ULTOMIRIS® (ravulizumab-cwvz) Treatment Initiation

A Guide to Meningococcal Vaccinations

Helpful information on the required vaccinations your patients need throughout treatment with ULTOMIRIS

INDICATION

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

SELECT IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

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

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

Because of the risk of serious meningococcal infections, ULTOMIRIS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called ULTOMIRIS REMS.

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

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

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

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

Meningococcal vaccinations and ULTOMIRIS® (ravulizumab-cwvz):

What you need to know

Vaccinations are an important part of treatment with ULTOMIRIS

Life-threatening meningococcal infections have occurred in patients treated with ULTOMIRIS. The use of ULTOMIRIS increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis).[1]

Signs and symptoms of meningococcal infection/sepsis include[1]:

- Headache with nausea or vomiting
- Headache and fever
- Headache with a stiff neck or back
- Fever with or without a rash
- Confusion
- Muscle aches with flu-like symptoms
- Eyes sensitive to light

Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Monitor patients for early signs of meningococcal infections and evaluate patients immediately if an infection is suspected. Meningococcal infections may become rapidly life-threatening or fatal if not recognized and treated early. Consider discontinuation of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection.[1]

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS, (continued)
Serious Meningococcal Infections, (continued)

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

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

ULTOMIRIS REMS

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

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

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

Other Infections

Patients may have increased susceptibility to infections, especially with encapsulated bacteria, such as infections caused by *Neisseria meningitidis* but also *Streptococcus pneumoniae*, *Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*. If ULTOMIRIS is administered to patients with active systemic infections, monitor closely for worsening infection.

Thromboembolic Event Management

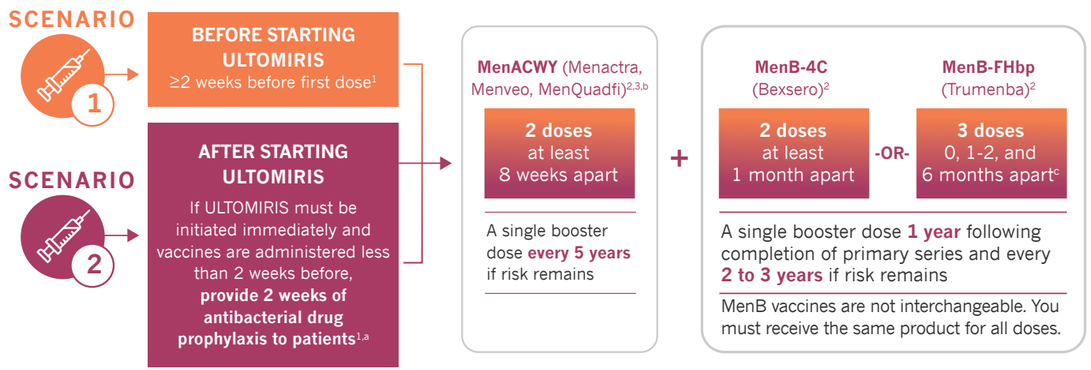
The effect of withdrawal of anticoagulant therapy during treatment with ULTOMIRIS has not been established. Treatment should not alter anticoagulant management.

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

How to approach vaccination in patients starting ULTOMIRIS®

When immunizing ULTOMIRIS patients against meningococcal infections, there are 2 potential scenarios[1]

- The 2022 Advisory Committee on Immunization Practices (ACIP) recommends the following meningococcal vaccination schedules for patients with persistent complement component deficiency or in patients receiving complement inhibitors, including patients receiving ULTOMIRIS[2]



[a]Several antibiotics are available for the treatment of meningococcal disease, including ceftriaxone, cefotaxime, and, when the diagnosis is confirmed, penicillin.[4]
[b]Menactra distribution is being discontinued.[5]
[c]For MenB-FHbp, if dose 2 was administered at least 6 months after dose 1, dose 3 is not needed.[2]

Vaccinate for meningococcal disease according to the most current ACIP recommendations for patients with complement deficiencies. Administer booster doses to patients in accordance with ACIP recommendations, considering the duration of ULTOMIRIS therapy.[1]

Immunize patients without a history of meningococcal vaccination at least 2 weeks prior to receiving the first dose of ULTOMIRIS. Patients who initiate ULTOMIRIS treatment less than 2 weeks after receiving meningococcal vaccine(s) must receive appropriate prophylactic antibiotics until 2 weeks after vaccination.[1]

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 Prescribing Information for complete details, including vaccine Warnings, Precautions, and Contraindications.

- If your patient received meningococcal vaccines in the past, they might need additional vaccination before starting ULTOMIRIS[2]
- 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[6]
- To help reduce the risk of meningococcal infections, the complete series for the MenACWY and MenB vaccines should be administered. Booster doses for the MenACWY vaccines are currently recommended every 5 years if a patient remains on ULTOMIRIS. Booster doses for the MenB vaccines are recommended 1 year following completion of the series and every 2 to 3 years if risk remains[2]

Access the latest adult vaccination recommendations from ACIP by visiting **CDC.gov/vaccines/schedules/hcp/imz/adult.html**.

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Additional steps required to start your patients on ULTOMIRIS®

1 **Enroll in the ULTOMIRIS (ravulizumab-cwvz) Risk Evaluation and Mitigation Strategy (REMS) program**

Due to the risk of meningococcal infections, ULTOMIRIS is available only through a restricted program under a REMS called ULTOMIRIS REMS. Under the ULTOMIRIS REMS, prescribers must enroll in the program. Prescribers must counsel patients about the risk of meningococcal infection/sepsis, provide patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccines.

Enrollment in the ULTOMIRIS REMS and additional information on the requirements are available at www.ultomirisrems.com or 1-888-765-4747.

2 **Give your adult patients an ULTOMIRIS Patient Safety Card and instruct them to carry it at all times**

This card identifies the signs and symptoms of meningococcal infection and advises patients to seek immediate medical attention if these signs or symptoms occur. Patients are recommended to carry this card for at least 8 months after discontinuing ULTOMIRIS due to increased risk of meningococcal infection.

Talk to your patients about OneSource™

OneSource is a comprehensive, complimentary, and personalized patient support program offered by Alexion that provides education, health insurance navigation, community connections, and ongoing support to patients and caregivers. OneSource can provide information about meningococcal vaccinations and can help your patients locate a vaccination center. OneSource is not mandatory for patients receiving ULTOMIRIS.

Contact your ULTOMIRIS representative for additional information on starting adult patients on ULTOMIRIS.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS, (continued)

Infusion-Related Reactions

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

ADVERSE REACTIONS

Most common adverse reactions in adult patients with gMG (incidence ≥10%) were diarrhea and upper respiratory tract infection. Serious adverse reactions were reported in 20 (23%) of patients treated with ULTOMIRIS and in 14 (16%) patients receiving placebo. The most frequent serious adverse reactions were infections reported in at least 8 (9%) patients treated with ULTOMIRIS and in 4 (4%) patients treated with placebo. Of these infections, one fatal case of COVID-19 pneumonia was identified in a patient treated with ULTOMIRIS and one case of infection led to discontinuation of ULTOMIRIS.

DRUG INTERACTIONS

Plasma Exchange, Plasmapheresis, and Intravenous Immunoglobulins

Concomitant use of ULTOMIRIS with plasma exchange (PE), plasmapheresis (PP), or intravenous immunoglobulin (IVIg) treatment can reduce serum ravulizumab concentrations and requires a supplemental dose of ULTOMIRIS.

Neonatal Fc Receptor Blockers

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

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

References: 1. ULTOMIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. **2.** Recommended adult immunization schedule for ages 19 and older. Centers for Disease Control and Prevention. Updated February 17, 2022. Accessed February 22, 2022. https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf **3.** Meningococcal vaccination: what everyone should know. Centers for Disease Control and Prevention. Updated October 12, 2021. Accessed February 10, 2022. https://www.cdc.gov/vaccines/vpd/mening/public **4.** Mbaeyi SA, et al; Advisory Committee on Immunization Practices. Centers for Disease Control and Prevention; 2020. Accessed August 6, 2022. https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6909a1-H.pdf **5.** Transition from Menactra to MenQuadfi Meningococal Conjugate Vaccine; 2022. Accessed October 13, 2022. Available at: https://portal.ct.gov/-/media/Departments-and-Agencies/DPH/dph/infectious_diseases/immunization/CVP-2020/2022-CVP-Communications/update-menactra-discontinuation-2-24-22.pdf. **6.** Administering meningococcal vaccines. Centers for Disease Control and Prevention. Updated October 12, 2021. Accessed August 6, 2022. https://www.cdc.gov/vaccines/vpd/mening/hcp/administering-vaccine.html

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