# ULTOMIRIS® (ravulizumab-cwvz) approved in the US for adults with generalized myasthenia gravis

April 28, 2022

**First and only long-acting C5 complement inhibitor to demonstrate clinical improvement in patients with generalized myasthenia gravis**

**ULTOMIRIS showed early effect and lasting improvement in activities of daily living and has potential to reduce treatment burden with dosing every 8 weeks**

WILMINGTON, Del., April 28, 2022 – ULTOMIRIS® (ravulizumab-cwvz) has been approved in the US for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive, which represents 80% of people living with the disease.1-5

The approval by the Food and Drug Administration (FDA) was based on positive results from the CHAMPION-MG Phase III trial, in which ULTOMIRIS was superior to placebo in the primary endpoint of change from baseline in the Myasthenia Gravis-Activities of Daily Living Profile (MG-ADL) total score at Week 26, a patient-reported scale that assesses patients' abilities to perform daily activities.1

This FDA action marks the first and only approval for a long-acting C5 complement inhibitor for the treatment of gMG.

gMG is a rare, debilitating, chronic, autoimmune neuromuscular disease that leads to a loss of muscle function and severe weakness.6 The diagnosed prevalence of gMG in the US is estimated at approximately 90,000.7

Professor James F. Howard, Jr, MD, Department of Neurology at The University of North Carolina School of Medicine and lead primary investigator in the CHAMPION-MG trial said: "Despite recent advances, managing gMG is complex. Earlier intervention can preserve function and quality of life. This approval offers patients, including those with milder symptoms, a long-acting C5 inhibitor with early onset and reliable efficacy."

Samantha Masterson, Chief Executive Officer, Myasthenia Gravis Foundation of America (MGFA), said: "gMG takes a physical and emotional toll on those living with the disease. We are grateful for continued innovation and research into new treatment and dosing options to meet the needs of more patients and reduce the treatment burden. With the approval of ULTOMIRIS, we're excited that MG patients now have another option to consider as part of their personalized treatment strategies that may offer more convenience and improve muscle weakness."

Marc Dunoyer, Chief Executive Officer, Alexion, said: "Since bringing forward the first complement inhibitor, we've continued to listen to the community and focused innovation on the needs of gMG patients. We're proud to deliver on this commitment with today's approval. ULTOMIRIS, the only long-acting C5 inhibitor, will benefit a broader range of patients, including those with milder symptoms. As presented at the 2022 American Academy of Neurology Annual Meeting, ULTOMIRIS has demonstrated clinical benefit through 60 weeks, with treatment every eight weeks, compared to SOLIRIS every two weeks."

In the trial, the safety profile of ULTOMIRIS was comparable to placebo and consistent with that observed in Phase III trials of ULTOMIRIS in paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS). The most common adverse reactions in patients receiving ULTOMIRIS were upper respiratory tract infection and diarrhea.1

Results from the CHAMPION-MG trial were recently published online in NEJM Evidence and presented at the 2022 American Academy of Neurology Annual Meeting in April.

Regulatory submissions for ULTOMIRIS for the treatment of gMG are currently under review with multiple health authorities, including in the European Union (EU) and Japan.

**INDICATION(S) & IMPORTANT SAFETY INFORMATION for ULTOMIRIS® (ravulizumab-cwvz)**

**What is ULTOMIRIS?**

ULTOMIRIS is a prescription medicine used to treat:

- adults and children 1 month of age and older with a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH).
- adults and children 1 month of age and older with a disease called atypical Hemolytic Uremic Syndrome (aHUS). ULTOMIRIS is not used in treating people with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).
- adults with a disease called generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.

**It is not known if ULTOMIRIS is safe and effective in children younger than 1 month of age.**

**IMPORTANT SAFETY INFORMATION**

What is the most important information I should know about ULTOMIRIS?

ULTOMIRIS is a medicine that affects your immune system and can lower the ability of your immune system to fight infections.

- ULTOMIRIS increases your chance of getting serious and life-threatening meningococcal infections that may quickly become life-threatening and cause death if not recognized and treated early.

1. You must receive meningococcal vaccines at least 2 weeks before your first dose of ULTOMIRIS if you are not vaccinated.
2. If your doctor decided that urgent treatment with ULTOMIRIS is needed, you should receive meningococcal vaccination as soon as possible.
3. If you have not been vaccinated and ULTOMIRIS therapy must be initiated immediately, you should also receive 2 weeks of antibiotics with your vaccinations.
4. If you had a meningococcal vaccine in the past, you might need additional vaccination. Your doctor will decide if you need additional vaccination.
5. Meningococcal vaccines reduce but do not prevent all meningococcal infections. Call your doctor or get emergency medical care right away if you get any of these signs and symptoms of a meningococcal infection: headache with nausea or vomiting, headache and fever, headache with a stiff neck or stiff back, fever, fever and a rash, confusion, muscle aches with flu-like symptoms and eyes sensitive to light.

**Your doctor will give you a Patient Safety Card about the risk of meningococcal infection.** Carry it with you at all times during treatment and for 8 months after your last ULTOMIRIS dose. It is important to show this card to any doctor or nurse to help them diagnose and treat you quickly.

**ULTOMIRIS is only available through a program called the ULTOMIRIS REMS.** Before you can receive ULTOMIRIS, your doctor must: enroll in the ULTOMIRIS REMS program; counsel you about the risk of meningococcal infection; give you information and a **Patient Safety Card** about the symptoms and your risk of meningococcal infection (as discussed above); and make sure that you are vaccinated with a meningococcal vaccine, and if needed, get revaccinated with the meningococcal vaccine. Ask your doctor if you are not sure if you need to be revaccinated.

**ULTOMIRIS may also increase the risk of other types of serious infections.** Make sure your child receives vaccinations against Streptococcus pneumoniae and Haemophilis influenzae type b (Hib) if treated with ULTOMIRIS. Call your doctor right away if you have any new signs or symptoms of infection.

**Who should not receive ULTOMIRIS?**

**Do not** receive ULTOMIRIS if you have a meningococcal infection or have not been vaccinated against meningococcal infection unless your doctor decides that urgent treatment with ULTOMIRIS is needed.

**Before you receive ULTOMIRIS, tell your doctor about all of your medical conditions, including if you:** have an infection or fever, are pregnant or plan to become pregnant, and are breastfeeding or plan to breastfeed. It is not known if ULTOMIRIS will harm your unborn baby or if it passes into your breast milk. You should not breastfeed during treatment and for 8 months after your final dose of ULTOMIRIS.

**Tell your doctor about all the vaccines you receive and medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements which could affect your treatment.

**If you have PNH and you stop receiving ULTOMIRIS, your doctor will need to monitor you closely for at least 16 weeks after you stop ULTOMIRIS. Stopping ULTOMIRIS may cause breakdown of your red blood cells due to PNH. Symptoms or problems that can happen due to red blood cell breakdown include: drop in your red blood cell count, tiredness, blood in your urine, stomach-area (abdomen) pain, shortness of breath, blood clots, trouble swallowing, and erectile dysfunction (ED) in males.**

**If you have aHUS, your doctor will need to monitor you closely for at least 12 months after stopping treatment for signs of worsening aHUS or problems related to a type of abnormal clotting and breakdown of your red blood cells called thrombotic microangiopathy (TMA). Symptoms or problems that can happen with TMA may include: confusion or loss of consciousness, seizures, chest pain (angina), difficulty breathing and blood clots or stroke.**

**What are the possible side effects of ULTOMIRIS?**

**ULTOMIRIS can cause serious side effects including infusion-related reactions.** Symptoms of an infusion-related reaction with ULTOMIRIS may include lower back pain, tiredness, feeling faint, discomfort in your arms or legs, or bad taste. Tell your doctor or nurse right away if you develop these symptoms, or any other symptoms during your ULTOMIRIS infusion that may mean you are having a serious infusion reaction, including: chest pain, trouble breathing or shortness of breath, swelling of your face, tongue, or throat, and feel faint or pass out.

**The most common side effects of ULTOMIRIS in people treated for PNH are upper respiratory tract infection and headache.**

**The most common side effects of ULTOMIRIS in people with aHUS are upper respiratory tract infection, diarrhea, nausea, vomiting, headache, high blood pressure and fever.**

**The most common side effects of ULTOMIRIS in people with gMG are diarrhea and upper respiratory tract infection.**

Tell your doctor about any side effect that bothers you or that does not go away. These are not all the possible side effects of ULTOMIRIS. For more information, ask your doctor or pharmacist. Call your doctor right away if you miss an ULTOMIRIS infusion or for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

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

**Notes**

**gMG**

gMG is a rare autoimmune disorder characterized by loss of muscle function and severe muscle weakness.6

Eighty percent of people with gMG are AChR antibody positive meaning they produce specific antibodies (anti-AChR) that bind to signal receptors at

the neuromuscular junction (NMJ), the connection point between nerve cells and the muscles they control. 2-6 This binding activates the complement system, which is essential to the body's defense against infection, causing the immune system to attack the NMJ.6 This leads to inflammation and a breakdown in communication between the brain and the muscles.6

gMG can occur at any age, but it most commonly begins for women before the age of 40 and for men after the age of 60.8-10 Initial symptoms may include slurred speech, double vision, droopy eyelids and lack of balance; these can often lead to more severe symptoms as the disease progresses such as, impaired swallowing, choking, extreme fatigue and respiratory failure.11-12

**CHAMPION-MG**

The global Phase III randomized, double-blind, placebo-controlled, multicenter 26-week trial evaluated the safety and efficacy of ULTOMIRIS in adults with gMG. The trial enrolled 175 patients across North America, Europe, Asia-Pacific and Japan. Participants were required to have a confirmed myasthenia gravis diagnosis at least six months prior to the screening visit with a positive serologic test for anti-AChR antibodies, MG-ADL total score of at least 6 at trial entry and Myasthenia Gravis Foundation of America Clinical Classification Class II to IV at screening. Patients could stay on stable standard of care medicines, with a few exceptions, for the duration of the randomized control period.13

Patients were randomized 1:1 to receive ULTOMIRIS or placebo for a total of 26 weeks. Patients received a single weight-based loading dose on Day 1, followed by regular weight-based maintenance dosing beginning on Day 15, every eight weeks. The primary endpoint of change from baseline in the MG-ADL total score at Week 26 was assessed along with multiple secondary endpoints evaluating improvement in disease-related and quality-of-life measures.

Patients who completed the randomized control period were eligible to continue into an open-label extension period evaluating the safety and efficacy of ULTOMIRIS, which is ongoing.

**ULTOMIRIS**

ULTOMIRIS (ravulizumab-cwvz), the first and only long-acting C5 complement inhibitor, offers immediate, complete and sustained complement inhibition. The medication works by inhibiting the C5 protein in the terminal complement cascade, a part of the body's immune system. When activated in an uncontrolled manner, the complement cascade over-responds, leading the body to attack its own healthy cells. ULTOMIRIS is administered intravenously every eight weeks in adult patients, following a loading dose.

ULTOMIRIS is approved in the US for the treatment of certain adults with gMG.

ULTOMIRIS is also approved in the US, EU and Japan for the treatment of certain adults and children with PNH.

Additionally, ULTOMIRIS is approved in the US, EU and Japan for certain adults and children with aHUS to inhibit complement-mediated thrombotic microangiopathy.

As part of a broad development program, ULTOMIRIS is being assessed for the treatment of additional hematology and neurology indications.

**Alexion**

Alexion, AstraZeneca Rare Disease, is the group within AstraZeneca focused on rare diseases, created following the 2021 acquisition of Alexion Pharmaceuticals, Inc. As a leader in rare diseases for nearly 30 years, Alexion is focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and commercialization of life-changing medicines. Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its development efforts on hematology, nephrology, neurology, metabolic disorders, cardiology and ophthalmology. Headquartered in Boston, Massachusetts, Alexion has offices around the globe and serves patients in more than 50 countries. For more information, please visit www.alexion.com.

**About AstraZeneca**

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialization of prescription medicines in Oncology, Rare Diseases and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information, please visit www.astrazeneca-us.com and follow us on Twitter @AstraZenecaUS.

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