SAMPLE APPEAL LETTER FOR ULTOMIRIS® (ravulizumab-cwvz)

In Adult Patients Who Have Anti-Acetylcholine Receptor (AChR) Antibody-Positive Generalized Myasthenia Gravis (gMG)

When a payer (health plan or pharmacy benefit manager [PBM]) denies a prior authorization (PA), precertification, or reauthorization request for ULTOMIRIS prescribed for the treatment of anti-acetylcholine receptor (anti-AChR) antibody-positive generalized myasthenia gravis (gMG), your patient has the right to appeal the decision. If your patient wishes to appeal, you and your staff may assist by submitting an appeal letter and supporting documentation.

As part of the appeals process, payers may request additional documentation from you to support coverage of ULTOMIRIS when approval for its use has been denied. Your letter should explain why ULTOMIRIS is medically necessary for the specific patient and may include supporting documentation. The letter may be submitted in response to the denial letter or to a payer's request for additional documentation. The letter should include patient-specific information, address the reason for denial, be presented on the prescriber's letterhead, and be signed by the prescriber. The provided Sample Appeal Letter gives you a framework for composing an appeal.

This Sample Appeal Letter is provided for informational purposes only and is not legal advice or official guidance from payers. It is not intended to increase or maximize reimbursement by any payer. Alexion does not warrant, promise, guarantee, or make any statement that the use of this information will result in coverage or payment for ULTOMIRIS, or that any payment received will cover providers' costs.

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 Important Safety Information on pages 8-10 and the 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

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GENERAL TIPS FOR COMPLETING AN APPEAL LETTER

Understand the appeals process for the specific payer. It's important to follow the payer's guidelines when submitting an appeal. Payers may have their own appeal request forms, which are usually available on their website. If a form is required, include it with your own letter. Be sure to contact the payer with any questions and to obtain written instructions for their appeals process.

When submitting an appeal, timing is critical. Refer to the denial letter to find the timelines for submitting the appeal, as well as any payer-specific guidelines.

In cases of medical urgency, your patient may request an expedited review and can expect to receive a decision within 72 hours. For more information, please visit **HealthCare.gov**.

Understand the reason for denial. It's important to read the denial letter carefully to understand the reason(s) provided. You may also call the payer to discuss a denial with them; this may help inform you about ways to resolve it in a timely manner:

- **If the denial is due to inaccurate or incomplete information,** carefully review the PA or reauthorization request that you submitted to identify information that is incorrect or was omitted. Resubmit the PA or reauthorization request when all the required information is accurate and complete
- **If there is a medical reason for the denial,** ensure that your appeal letter includes specific and relevant medical information to support ULTOMIRIS use according to the payer's criteria. Your letter should clearly explain why you believe ULTOMIRIS is the most appropriate option for this patient
- **If the denial is due to step therapy protocols, emphasize specific reasons for exception to treatment. Reasons could include:**
  1. Contraindications to treatment
  2. Treatment could be ineffective due to clinical characteristics of patient
  3. Patient has tried and failed required treatment while on a previous health benefit plan
  4. Medication is not in the best interest of the patient based on medical necessity
  5. Patient is already stable on current treatment and should not disrupt continuity of care by switching to required step therapy

Provide all supporting documentation at the same time and in the requested order, as shown in the individual payer's appeal instructions. This might include:

- The payer's appeal form (if required)
- Your appeal letter
- A copy of the payer's denial letter
- Supporting documentation, such as clinical notes, lab results, etc

Our dedicated Field Reimbursement Managers (FRMs) can work with you. In the event of a PA denial, FRMs can provide you or your office staff with educational support and guidance. FRMs can help with:

- Payer options for PA resubmission, including details about the resubmission process, peer-to-peer review, appeals process, and associated timelines
- Review of the redacted denial letter or Explanation of Benefits (EOB) letter to provide specific guidance on next steps and best practices

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

[John Doe, MD]
[Address]
[City, State ZIP Code]
[(888) 555-5555]

SAMPLE ONLY
PLEASE COPY ONTO YOUR LETTERHEAD.

[Date]
[Contact Name], [Title] [Name of Health Insurance Plan or PBM]
[Address]
[City, State ZIP Code]

Re: [First/Second]-Level Appeal for Coverage Denial of ULTOMIRIS® (ravulizumab-cwvz)
[Request for Expedited Review Due to Medical Urgency]

Denial Letter Date: [MM/DD/YYYY]
Denial Reference #: [Denial Reference #]

Patient: [Name]
Date of Birth: [MM/DD/YYYY]
Member ID Number: [Insurance ID Number] Group Number: [Insurance Group Number]
Rx Bin: [Rx Bin Number] Rx PCN: [Rx PCN Number] Rx Group: [Rx Group Number]

Dear [Contact Name],

I am writing to appeal the coverage denial for [name of patient]'s treatment with ULTOMIRIS® (ravulizumab-cwvz) for anti-AChR antibody-positive generalized myasthenia gravis (gMG). In the letter referenced above, you stated that the reason for denial was [insert reason for denial]. This letter provides information about my patient's medical history and my treatment rationale.

1 **REASON(S) FOR DENIAL AND TREATMENT RATIONALE (Refer to "Treatment Rationale to Support Appeal" and "Key Resources Available to You")**

[In the appeal letter, you need to address every denial reason(s) stated in the denial letter from the insurance plan. Clearly explain why the reason(s) stated by the insurance plan as a cause for denial of coverage do not preclude use of ULTOMIRIS. During the appeal process, it is generally not helpful to provide additional information beyond the specific denial reasons.]

In my medical opinion, ULTOMIRIS remains the most appropriate treatment for [name of patient]. The stated reason(s) for denial was [insert each denial reason and address each reason point by point and provide any laboratory results if applicable].

2 **SUMMARY AND OPTIONAL MEDICAL HISTORY (Refer to "Optional Medical History")**

As stated in my initial authorization request, [name of patient] presented with [insert specific clinical presentations and treatments for anti-AChR antibody-positive gMG, including any relevant patient-specific clinical scenarios demonstrating serious medical need]. For the above reasons, I request that you reverse the coverage determination.

3 For your additional information, I am enclosing [list enclosures, such as a copy of the denial letter, supporting clinical documentation, etc]. If you have any further questions, please feel free to call me at [physician's telephone number] to discuss.

Thank you in advance for your immediate attention to this request.
[Provider Name]
[Provider Identification Number]
[Provider Practice Name]
[Provider Phone Number]
[Provider Fax Number]
[Provider Email]

Enclosures
[At the bottom of your letter, list the items you have enclosed, such as the original denial letter and ULTOMIRIS Full Prescribing Information. Be sure to include every article that you referenced or any new documentation.]

1 TREATMENT RATIONALE TO SUPPORT APPEAL

Below are some common reasons your patient's PA, precertification, or reauthorization request may be denied. In your appeal letter, ensure that each reason for denial is addressed by sharing your medical expertise on why the requirement is satisfied or should not apply in your patient's individual case. Be sure to attach the supporting references and any additional documentation in your reply.

- **Denial due to indication:** ULTOMIRIS is indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive
- **Denial due to previous failed treatments:** Upon diagnosis with anti-AChR antibody-positive gMG, [Patient Name] was treated with [list treatments and the respective clinical responses here]. My rationale for treatment with ULTOMIRIS at this time is [include rationale here]
- **Denial due to required use of immunosuppressive therapy (IST):** [Patient Name] has tried and failed [list treatment names]. [He/she] has not shown adequate response due to [insert rationale and list specific reasons]
- **Denial due to pyridostigmine:** Pyridostigmine treatment was tried with the following results: [Describe clinical response and/or failure with pyridostigmine treatment]. For [this reason/these reasons], [include rationale for treatment with ULTOMIRIS]
- **Denial due to required use of efgartigimod alfa-fcab and efgartigimod alfa and hyaluronidase-qvfc[1-3]:** In my medical opinion, efgartigimod is not an appropriate step for my patient due to [list specific reason(s) based on the following below]:

  ADAPT study design—select patient exclusion criteria

  - Pregnant and lactating women, and those intending to become pregnant during the trial or within 90 days after the last dosing
  - Male patients who are sexually active and do not intend to use effective methods of contraception during the trial or within 90 days after the last dosing or male patients who plan to donate sperm during the trial or within 90 days after the last dosing
  - Patients with worsening muscle weakness secondary to concurrent infections or medications
  - Patients with known seropositivity or who test positive for an active viral infection for HBV (except patients who are seropositive because of HBV vaccination), HCV, or HIV
  - Patients with serum IgG levels less than 6 g/L
  - Patients with MG-ADL total score less than 5, or at least 5 with >50% of the total score due to ocular symptoms

  Effect of efgartigimod alfa-fcab or efgartigimod alfa and hyaluronidase-qvfc on other drugs

  - Based on the VYVGART and VYVGART HYTRULO PIs (Section 7.1), discontinuing efgartigimod should be considered when concomitant long-term use of medications that bind to the human neonatal Fc receptor is essential for patient care. Examples of these medications include immunoglobulin products, monoclonal antibodies, or antibody derivates containing the human Fc domain of the IgG subclass. Alternative therapies should be considered[3,4]
  - Patients with certain comorbid conditions (including asthma, rheumatoid arthritis, psoriasis, osteoporosis, atopic dermatitis, ulcerative colitis, etc) may be on medications that have these drug-drug interactions[5]
  - Include details of reactions from these drug-drug interactions, such as decreased effectiveness of gMG treatment[6]

HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IgG, immunoglobulin G; MG-ADL, Myasthenia Gravis Activities of Daily Living scale.

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- **Denial due to use with eculizumab:**
  - The patient had a previous diagnosis of gMG that met requirements for initiating eculizumab, was clinically stable on eculizumab, and has had a beneficial response as evidenced by [change from baseline in MG-ADL total score, change from baseline in QMG total score][7,8]
  - Switching to ULTOMIRIS reduces maintenance dosing frequency to 6 to 7 infusions per year, from 26 infusions per year with eculizumab[7,8]
  - ULTOMIRIS was engineered through the modification of eculizumab to result in an extended half-life with the same mechanism of action[7,8]
  - The annualized cost of treatment is expected to be reduced by ~26% to 39% with ULTOMIRIS compared with eculizumab based on wholesale acquisition cost (WAC)[7-9]
- **Denial due to use with rozanolixizumab[10,11]:** In my medical opinion, rozanolixizumab is not an appropriate step for my patient due to [list specific reason(s) based on the following below]:

  MycarinG study design—select patient exclusion criteria:

  - Patients with severe oropharyngeal or respiratory weakness
  - Patients' total IgG concentration of ≤5.5 g/L
  - Patients who experienced hypersensitivity reaction to any components of the medication
  - Pregnant and lactating women

  Effect of rozanolixizumab on other drugs:

  - Based on the RYSTIGGO PI (Section 7.1), discontinuing rozanolixizumab should be considered when concomitant long-term use of medications that bind to the human neonatal Fc receptor is essential for patient care. Examples of these medications include immunoglobulin products, monoclonal antibodies, or antibody derivates containing the human Fc domain of the IgG subclass. Alternative therapies should be considered[11]
  - Patients with certain comorbid conditions (including asthma, rheumatoid arthritis, psoriasis, osteoporosis, atopic dermatitis, ulcerative colitis, etc) may be on medications that have these drug-drug interactions[5]
  - Include details of reactions from these drug-drug interactions such as decreased effectiveness of gMG treatment[11]
- **Denial due to zilucoplan[12,13]:** In my medical opinion, zilucoplan is not an appropriate step for my patient due to [challenges with self-administered medication or list other specific reason(s) based on the following below]:

  RAISE trial design—select patient exclusion criteria:

  - Patients who are ≥75 years
  - Patients with abnormal thyroid function
  - Patients with known positive serology for muscle-specific tyrosine kinase autoantibodies
  - Patients with fixed weakness according to investigator judgment

QMG, Quantitative Myasthenia Gravis.

- **Denial due to absence of thymectomy for non-thymomatous patients who are 50 years of age or younger[14-16]:** In my medical opinion, a thymectomy is not appropriate for [Patient Name] for [this reason/these reasons:
  - Absence of thymomas and age.] Thymectomy is applicable only to patients with thymomas or non-thymomatous patients who are 50 years of age or younger. The MGTX study, which demonstrated clinical benefit of thymectomy in non-thymomatous gMG patients, was only designed to assess benefit in patients who had disease duration of less than 5 years and did not show benefit in patients aged 50 or older. Furthermore, the MGTX study was conducted prior to C5 inhibitors
  - Clinical guidance for MG.] The most recent International Consensus Guidance for Management of Myasthenia Gravis (updated in 2020) highlights that thymectomy for MG is an elective procedure
  - CHAMPION-MG inclusion/exclusion criteria.] The CHAMPION-MG trial, the Phase 3 pivotal trial that studied ravulizumab in adult gMG patients who are anti-acetylcholine receptor antibody positive, did not include thymectomy as an inclusion criterion. Patients were excluded from the study if they had a history of thymectomy in the 12 months before screening
- **Denial due to Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score*:** Documentation of current score ≥6 on the MG-ADL scale, including case notes and other clinical impressions. If patient or caregiver has tracked changes in their MG-ADL total score, include the score history; payers may require the MG-ADL total scores for initial approval and reauthorizations of treatment
- **Denial due to QMG score[17]:** Documentation of current QMG score. Include rationale why this score may not be an accurate depiction of patient's gMG status [eg, despite an improved QMG score, patient is incapacitated due to poor strength in 1 or 2 areas]
- **Denial due to anti-AChR antibody test:** Evidence of a positive serological test for AChR antibodies (include laboratory results and date) and any other context you consider relevant around this laboratory result
- **Denial due to meningococcal vaccinations:** Provide documentation of initial series and/or most recent booster(s) for MenACWY and MenB vaccinations
- **Denial due to required use of rituximab[18]:** In my medical opinion, rituximab is not an appropriate step for my patient due to [his/her] history of [describe relevant medical history which may include the following (not all inclusive):
  - Heart issues (eg, angina, acute myocardial infarction, heart arrhythmia, etc).] This condition is listed in the rituximab prescribing information as a warning and precaution in Section 5.7 under "Cardiovascular Adverse Reactions"
  - Renal failure or insufficiencies.] This condition is listed in the rituximab prescribing information as a warning and precaution in Section 5.8 under "Renal Toxicity"
  - Cytopenias and/or hypogammaglobulinemia.] This condition is listed in the rituximab prescribing information as a warning and precaution in Section 5.6 under "Infections," and Section 6.1 under "Cytopenias and hypogammaglobulinemia"

*MG-ADL total score is based on a scale of 0 to 24; MG-ADL total score of ≥6 assessed in CHAMPION-MG clinical trial population.[7]
MenACWY, meningococcal serogroups A, C, W, Y; MenB, meningococcal serogroup B.

2 OPTIONAL MEDICAL HISTORY

- [Name of patient] is a[n] [age]-year-old [male/female] born [MM/DD/YYYY] who requires treatment with ULTOMIRIS after being diagnosed with anti-AChR antibody-positive gMG on [date of diagnosis MM/DD/YYYY]
- **Current symptoms[19]:** Examples such as profound muscle weakness throughout the body, as demonstrated by slurred speech, impaired swallowing, double vision, upper and lower extremity weakness, disabling fatigue, and/or shortness of breath due to respiratory muscle weakness
  - It may be helpful to highlight in particular your patient's severity of disease based on your medical opinion and disease progression (eg, history of myasthenic crises, likelihood of impending crises, etc)
- **Myasthenia Gravis Foundation of America (MGFA) Clinical Classification**[†]
  Documentation of status on the MGFA Clinical Classification Class II to V; include patient-specific clinical features/presentations and symptom severity. If classification has been tracked, include past MGFA Clinical Classification statuses
- Attestation that the patient has tried and failed therapies the plan requires before use of ULTOMIRIS is permitted, such as 2 immunosuppressants; oral corticosteroids; intravenous immunoglobulin, plasmapheresis, pyridostigmine, and/or rituximab in order to meet the plan's medical policy; pre-certification; or PA criteria
- Documentation of your clinical rationale to initiate ULTOMIRIS for this patient, such as contraindications to other therapies, clinical presentation, recent medical history, or visits related to gMG, etc
- Current medication regimen from comorbidities that could create drug-drug interactions[5]
- Documentation of clinical stability and beneficial response of eculizumab as evidenced by [change from baseline in MG-ADL total score, change from baseline in QMG total score][7,8]
- Documentation of efficacy and tolerability of ULTOMIRIS as evidenced by [change from baseline in MG-ADL total score, change from baseline in QMG total score][20]

3 KEY RESOURCES AVAILABLE TO YOU

- Connect with an FRM—Alexion Field Reimbursement Managers (FRMs) provide education and support to HCP offices to facilitate patient access to their prescribed Alexion medications
- The Compendium of Generalized Myasthenia Gravis (gMG) References for ULTOMIRIS provides information about specific scientific data and publications that may provide additional evidence for your Appeal Letter
- The Preparing for a Peer-to-Peer Medical Review resource provides education and support for HCPs, HCP offices, and infusion centers about using a peer-to-peer review as a potential next step before submitting a formal appeal

For additional access resources, please visit:

Explore Alexion Access Navigator

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® (ravulizumab-cwvz).

Online: https://alexionaccessnavigator.com

[†]MGFA Clinical Classification is based on Class I to V; MGFA Class II-IV assessed in CHAMPION-MG clinical trial population.[7]
HCP, healthcare provider.

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INDICATION & IMPORTANT SAFETY INFORMATION FOR ULTOMIRIS® (ravulizumab-cwvz)

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.

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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.

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.

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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.

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 Important Safety Information on pages 8-10 and the full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

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