ULTOMIRIS® (ravulizumab-cwvz)

SOLIRIS® (eculizumab)

ULTOMIRIS and SOLIRIS REMS

Healthcare Provider Safety Brochure

This brochure provides information for healthcare providers who will prescribe or dispense ULTOMIRIS® and SOLIRIS®.

It describes:

- What are ULTOMIRIS and SOLIRIS?
- What is the ULTOMIRIS and SOLIRIS REMS?
- Prescriber Requirements
- Healthcare Setting and Pharmacy Requirements
- ULTOMIRIS and SOLIRIS REMS Resources
- Adverse Event Reporting

What are ULTOMIRIS and SOLIRIS?

ULTOMIRIS is indicated for the treatment of:

- Adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH).
- Adult and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).
- Adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.
- Adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive.

SOLIRIS is indicated for the treatment of:

- Patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.
- Patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.
- Generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.
- Neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

Limitation of Use

ULTOMIRIS and SOLIRIS are not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

Risk of Serious Meningococcal Infections

- ULTOMIRIS and SOLIRIS, complement inhibitors, increase 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 such as ULTOMIRIS and SOLIRIS.
- The initiation of ULTOMIRIS and SOLIRIS treatment is contraindicated in patients with unresolved serious *Neisseria meningitidis* infection.
- At least 2 weeks prior to administration of the first dose of ULTOMIRIS or SOLIRIS, complete or update meningococcal vaccination (for serogroups A, C, W, Y and B) according to current Advisory Committee on Immunization Practices (ACIP) recommendations for patients receiving a complement inhibitor.
- If urgent ULTOMIRIS or SOLIRIS therapy is indicated in a patient who is not up to date with meningococcal vaccines according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer meningococcal vaccines as soon as possible.
- 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. Promptly treat known infections.
- Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.
- Inform patients of the signs and symptoms of serious meningococcal infection and instruct patients to seek immediate medical care if these signs and symptoms occur.
- Consider interruption of ULTOMIRIS and SOLIRIS in patients who are undergoing treatment for serious meningococcal infection, depending on the risks of interrupting treatment in the disease being treated.

What is the ULTOMIRIS and SOLIRIS REMS?

A Risk Evaluation and Mitigation Strategy (REMS) is a program required by the Food and Drug Administration (FDA) to help ensure that the benefits of a drug outweigh its risks.

Because of the risk of serious meningococcal infections, ULTOMIRIS and SOLIRIS are available only through the ULTOMIRIS and SOLIRIS REMS, a restricted distribution program.

Prescriber Requirements

What do Prescribers Need to do When Prescribing ULTOMIRIS and SOLIRIS?

Healthcare providers who prescribe ULTOMIRIS and SOLIRIS must be specially certified. To become certified in the ULTOMIRIS and SOLIRIS REMS and prescribe ULTOMIRIS and SOLIRIS, prescribers must:

1. Review the ULTOMIRIS and SOLIRIS Prescribing Information, **Healthcare Provider Safety Brochure** (this document), **Patient Safety Card**, and **Patient Guide**.
2. Complete and submit the **Prescriber Enrollment Form** to the REMS:
    - online at www.UltSolREMS.com
    - by fax at 1-866-750-0481
    - by scanning and emailing to UltSol@AlexionREMS.com

Before initiating a patient's ULTOMIRIS or SOLIRIS treatment, prescribers must:

- Assess the patient for unresolved meningococcal infections and not initiate ULTOMIRIS or SOLIRIS in any patient with these infections.
- Assess the patient's vaccination status for meningococcal serogroups A, C, W, Y and B and vaccinate as needed according to the current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccinations in patients receiving a complement inhibitor.
- For patients who are not up to date with meningococcal vaccines at least two weeks prior to initiation of treatment and who must start ULTOMIRIS or SOLIRIS urgently: Provide the patient with a prescription for antibacterial drug prophylaxis.
- Counsel the patient using the **Patient Safety Card** and **Patient Guide**. Provide a copy of the materials to the patient.
    - The **Patient Guide** provides information for your patients about the risk of serious meningococcal infections including:
        - The need to complete or update their meningococcal vaccines for serotypes A, C, W, Y, and B at least 2 weeks prior to receiving the first dose of ULTOMIRIS or SOLIRIS or receive antibacterial drug prophylaxis if ULTOMIRIS or SOLIRIS must be initiated immediately, and they have not previously been vaccinated.
        - Additional vaccines may be necessary during treatment with ULTOMIRIS and SOLIRIS.
        - Meningococcal vaccines do not prevent all meningococcal infections.
    - The **Patient Safety Card** has important safety information for both patients and any healthcare providers that may see or treat your patient. It describes the following signs and symptoms which, if experienced, should prompt the patient to seek immediate medical care:
        - fever
        - fever and a rash
        - fever with high heart rate
        - headache with nausea or vomiting
        - headache and fever
        - headache with stiff neck or stiff back
        - confusion
        - eyes sensitive to light
        - muscle aches with flu-like symptoms

- Counsel the patient on the need to carry the **Patient Safety Card**. Instruct your patient to show the card to any healthcare provider involved in their care.
  - For ULTOMIRIS, instruct the patient to carry the **Patient Safety Card** at all times and for 8 months after their last dose.
  - For SOLIRIS, instruct the patient to carry the **Patient Safety Card** at all times and for 3 months after their last dose.

During ULTOMIRIS or SOLIRIS treatment, prescribers must:

- Assess the patient for early signs and symptoms of meningococcal infection and evaluate immediately if infection is suspected.
- Vaccinate patients as needed according to the current ACIP recommendations for meningococcal vaccinations for patients receiving a complement inhibitor.

At all times, prescribers must:

- Report adverse events suggestive of meningococcal infection, including the patient's clinical outcomes, to Alexion Pharmaceuticals, Inc. by phone at 1-844-259-6783.
- Comply with the ULTOMIRIS and SOLIRIS REMS requirements to maintain certification to prescribe.

Before dispensing, certified healthcare settings and pharmacies must assess the patient's vaccination status for up to date meningococcal vaccines for serogroups A, C, W, Y, and B according to the current ACIP recommendations including antibacterial drug prophylaxis, if needed. If you have not provided this information already, you may receive a call from the healthcare setting and pharmacy to collect information confirming that the patient has received the appropriate vaccinations or antibacterial drug prophylaxis.

Healthcare Setting and Pharmacy Requirements

What do Healthcare Settings and Pharmacies Need to do When Dispensing ULTOMIRIS and SOLIRIS?

ULTOMIRIS and SOLIRIS may only be dispensed by healthcare settings and pharmacies that are certified to dispense. To become certified, the healthcare setting and pharmacy must designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS on behalf of the healthcare setting or pharmacy. To become certified, the Authorized Representative must:

- Review the **Healthcare Provider Safety Brochure** (this document)
- Complete and submit the **Healthcare Setting and Pharmacy Enrollment Form** to the REMS:
  - online at www.UltSolREMS.com
  - by fax at 1-866-750-0481
  - by scanning and emailing to UltSol@AlexionREMS.com

By completing and submitting the Healthcare Setting and Pharmacy Enrollment Form, the Authorized Representative agrees to:

- Train all relevant staff involved in dispensing ULTOMIRIS and SOLIRIS using the **Healthcare Provider Safety Brochure**.
- Establish processes and procedures to assess the patient's vaccination status for up to date meningococcal vaccines for serogroups A, C, W, Y, and B according to the current Advisory Committee on Immunization Practices (ACIP) recommendations including antibacterial drug prophylaxis, if needed, before treatment initiation and document the findings.
- For patients who are not up to date with meningococcal vaccines when starting treatment: Establish processes and procedures to assess the patient's vaccination status for up to date meningococcal vaccines including antibacterial drug prophylaxis, if needed, before dispensing prescriptions up to 6 months after the first dose and document the findings.

Before dispensing the first dose, all healthcare setting and pharmacy staff must:

- Obtain authorization to dispense each prescription by contacting the REMS to verify the prescriber is certified.
- Assess the patient's vaccination status for up to date meningococcal vaccines for serogroups A, C, W, Y, and B including antibacterial drug prophylaxis, if needed, and document the findings through the processes and procedures established as a requirement of the REMS.

Before dispensing, up to 6 months after the first dose, all healthcare setting and pharmacy staff must:

- Obtain authorization to dispense each prescription by contacting the REMS to verify the prescriber is certified.
- For patients who are not initially up to date with meningococcal vaccines when starting treatment: Assess the patient's vaccination status for up to date meningococcal vaccines for serogroups A, C, W, Y, and B including antibacterial drug prophylaxis, if needed, and document the findings through the processes and procedures established as a requirement of the REMS.

Before dispensing, 6 months after the first dose and thereafter, all healthcare setting and pharmacy staff must:

- Obtain authorization to dispense each prescription by contacting the REMS to verify the prescriber is certified.

At all times, all healthcare setting and pharmacy staff must:

- Report adverse events suggestive of meningococcal infections to Alexion Pharmaceuticals, Inc. by phone at 1-844-259-6783.
- Not distribute, transfer, loan, or sell ULTOMIRIS or SOLIRIS, except to other certified healthcare settings or certified pharmacies.
- Maintain records of staff's completion of REMS training.
- Maintain records that all processes and procedures are in place and are being followed.
- Comply with audits carried out by Alexion Pharmaceuticals, Inc. or a third party acting on behalf of Alexion Pharmaceuticals, Inc., to ensure that all processes and procedures are in place and are being followed.

To maintain certification to dispense, any new Authorized Representative must:

- Enroll by completing and submitting this **Healthcare Setting and Pharmacy Enrollment Form** to the REMS.

ULTOMIRIS and SOLIRIS REMS Resources

Visit www.UltSolREMS.com or call 1-888-765-4747 to learn more about the ULTOMIRIS and SOLIRIS REMS.

Adverse Event Reporting

Report adverse events suggestive of meningococcal infections, including the patient's clinical outcomes, immediately to Alexion Pharmaceuticals, Inc. by phone at 1-844-259-6783.

You are encouraged to report other adverse reactions of ULTOMIRIS and SOLIRIS to Alexion Pharmaceuticals, Inc. by phone at 1-844-259-6783 or the FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

This brochure does not provide all risk information for ULTOMIRIS and SOLIRIS. Please see Prescribing Information for ULTOMIRIS and SOLIRIS, including BOXED WARNING regarding serious meningococcal infection for more detailed safety information.