individual symptom domains was an exploratory endpoint. Efficacy or clinical significance should be interpreted with caution

BL, baseline; CI, confidence interval; LS, least squares; QMG, Quantitative Myasthenia Gravis; SD, standard deviation.

SELECT IMPORTANT SAFETY INFORMATION, (continued)
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.

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.

Improvement in MG-ADL total score seen in CHAMPION-MG was observed through Week 60 in the open-label extension (OLE) period[4]

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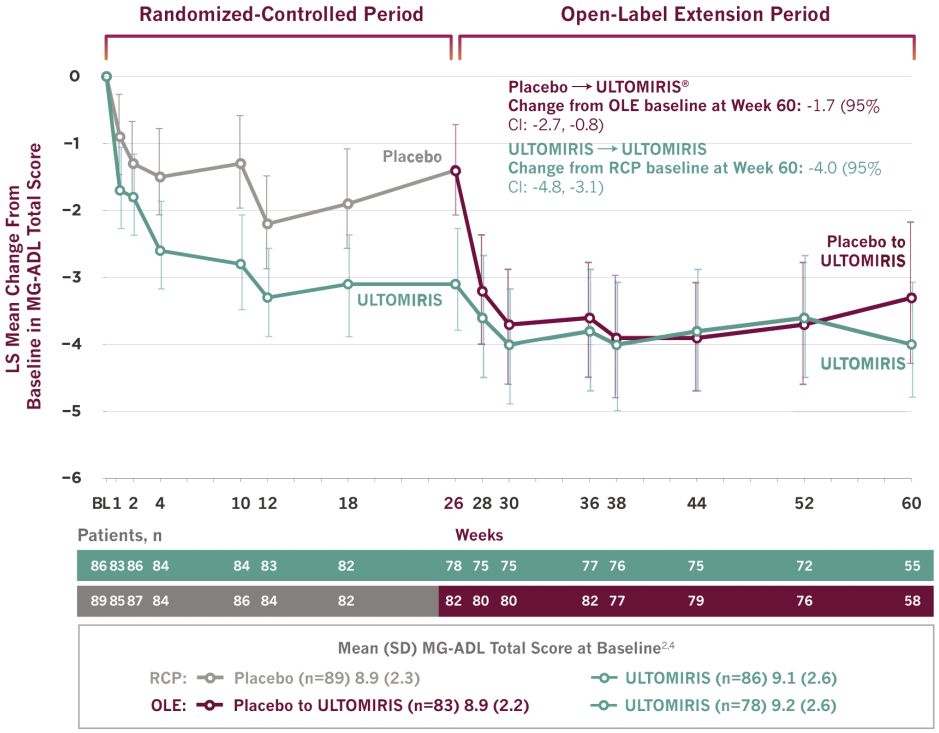
MG-ADL total score observed through Week 60 in the OLE period[4]



The OLE period began following Week 26, when all patients received ULTOMIRIS®, and results were observed through Week 60.[4]

CHAMPION-MG OLE STUDY LIMITATION: Any inference of efficacy or clinical significance should be interpreted with caution since the study was designed to evaluate safety and lacked a control group.

BL, baseline; CI, confidence interval; LS, least squares; MG-ADL, Myasthenia Gravis Activities of Daily Living; RCP, randomized-controlled period; SD, standard deviation.

SELECT IMPORTANT SAFETY INFORMATION, (continued)

WARNINGS AND PRECAUTIONS, (continued)

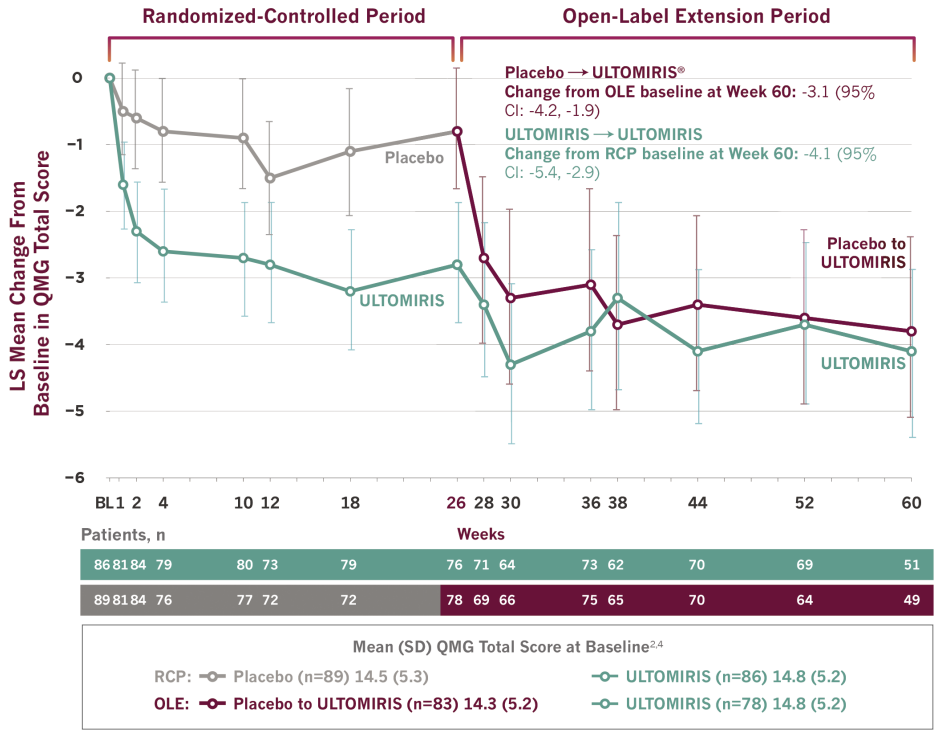
Infusion-Related Reactions

Intravenous administration may result in systemic infusion-related reactions, including anaphylaxis and hypersensitivity reactions. In clinical trials, infusion-related reactions occurred in approximately 1 to 7% of patients treated with ULTOMIRIS.

Improvement in QMG total score seen in CHAMPION-MG was observed through Week 60 in the open-label extension (OLE) period[4]

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

QMG total score observed through Week 60 in the OLE period[4]



The OLE period began following Week 26, when all patients received ULTOMIRIS®, and results were observed through Week 60.[4]

CHAMPION-MG OLE STUDY LIMITATION: Any inference of efficacy or clinical significance should be interpreted with caution since the study was designed to evaluate safety and lacked a control group.

BL, baseline; CI, confidence interval; LS, least squares; QMG, Quantitative Myasthenia Gravis; RCP, randomized-controlled period; SD, standard deviation.

SELECT IMPORTANT SAFETY INFORMATION, (continued)

WARNINGS AND PRECAUTIONS, (continued)

Infusion-Related Reactions, (continued)

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

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.

Improvement in scores across a range of secondary endpoints

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Endpoints related to quality of life[2]

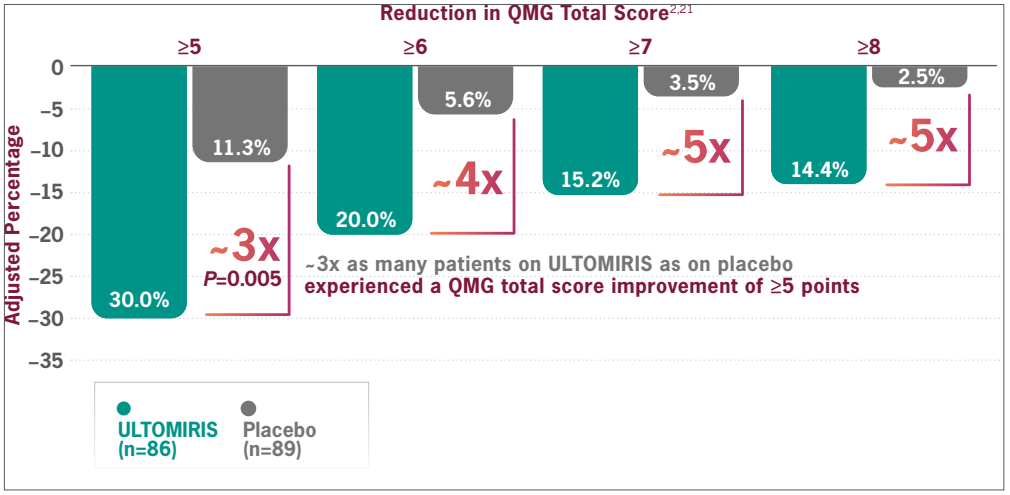
- Change from baseline to Week 26 in MG-QoL15r: -3.3 for ULTOMIRIS® and -1.6 for placebo
- Change from baseline to Week 26 in the Neuro-QoL Fatigue score: -7.0 for ULTOMIRIS and -4.8 for placebo
- MG-QoL15r didn't reach statistical significance. Due to hierarchical testing, Neuro-QoL wasn't considered for statistical significance

Observed MG-ADL total score changes with ULTOMIRIS[1,2]

- More patients taking ULTOMIRIS achieved a ≥3-point improvement in MG-ADL total score vs placebo
- 57% of patients taking ULTOMIRIS had a ≥3-point improvement in MG-ADL total score vs 34% of patients taking placebo

Observed improvements in QMG total score at Week 26[1]

Patients treated with ULTOMIRIS were more likely to experience a larger improvement in QMG total score[1]



The proportion of patients taking ULTOMIRIS who achieved a ≥5-point improvement in QMG total score was greater than the proportion of patients taking placebo.[1]

30% of patients taking ULTOMIRIS had a ≥5-point improvement in QMG total score vs 11.3% taking placebo (*P*=0.005).[1]

MG-ADL, Myasthenia Gravis Activities of Daily Living; MG-QoL15r, Myasthenia Gravis Quality of Life 15-item scale; Neuro-QoL, Neurological Quality of Life; QMG, Quantitative Myasthenia Gravis.

SELECT IMPORTANT SAFETY INFORMATION, (continued)
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.

Improvements observed in a range of exploratory endpoints and post hoc analyses

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Post hoc analyses

- MG-ADL total score reduction with earlier use[23]
- Reduction in clinical deterioration[4]
- Cumulative MG-ADL response rates[24]

Exploratory endpoint

- Minimal manifestation status[2]

The efficacy or clinical significance of exploratory endpoints and post hoc analyses should be interpreted with caution.

In an interim analysis, 28% of patients reduced and 6.2% of patients stopped steroid use during the 34-week OLE period (45 and 10 patients, respectively).[4,a,b,c,d]

CHAMPION-MG OLE STUDY LIMITATION: Any inference of efficacy or clinical significance 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.[2]
[b]Dose changes were only allowed in the OLE period beginning after Week 26 of the RCP.[2]
[c]Data cutoff date of November 9, 2021.[2]
[d]By Week 60, 8% of patients increased their daily dose of corticosteroids or added steroids to their treatment regimen. Percentages based on all patients in OLE, not just those on steroids.[4]

MG-ADL, Myasthenia Gravis Activities of Daily Living; OLE, open-label extension; RCP, randomized-controlled period.

SELECT IMPORTANT SAFETY INFORMATION, (continued)
ADVERSE REACTIONS, (continued)
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.

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.

MG-ADL total score reduction with earlier use[23]

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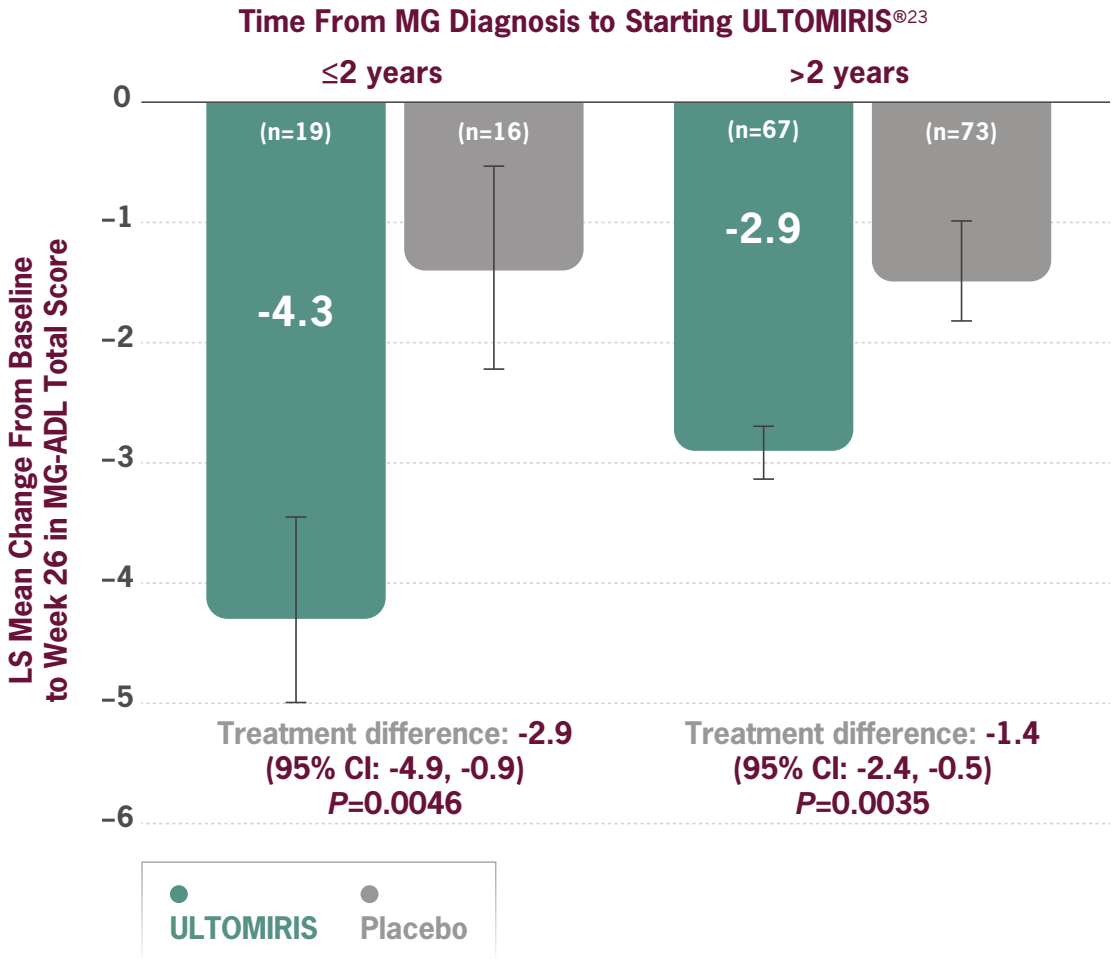

Patients who started ULTOMIRIS within 2 years of gMG diagnosis experienced a 4.3-point reduction in MG-ADL total scores from baseline, while patients who started after 2 years experienced a 2.9-point reduction.[23,a]

CHAMPION-MG STUDY LIMITATION: Change in MG-ADL total score reduction with earlier use was not a prespecified endpoint. Efficacy or clinical significance should be interpreted with caution.

[a]In a post hoc analysis of 175 patients at Week 26.[23]

CI, confidence interval; gMG, generalized myasthenia gravis; LS, least squares; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living.

SELECT IMPORTANT SAFETY INFORMATION, (continued)

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.

Baseline demographics and clinical characteristics by time from MG diagnosis[23]

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Characteristic	≤2 years from MG diagnosis			>2 years from MG diagnosis		
	ULTOMIRIS® (n=19)	Placebo (n=16)	All patients (n=35)	ULTOMIRIS (n=67)	Placebo (n=73)	All patients (n=140)
Female sex, n (%)	5 (26.3)	6 (37.5)	11 (31.4)	39 (58.2)	39 (53.4)	78 (55.7)
Age at first trial infusion, years, mean±SD	62.9±11.97	58.6±13.46	60.9±12.67	56.6±14.08	52.1±16.42	54.3±15.45
Age at MG diagnosis, years, mean±SD	62.0±11.82	57.7±13.47	60.0±12.60	44.8±18.41	40.7±18.78	42.6±18.65
Baseline MG-ADL score, mean±SD	8.8±1.74	9.8±2.51	9.3±2.15	9.2±2.83	8.8±2.22	9.0±2.53
Baseline QMG score, mean±SD	13.5±4.57	13.7±5.65	13.6±5.02	15.2±5.34	14.6±5.20	14.9±5.26
Baseline MGFA classification, n (%)						
Class II	9 (47.4)	12 (75.0)	21 (60.0)	30 (44.8)	27 (37.0)	57 (40.7)
Class III	10 (52.6)	4 (25.0)	14 (40.0)	31 (46.3)	41 (56.2)	72 (51.4)
Class IV	0	0	0	6 (9.0)	5 (6.8)	11 (7.9)
Use of any ISTs[a] at baseline, n (%)	18 (94.7)	14 (87.5)	32 (91.4)	58 (86.6)	67 (91.8)	125 (89.3)
Corticosteroids only	8 (42.1)	5 (31.3)	13 (37.1)	12 (17.9)	13 (17.8)	25 (17.9)
One NSIST only	5 (26.3)	1 (6.3)	6 (17.1)	15 (22.4)	15 (20.5)	30 (21.4)
Corticosteroids + one NSIST	5 (26.3)	8 (50.0)	13 (37.1)	31 (46.3)	39 (53.4)	70 (50.0)

[a]Including corticosteroids; no patients were being treated with >2 ISTs and no patients were being treated with >1 NSIST.[23]

IST, immunosuppressive therapy; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NSIST, nonsteroidal immunosuppressive therapy; QMG, Quantitative Myasthenia Gravis; SD, standard deviation.

SELECT IMPORTANT SAFETY INFORMATION, (continued)

DRUG INTERACTIONS, (continued)

Neonatal Fc Receptor Blockers

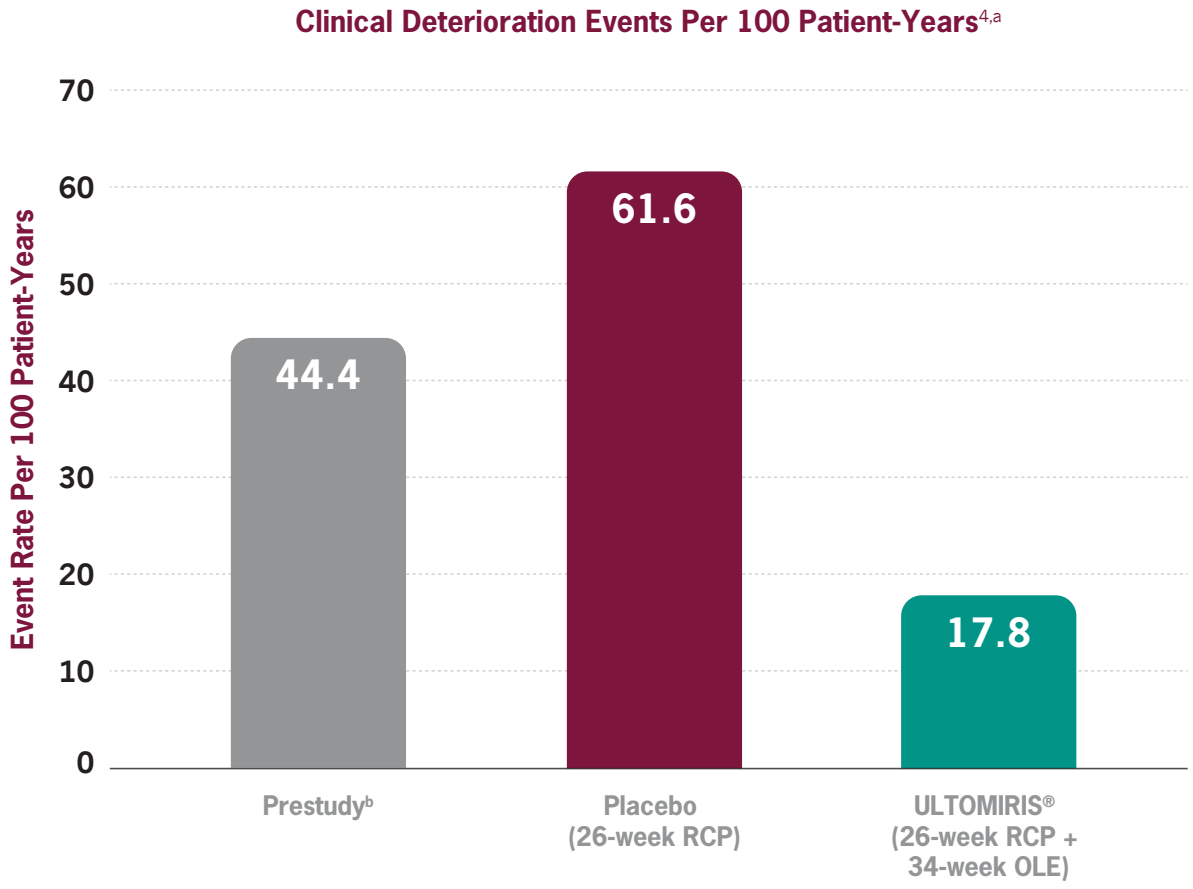
Concomitant use of ULTOMIRIS with neonatal Fc receptor (FcRn) blockers (e.g., efgartigimod) may lower systemic exposures and reduce effectiveness of ULTOMIRIS. Closely monitor for reduced effectiveness of ULTOMIRIS.

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

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

Reduction in clinical deterioration events[4]

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



Patients receiving ULTOMIRIS experienced clinical deteriorations at an event rate of 17.8 events per 100 patient-years vs 61.6 events per 100 patient-years in patients receiving placebo.[4,c]

CHAMPION-MG STUDY LIMITATION: Clinical deterioration was not a prespecified endpoint. Efficacy or clinical significance should be interpreted with caution.

[a]Clinical deterioration was defined as myasthenic crisis, need for rescue therapy, or significant symptom worsening on any MG-ADL item, other than double vision or eyelid droop.[4]

[b]1-year prestudy period, events reported by investigators. Patients may have been on other medications to treat generalized myasthenia gravis during this period.[4]

[c]ULTOMIRIS event rate is based on combined RCP and OLE data. Placebo event rate is based on RCP data only.[4]

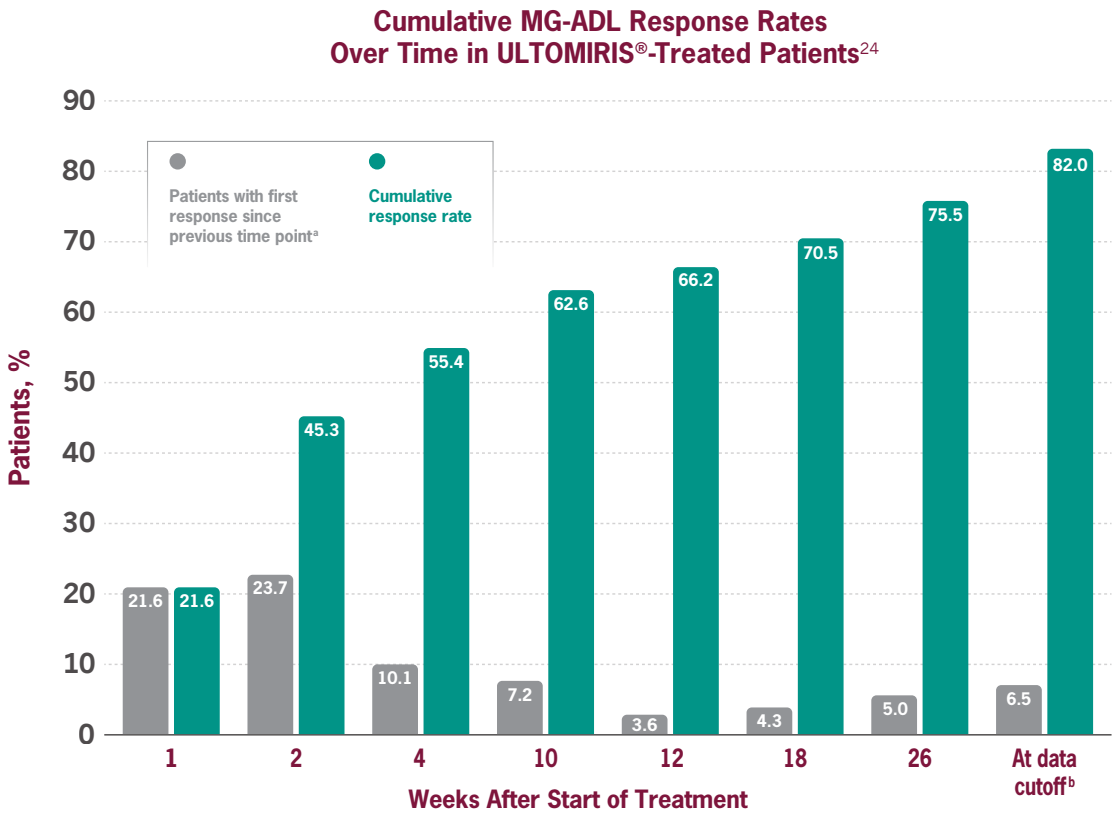
MG-ADL, Myasthenia Gravis Activities of Daily Living; OLE, open-label extension; RCP, randomized-controlled period.

SELECT IMPORTANT SAFETY INFORMATION, (continued)

CONTRAINDICATIONS

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

Cumulative MG-ADL response[24]



At Week 60, 82% of patients treated with ULTOMIRIS experienced a 3-point improvement in MG-ADL total score from baseline.[24,a,b,c]

CHAMPION-MG STUDY LIMITATION: Cumulative MG-ADL response was not a prespecified endpoint. Efficacy or clinical significance should be interpreted with caution.

[a]n=139 at data cutoff.[24]

[b]Date of data cutoff: November 9, 2021.[2]

[c]Response defined as improvement from baseline in MG-ADL total score ≥3 points.[24]

MG-ADL, Myasthenia Gravis Activities of Daily Living.

SELECT IMPORTANT SAFETY INFORMATION, (continued)

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.

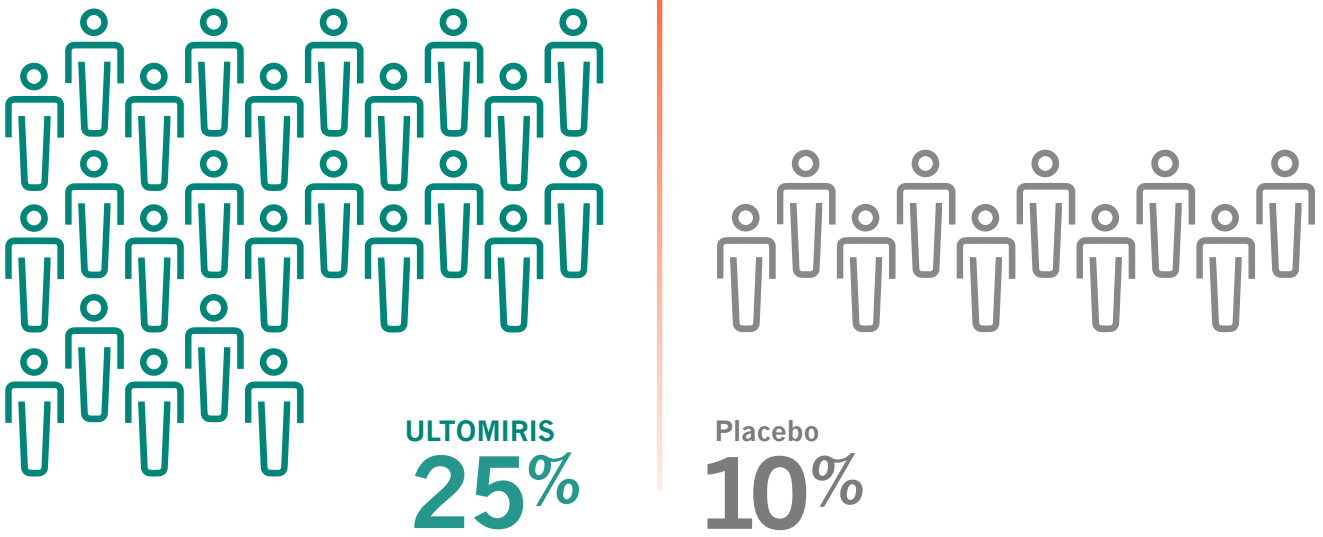
Revaccinate patients in accordance with ACIP recommendations considering the duration of ULTOMIRIS therapy. Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information.

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.

MGFA post-intervention status: minimal manifestation observed at Week 26[2]

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

1 in 4 patients treated with ULTOMIRIS® achieved minimal manifestation status vs 1 in 10 on placebo[2]



Minimal manifestation status is achieved when a patient has no symptoms of functional limitations from MG but has some weakness on examination of some muscles. It's another way to assess a patient's symptoms after treatment initiation.[25,a,b]

Patients reaching minimal manifestation status may be better able to perform everyday activities.[25]

CHAMPION-MG STUDY LIMITATION: Minimal manifestation was an exploratory endpoint. Any inference of efficacy should be interpreted with caution.[2]

[a]Per MGFA post-intervention status.[25]

[b]This class recognizes that some patients who otherwise meet the definition of pharmacologic remission do have weakness that is only detectable by careful examination.[25]

MG, myasthenia gravis; MGFA, Myasthenia Gravis Foundation of America.

SELECT IMPORTANT SAFETY INFORMATION, (continued)

WARNINGS AND PRECAUTIONS, (continued)

Serious Meningococcal Infections, (continued)

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.

All images depict hypothetical patients.

Safety evaluated for 26 weeks in CHAMPION-MG[1,2]

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

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)

- Serious adverse reactions were reported in 20 (23%) patients with gMG receiving ULTOMIRIS and in 14 (16%) patients receiving placebo[1]
- 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[1]
- 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[1]
- The most frequent adverse reactions occurring in ≥10% of patients taking ULTOMIRIS were diarrhea and upper respiratory tract infection[1]

ULTOMIRIS has[1,2]:
- 5+ years of postmarketing experience
- 12,300+ patient-years of exposure across 4 rare, complement-mediated diseases

gMG, generalized myasthenia gravis.

SELECT IMPORTANT SAFETY INFORMATION, (continued)
WARNINGS AND PRECAUTIONS, (continued)
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.

Safety was also evaluated in an open-label extension study[4]

Adverse reactions reported in >5% of patients treated with ULTOMIRIS® during the randomized-controlled period or the open-label extension period up to Week 60[4]

Adverse Reactions	ULTOMIRIS (n=169),[a] n (%)
INFECTIONS AND INFESTATIONS	
Nasopharyngitis	15 (8.9)
Urinary tract infection	15 (8.9)
COVID-19	9 (5.3)
Upper respiratory tract infection	9 (5.3)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	
Fatigue	16 (9.5)
Dizziness	14 (8.3)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	
Back pain	16 (9.5)
Arthralgia	15 (8.9)
NERVOUS SYSTEM DISORDERS	
Headache	28 (16.6)
GASTROINTESTINAL DISORDERS	
Abdominal pain	9 (5.3)
Diarrhea	23 (13.6)
Nausea	16 (9.5)

[a]Includes data available for all patients who received ≥1 dose of ULTOMIRIS in the randomized-controlled period or the open-label extension period, up to Week 60 at data cutoff (November 9, 2021).[4]

SELECT IMPORTANT SAFETY INFORMATION, (continued)
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 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.

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.

Meningococcal vaccination is part of a risk-mitigation strategy that takes into account how C5 inhibitors work[1,26]

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

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, per the current Advisory Committee on Immunization Practices (ACIP) recommendations for patients receiving a complement inhibitor.[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.[27]
- Revaccinate patients in accordance with ACIP recommendations considering the duration of ULTOMIRIS therapy.[1,a]

Vaccine	Primary Vaccination	Booster Vaccination
MenACWY (Menveo, MenQuadfi®)[28,29]	**2 doses** at least 8 weeks apart	1 dose every 5 years, if risk remains
+		
MenB-4C[b] (Bexsero)[28,29]	**2 doses** at least 1 month apart	1 dose 1 year following completion of primary series and every 2 to 3 years, if risk remains
OR		
MenB-FHbp[b] (Trumenba®)[28,29]	**3 doses** 0, 1-2, and 6 months apart[c]	1 dose 1 year following completion of primary series and every 2 to 3 years, if risk remains

[a]Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information.[1]

[b]MenB vaccines are not interchangeable. Patients must receive the same product for all doses.[28]

[c]For MenB-FHbp, if dose 2 was administered at least 6 months after dose 1, dose 3 is not needed.[28]

SELECT IMPORTANT SAFETY INFORMATION, (continued)

WARNINGS AND PRECAUTIONS, (continued)

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.

If patients have not been vaccinated and ULTOMIRIS® must be started right away, antibacterial drug prophylaxis should be administered[1,27,a,b]

The benefits and risks of antibiotic prophylaxis for prevention of meningococcal infections in patients receiving ULTOMIRIS have not been established.[1]

Please see the respective meningococcal vaccine's Prescribing Information for complete details, including the vaccine's Warnings, Precautions, and Contraindications.

- If your patient received meningococcal vaccines in the past, they might need additional vaccination before starting ULTOMIRIS[28]
- The choice of vaccine deemed medically appropriate is your independent decision
- In most cases, your patients can receive meningococcal vaccines at a physician's office or retail pharmacy
- MenACWY and MenB vaccines may be administered during the same visit but at different injection sites[30]
- To help reduce the risk of meningococcal infections, the complete series for the MenACWY and MenB vaccines should be administered[28]

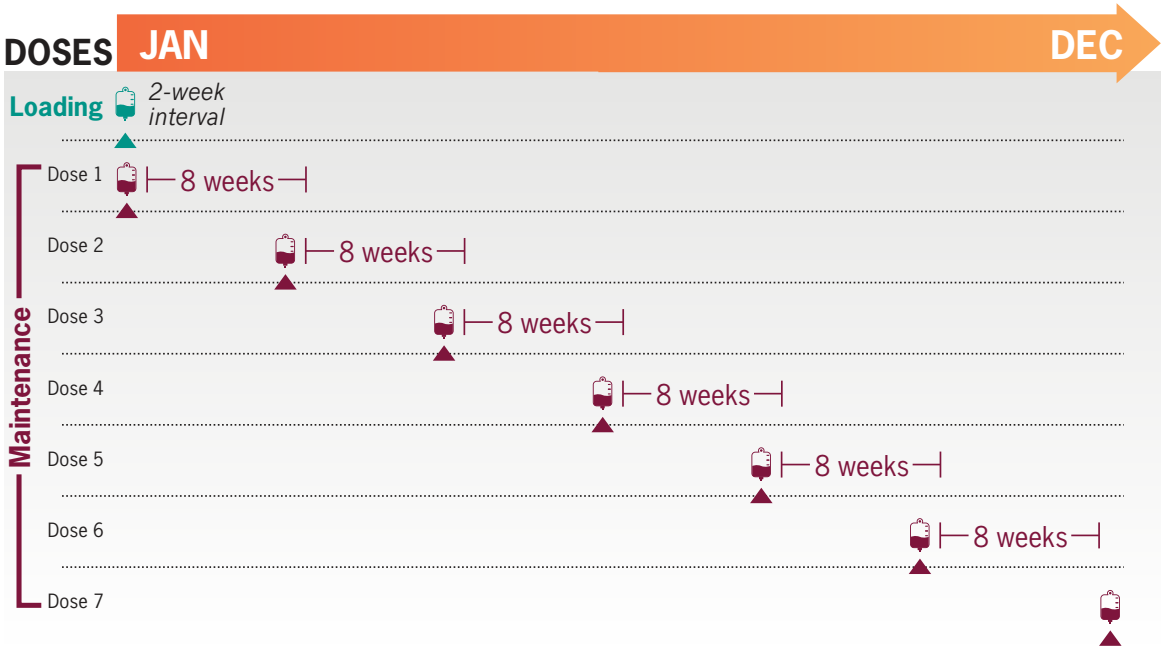
[a]Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information.[1]
[b]Several antibiotics are available for the treatment of meningococcal disease, including ceftriaxone, cefotaxime, and, when the diagnosis is confirmed, penicillin.[27]

SELECT IMPORTANT SAFETY INFORMATION, (continued)
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.

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.

Providing adult patients with predictable, once-every-8-week maintenance dosing for lasting symptom control[1,4,a]

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



1 infusion every 8 weeks[a]; 6-7 maintenance infusions per year after a loading dose

Each infusion typically lasts less than 1 hour for the majority of patients. Patients are monitored for at least 1 hour after infusions for signs or symptoms of an infusion-related reaction.[1,b]

- If an adverse reaction occurs during the administration of ULTOMIRIS®, the infusion may be slowed or stopped at the discretion of the physician[1]
- The recommended weight-based dosing regimen in adult patients with gMG (≥40 kg [88 lb]) consists of a loading dose followed 2 weeks later by the start of maintenance dosing every 8 weeks[1]
- The dosing schedule is allowed to occasionally vary within 7 days of the scheduled infusion day (except for the first maintenance dose of ULTOMIRIS), but subsequent doses should be administered according to the original schedule[1]
- Following a missed intravenous ULTOMIRIS dose, the patient should contact their healthcare provider immediately[1]

[a]Starting 2 weeks after an initial loading dose.[1]
[b]Minimum infusion time for ULTOMIRIS 100 mg/mL maintenance doses ranges from 30 minutes to less than 1 hour, depending on body weight.[1]

gMG, generalized myasthenia gravis.

SELECT IMPORTANT SAFETY INFORMATION, (continued)

WARNINGS AND PRECAUTIONS, (continued)

Infusion-Related Reactions

Intravenous administration may result in systemic infusion-related reactions, including anaphylaxis and hypersensitivity reactions. In clinical trials, infusion-related reactions occurred in approximately 1 to 7% of patients treated with ULTOMIRIS.

Doses and infusion times for ULTOMIRIS® 100 mg/mL[1]

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

Body Weight Range[a,b]	Loading Dose	Maintenance Dose	Minimum Infusion Time (loading, maintenance dose)
40 kg (88 lb) to less than 60 kg (132 lb)	2400 mg	3000 mg	48 min, 54 min
60 kg (132 lb) to less than 100 kg (220 lb)	2700 mg	3300 mg	36 min, 42 min
100 kg (220 lb) or greater	3000 mg	3600 mg	24 min, 30 min

[a]Body weight at time of treatment.[1]
[b]Approximate weight in pounds was calculated using standard weight conversion of 1 kg=2.205 lb.

If an adverse reaction occurs during the administration of ULTOMIRIS, the infusion may be slowed or stopped at the discretion of the physician. Monitor the patient for at least 1 hour following completion of the infusion for signs or symptoms of an infusion-related reaction.[1]

With a predictable, patient-friendly infusion schedule, ULTOMIRIS **decreases the treatment burden for adult patients with gMG** who are anti-AChR antibody positive. ULTOMIRIS offers **the only once-every-8-week maintenance dosing** schedule[1]

AChR, acetylcholine receptor; gMG, generalized myasthenia gravis.

SELECT IMPORTANT SAFETY INFORMATION, (continued)
WARNINGS AND PRECAUTIONS, (continued)
Infusion-Related Reactions, (continued)
These events included lower back pain, drop in blood pressure, limb discomfort, drug hypersensitivity (allergic reaction), dysgeusia (bad taste), and drowsiness. These reactions did not require discontinuation of ULTOMIRIS. If signs of cardiovascular instability or respiratory compromise occur, interrupt ULTOMIRIS infusion and institute appropriate supportive measures.

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® 100 mg/mL dosing at a glance[1]

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

	Body Weight Range[a]	ULTOMIRIS Volume		Volume of 0.9% of NaCl[b]		Total Volume (dose)	Minimum Infusion Time[c]	Maximum Infusion Rate	ULTOMIRIS Vial Combinations	
									1100 mg/ 11 mL	300 mg/ 3 mL
Loading Dose Administration	40 kg (88 lb) to <60 kg (132 lb)	24 mL	+	24 mL	=	48 mL (2400 mg)	48 min	60 mL/hr	—	8
	60 kg (132 lb) to <100 kg (220 lb)	27 mL	+	27 mL	=	54 mL (2700 mg)	36 min	90 mL/hr	—	9
	100 kg (220 lb) or greater	30 mL	+	30 mL	=	60 mL (3000 mg)	24 min	150 mL/hr	—	10
Maintenance Dose Administration	40 kg (88 lb) to <60 kg (132 lb)	30 mL	+	30 mL	=	60 mL (3000 mg)	54 min	67 mL/hr	—	10
	60 kg (132 lb) to <100 kg (220 lb)	33 mL	+	33 mL	=	66 mL (3300 mg)	42 min	95 mL/hr	3	—
	100 kg (220 lb) or greater	36 mL	+	36 mL	=	72 mL (3600 mg)	30 min	144 mL/hr	3	1

[a]Body weight at time of treatment.[1]
[b]Dilute ULTOMIRIS only using 0.9% Sodium Chloride Injection, USP.[1]
[c]Minimum infusion time for ULTOMIRIS 100 mg/mL maintenance doses ranges from 30 minutes to less than 1 hour, depending on body weight.[1]

NaCl, sodium chloride; USP, United States Pharmacopeia.

SELECT IMPORTANT SAFETY INFORMATION, (continued)
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.

Supplemental dosing of ULTOMIRIS® after PE, PP, or IVIg[1]

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

Concomitant use of ULTOMIRIS with PE, PP, or IVIg treatment can reduce serum ULTOMIRIS concentrations and requires a supplemental dose of ULTOMIRIS.

Body Weight Range[a]	Most Recent ULTOMIRIS Dose	Supplemental Dose Following Each PE or PP Intervention	Supplemental Dose Following Completion of an IVIg Cycle
40 kg (88 lb) to <60 kg (132 lb)	2400 mg	1200 mg	600 mg
	3000 mg	1500 mg	
60 kg (132 lb) to <100 kg (220 lb)	2700 mg	1500 mg	600 mg
	3300 mg	1800 mg	
100 kg (220 lb) or greater	3000 mg	1500 mg	600 mg
	3600 mg	1800 mg	
Timing of ULTOMIRIS supplemental dose		Within 4 hours following each PE or PP intervention	Within 4 hours following completion of an IVIg cycle

Neonatal Fc receptor (FcRn) blockers

Concomitant use of ULTOMIRIS with FcRn blockers (eg, efgartigimod) may lower systemic exposures and reduce the effectiveness of ULTOMIRIS. Closely monitor for reduced effectiveness.

[a]Body weight at time of treatment.

IVIg, intravenous immunoglobulin; PE, plasma exchange; PP, plasmapheresis.

SELECT IMPORTANT SAFETY INFORMATION, (continued)

ADVERSE REACTIONS, (continued)

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.

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.

Comprehensive support for your patients and your practice

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

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 your patients' needs from diagnosis through treatment.

We can help make sense of health insurance coverage, answer questions about treatment with ULTOMIRIS®, and foster connections to community resources. With our experience and resources, we're here to help you and your patients feel supported every step of the way.

Alexion OneSource Specialists assist with:

Education

- Providing your patients with educational resources and materials related to generalized myasthenia gravis (gMG)
- Helping to answer your patients' questions about the disease or treatment logistics
- Providing information about meningococcal vaccinations and can help your patients locate a vaccination center

Health insurance navigation

- Helping your patients understand ULTOMIRIS health insurance coverage
- Exploring alternative funding options and financial resources

Ongoing support

- Personalized support for your patients in maintaining therapy during their major life events, such as a change in job, insurance status, provider, or relocation

Community connections

- Providing information to patients regarding in-person and online meetings and events
- Connecting patients with other people living with gMG

For more information, please visit:
AlexionOneSource.com | UltomirisHCP.com/gmg

Scan to visit
UltSolREMS.com

OneSource gives patients the confidence of comprehensive, personalized support throughout their gMG treatment journey

Call 1-888-765-4747 or email OneSource@alexion.com to connect with our OneSource team

Comprehensive support for your patients and your practice, (continued)

ALEXION ACCESS NAVIGATOR

Alexion Access Navigator is a dedicated resource website for US healthcare professionals and their offices that contains downloadable access and reimbursement materials for ULTOMIRIS® in generalized myasthenia gravis (gMG).

Scan to visit
alexionaccessnavigator.com/ULTOMIRIS

Resources include:

ULTOMIRIS Access & Reimbursement Guide

- An access and reimbursement educational support resource for HCPs, HCP offices, and infusion centers that administer ULTOMIRIS in gMG

ULTOMIRIS gMG Common Prior Authorization Criteria

- Presents the common criteria that may be requested by payers for prior authorization of ULTOMIRIS in gMG as well as general information about the prior authorization processes

ULTOMIRIS gMG Appeal Letter

- This template is a resource a healthcare provider may use when responding to a request from a patient's insurance company to provide a letter of medical necessity when prescribing ULTOMIRIS in gMG

Call 1-888-765-4747 to be connected to your local Field Reimbursement Manager (FRM)

Meet Madison, a 32-year-old professional recently diagnosed with gMG and experiencing 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

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 steroid 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 due to incomplete response, then reduced to 40 mg per day due to steroid-related adverse reactions but has been unable to reduce further

Current medications

- Prednisone 40 mg once per day
- 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 steroid-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 steroid 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.

SELECT IMPORTANT SAFETY INFORMATION, (continued)

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.

Meet Jacob, a 55-year-old father with gMG worried about treatment burden[a]

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

Jacob

Age:	55
Profession:	Grocery clerk
Length of Disease:	2 years
Location:	Boston, Massachusetts

Past medical history

- Jacob has no significant medical history except for a diagnosis of anti-AChR antibody-positive gMG 2 years ago

History of present illness

- He has been on an infusion therapy with concomitant steroids for the past 6 months
- MGFA class IIa
- His daily medication regimen previously included azathioprine, which was discontinued because he could not tolerate it
- He was still experiencing gMG symptoms, which prompted more frequent doses of infusion therapy

Current medications

- Frequent IV biologic therapy
- Prednisone 20 mg once daily

Current chief complaints

- Despite more frequent infusions, Jacob is still experiencing fluctuating and unpredictable symptoms between treatment doses, making it difficult to drive to work and keep up with his children's extracurricular activities
- Jacob has concerns about his current treatment regimen due to its unpredictable infusion schedules and frequent lengthy infusion center visits
- Based on conversations with his doctor, Jacob is also interested in a treatment option that might allow him to lower or discontinue steroids

[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; IV, intravenous; MGFA, Myasthenia Gravis Foundation of America.

SELECT IMPORTANT SAFETY INFORMATION, (continued)
DRUG INTERACTIONS, (continued)

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

MG-ADL Scale[31]

	0=Normal	1	2	3=Most severe	
Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal speech, but can be understood	Difficult-to-understand speech	
Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube	
Swallowing	Normal	Rare episode of choking	Frequent choking necessitating changes in diet	Gastric tube	
Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence	
Impairment of ability to brush teeth or comb hair	None	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions	
Impairment of ability to arise from a chair	None	Mild, sometimes uses arms	Moderate, always uses arms	Severe, requires assistance	
Double vision	None	Occurs, but not daily	Daily, but not constant	Constant	
Eyelid droop	None	Occurs, but not daily	Daily, but not constant	Constant	

MG-ADL, Myasthenia Gravis Activities of Daily Living.
The information on this page is intended as educational information for healthcare providers. It does not replace a healthcare provider's judgment or clinical diagnosis.
Assessment adapted from: myasthenia.org/Portals/0/ADL.pdf.

Add items for MG-ADL total score

QMG Scale[32]

	0=None	1=Mild	2=Moderate	3=Severe	
Double vision on lateral gaze right or left (circle one), seconds	61	11-60	1-10	Spontaneous	
Ptosis (upward gaze), seconds	61	11-60	1-10	Spontaneous	
Facial muscles	Normal lid closure	Complete, weak, some resistance	Complete, without resistance	Incomplete	
Swallowing 4 oz of water (1/2 cup)	Normal	Minimal coughing or throat clearing	Severe coughing/ choking or nasal regurgitation	Cannot swallow (test not attempted)	
Speech after counting aloud from 1 to 50 (onset of dysarthria)	None at 50	Dysarthria at 30-49	Dysarthria at 10-29	Dysarthria at 9	
Right arm outstretched (90-degree sitting), seconds	240	90-239	10-89	0-9	
Left arm outstretched (90-degree sitting), seconds	240	90-239	10-89	0-9	
Forced vital capacity	≥80	65-79	50-64	<50	
Right-hand grip, kgW **Men** **Women**	 ≥45 ≥30	 15-44 10-29	 5-14 5-9	 0-4 0-4	
Left-hand grip, kgW **Men** **Women**	 ≥35 ≥25	 15-34 10-24	 5-14 5-9	 0-4 0-4	
Head lifted (45-degree supine), seconds	120	30-119	1-29	0	
Right leg outstretched (45-degree supine), seconds	100	31-99	1-30	0	
Left leg outstretched (45-degree supine), seconds	100	31-99	1-30	0	
				Add items for QMG total score	

QMG, Quantitative Myasthenia Gravis.
The information on this page is intended as educational information for healthcare providers. It does not replace a healthcare provider's judgment or clinical diagnosis.
Assessment adapted from: myasthenia.org/Portals/0/QMG.pdf.

INDICATION & IMPORTANT SAFETY INFORMATION

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

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.

ULTOMIRIS and SOLIRIS REMS, (continued)
Prescribers must enroll in the REMS, counsel patients about the risk of serious meningococcal infection, provide patients with the REMS educational materials, assess patient vaccination status for meningococcal vaccines (against serogroups A, C, W, Y, and B) and vaccinate if needed according to current ACIP recommendations two weeks prior to the first dose of ULTOMIRIS. Antibacterial drug prophylaxis must be prescribed if treatment must be started urgently, and the patient is not up to date with both meningococcal vaccines according to current ACIP recommendations at least two weeks prior to the first dose of ULTOMIRIS. Patients must receive counseling about the need to receive meningococcal vaccines and to take antibiotics as directed, signs and symptoms of meningococcal infection, and be instructed to carry the Patient Safety Card at all times during and for 8 months following ULTOMIRIS treatment.

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

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

ULTOMIRIS blocks terminal complement activation; therefore, patients may have increased susceptibility to infections, especially with encapsulated bacteria, such as infections caused by *Neisseria meningitidis* but also *Streptococcus pneumoniae*, *Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*. Patients receiving ULTOMIRIS are at increased risk for infections due to these organisms, even if they develop antibodies following vaccination.

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

Infusion-Related Reactions
Intravenous administration may result in systemic infusion-related reactions, including anaphylaxis and hypersensitivity reactions. In clinical trials, infusion-related reactions occurred in approximately 1 to 7% of patients treated with ULTOMIRIS. These events included lower back pain, drop in blood pressure, limb discomfort, drug hypersensitivity (allergic reaction), dysgeusia (bad taste), and drowsiness. These reactions did not require discontinuation of ULTOMIRIS. If signs of cardiovascular instability or respiratory compromise occur, interrupt ULTOMIRIS infusion and institute appropriate supportive measures.

ADVERSE REACTIONS
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.

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.

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

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

Symptom control for the journey ahead[1-4,a]

ULTOMIRIS® offers adult patients:

All images depict hypothetical patients.

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])[1,2,a]

8 WEEKS **Predictable, once-every-8-week maintenance dosing**[1,b]

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

Comprehensive, personalized support through the Alexion OneSource program

[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]Once-every-8-week dosing after an initial loading dose.[1]

MG-ADL, Myasthenia Gravis Activities of Daily Living.

References: 1. ULTOMIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. **2.** Data on file. Alexion Pharmaceuticals, Inc. **3.** Muppidi S, et al; MG Composite and MG-QOL15 Study Group. *Muscle Nerve.* 2011;44(5):727-731. **4.** Meisel A, et al. *J Neurol.* 2023;1-14. **5.** Gilhus NE, et al. *Nat Rev Dis Primers.* 2019;5(1):30. **6.** Johnson S, et al. *Med Sci Monit.* 2021;27:e933296. **7.** Sanders DB, et al. *Neurology.* 2016;87(4):419-425. **8.** Harris L, et al. *BMC Neurol.* 2022;22(1):172. **9.** Mahic M, et al. *Muscle Nerve.* 2023;67(4):297-305. **10.** Sanders DB, Evoli A. *Autoimmunity.* 2010;43(5-6):428-435. **11.** Kusner LL, Kaminski HJ. *Ann N Y Acad Sci.* 2012;1274(1): 127-132. **12.** Meriggioli MN, Sanders DB. *Lancet Neurol.* 2009;8(5):475-490. **13.** Conti-Fine BM, et al. *J Clin Invest.* 2006;116(11):2843-2854. **14.** Howard JF Jr. *Ann N Y Acad Sci.* 2018;1412(1):113-128. **15.** Engel AG, Lambert EH, Howard FM. *Mayo Clin Proc.* 1977;52(5):267-280. **16.** Sahashi K, Engel AG, Lambert EH, Howard FM Jr. *J Neuropathol Exp Neurol.* 1980;39(2):160-172. **17.** Kulasekararaj AG, et al. *Blood.* 2019;133(6):540-549. **18.** Lee JW, et al. *Blood.* 2019;133(6):530-539. **19.** Murphy K, Weaver C. Innate immunity: the first lines of defense. In: *Janeway's Immunobiology.* 9th ed. Garland Science, Taylor & Francis Group, LLC; 2017:chap 2. **20.** Rother RP, et al. *Nat Biotechnol.* 2007;25(11):1256-1264. **21.** Vu T, et al. *NEJM Evid.* 2022;1(5). **22.** VYVGART. Prescribing information. Argenx SE. **23.** Howard JF Jr, et al. Poster presented at: the 14th Myasthenia Gravis Foundation of America International Conference; May 10-12, 2022; Miami, FL. **24.** Habib AA, et al. Poster presented at: the American Association of Neuromuscular & Electrodiagnostic Medicine Annual Myasthenia Gravis Foundation of America Scientific Session; September 21, 2022; Nashville, TN. **25.** Jaretzki A III, et al. *Neurology.* 2000;55(1):16-23. **26.** Centers for Disease Control and Prevention. Accessed June 23, 2023. https://www.cdc.gov/meningococcal/about/soliris-patients.html **27.** Mbaeyi SA, et al; Advisory Committee on Immunization Practices. Centers for Disease Control and Prevention; 2020. Accessed June 23, 2023. https://www.cdc.gov/mmwr/volumes/69/rr/rr6909a1.htm **28.** Centers for Disease Control and Prevention. Updated April 21, 2023. Accessed June 23, 2023. https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf **29.** Centers for Disease Control and Prevention. Updated October 12, 2021. Accessed June 23, 2023. https://www.cdc.gov/vaccines/vpd/mening/public **30.** Centers for Disease Control and Prevention. Updated October 18, 2022. Accessed June 23, 2023. https://www.cdc.gov/vaccines/vpd/mening/hcp/administering-vaccine.html **31.** Myasthenia Gravis Foundation of America. Accessed June 23, 2023. https://myasthenia.org/Portals/0/ADL.pdf **32.** Myasthenia Gravis Foundation of America. Accessed June 23, 2023. https://myasthenia.org/Portals/0/QMG.pdf

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Scan QR code or visit the link: https://bit.ly/3KEpmzp

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ALEXION®
AstraZeneca Rare Disease

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