

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**761108Orig1s000**

**REMS**

# Risk Evaluation and Mitigation Strategy (REMS) Document

## ULTOMIRIS (ravulizumab-cwvz) REMS Program

### I. Administrative Information

Application Number: BLA 761108

Application Holder: Alexion Pharmaceuticals Inc.

Initial REMS approval: 12/2018

### II. REMS Goals

The goals of the REMS are:

- To mitigate the occurrence and morbidity associated with meningococcal infections
- To educate healthcare providers and patients regarding:
  - the increased risk of meningococcal infections with ULTOMIRIS
  - the early signs of invasive meningococcal infections, and
  - the need for immediate medical evaluation of signs and symptoms consistent with possible meningococcal infections

### III. REMS Requirements

**Alexion Pharmaceuticals, Inc. must ensure that healthcare providers and patients comply with the following requirements:**

#### 1. Healthcare Providers who prescribe ULTOMIRIS must:

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To become certified to prescribe

1. Review the drug's Prescribing Information.
2. Review the following: [Patient Safety Card](#), [Prescriber Safety Brochure](#), and [Patient Safety Brochure](#).
3. Enroll in the REMS by completing the [Prescriber Enrollment Form](#) and submitting it to the REMS Program.

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Before treatment initiation at least 2 weeks prior to first dose

4. Assess the patient's meningococcal vaccine status and immunize patients.
5. Provide the patient with a prescription for a 2-week course of antibiotic prophylaxis if ULTOMIRIS must be started less than 2 weeks after the patient was immunized.

	6. Counsel the patient using the <a href="#">Patient Safety Card</a> and <a href="#">Patient Safety Brochure</a> . Provide a copy of the materials to the patient.
During treatment	7. Assess the patient for early signs of meningococcal infection and evaluate immediately, if infection is suspected.  8. Consider discontinuation of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection.  9. Revaccinate patients according to the Advisory Committee on Immunization Practices recommendations.
At all times	10. Report cases of meningococcal infection, including the patient's clinical outcomes to Alexion Pharmaceuticals, Inc.

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## 2. Patients who are prescribed ULTOMIRIS:

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Before treatment initiation, at least 2 weeks prior to the first dose	1. Get meningococcal vaccines as directed by your doctor.  2. Take antibiotics as directed by your doctor for two weeks after you get your vaccine if you have to start ULTOMIRIS right away.  3. Receive counseling from the prescriber using the <a href="#">Patient Safety Card</a> and <a href="#">Patient Safety Brochure</a> .
During treatment	4. Get meningococcal vaccines as directed by your doctor.
At all times	5. Inform the prescriber or get emergency medical care right away if you experience headache with nausea or vomiting; headache and a fever; headache with a stiff neck or stiff back; fever; fever and a rash; confusion; muscle aches with flu-like symptoms; eyes sensitive to light.  6. Have the <a href="#">Patient Safety Card</a> with you.

### **Alexion Pharmaceuticals, Inc. must provide training to healthcare providers who prescribe ULTOMIRIS.**

The training includes the following educational materials: [Prescriber Enrollment Form](#), [Prescriber Safety Brochure](#), [Patient Safety Brochure](#), and [Patient Safety Card](#). The training must be available online or in hardcopy format via mail.

### **To support REMS Program operations, Alexion Pharmaceuticals, Inc. must:**

1. Establish and maintain a REMS Program website, [www.ultomirisrems.com](http://www.ultomirisrems.com). The REMS program must include the capability to complete the prescriber certification and enrollment online, and the option to print the PI and REMS materials. All ULTOMIRIS product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS program website. The REMS program website must not link back to the promotional product website(s).
2. Make the REMS Program website fully operational and all REMS materials available through the website and call center by the date ULTOMIRIS is first commercially distributed.
3. Establish and maintain a REMS Program call center for REMS participants at (1-888-765-4747).
4. Establish and maintain a validated, secure database of all REMS participants who are certified in the ULTOMIRIS REMS Program.
5. Ensure prescribers are able to enroll by fax, mail, email, and online.
6. Provide [Patient Safety Brochure](#), [Patient Safety Card](#), and [Prescriber Safety Brochure](#) to prescribers annually.
7. Provide [Prescriber Enrollment Form](#), [Prescriber Safety Brochure](#), [Patient Safety Brochure](#), and [Patient Safety Card](#), and the Prescribing Information to health care providers who (1) attempt to prescribe ULTOMIRIS and are not yet certified or (2) inquire about how to become certified.

**To ensure REMS participants' compliance with the REMS Program, Alexion Pharmaceuticals, Inc. must:**

8. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: ULTOMIRIS distribution and dispensing and certification of prescribers. These records must be readily available for FDA inspections.
9. Establish a plan for addressing noncompliance with REMS Program requirements.
10. Monitor prescribers on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if non-compliance is identified including de-certification.

#### **IV. REMS Assessment Timetable**

Alexion Pharmaceuticals, Inc. must submit REMS assessments 6 months, 12 months, and annually thereafter from the date of the initial approval of the REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Alexion Pharmaceuticals, Inc. must submit each assessment so that it will be received by the FDA on or before the due date.

## **V. REMS Materials**

The following materials are part of the ULTOMIRIS REMS:

### **Enrollment Forms**

Prescriber:

1. [Prescriber Enrollment Form](#)

### **Training and Educational Materials**

Prescriber:

2. [Prescriber Safety Brochure](#)

Patient:

3. [Patient Safety Card](#)
4. [Patient Safety Brochure](#)

### **Other Materials**

5. [ULTOMIRIS REMS Program Website](#)

# PATIENT SAFETY CARD



## Important Safety Information for Patients Taking ULTOMIRIS™

ULTOMIRIS can lower the ability of your immune system to fight infections, **especially meningococcal infection, which requires immediate medical attention.** If you experience any of the following symptoms, you should immediately call your doctor or seek emergency medical care, preferably in a major emergency medical care center:

- headache with nausea or vomiting
- headache and a fever
- headache with a stiff neck or stiff back
- fever
- fever and a rash
- confusion
- muscle aches with flu-like symptoms
- eyes sensitive to light



**Get emergency medical care right away if you have any of these signs or symptoms and show this card.**

Keep this card with you at all times, even if you stop using ULTOMIRIS. Your risk of meningococcal infection may continue for several months after your last dose of ULTOMIRIS.



## Information for the Treating Physician



This patient has been prescribed **ULTOMIRIS (ravulizumab-cwvz) therapy, which increases the patient's susceptibility to meningococcal infection (*Neisseria meningitides*) or other general infections.**

- Meningococcal infections may become rapidly life-threatening or fatal if not recognized and treated early
- **Evaluate immediately if infection is suspected and treat with appropriate antibiotics if necessary**
- Contact prescribing physician (below) as soon as possible

For more information about ULTOMIRIS, please refer to the full Prescribing Information. In case of safety concerns, call **1-888-765-4747**. In case of adverse event experiences, call **1-844-259-6783**.

 Patients receiving **ULTOMIRIS** should carry this card at all times. Show this card to any doctor involved in your health care.

Patient Name \_\_\_\_\_

Prescriber Name \_\_\_\_\_

Prescriber Number \_\_\_\_\_



# What You Need to Know About ULTOMIRIS

## What is ULTOMIRIS?

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

## What are the serious risks of ULTOMIRIS?

ULTOMIRIS increases your chance of getting serious and life-threatening meningococcal infections.

Meningococcal infections may quickly become life threatening and cause death if not recognized and treated early.

## Getting Your Meningococcal Vaccine

- Meningococcal vaccines lower the risk of getting a meningococcal infection. However, this vaccine will not prevent all meningococcal infections.
- You must receive a meningococcal vaccination at least 2 weeks before your first dose of ULTOMIRIS unless you have already had this vaccine(s).
- If your doctor decides that urgent treatment with ULTOMIRIS is needed, you should receive the meningococcal vaccination as soon as possible.
- If you have not been vaccinated and you must take ULTOMIRIS right away, you should also receive 2 weeks of antibiotics with your vaccinations
- If you had a meningococcal vaccine in the past, you might need additional vaccination before you start ULTOMIRIS. Your doctor will decide if you need additional meningococcal vaccination.

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 with a stiff neck or stiff back
- Fever and a rash
- Muscle aches with flu-like symptoms
- Headache and a fever
- Fever
- Confusion
- Eyes sensitive to light

## Patient Safety Card

You will receive a Patient Safety Card from your health care provider.

- Carry this card at all times.
- **Show this card to any healthcare professional who treats you. This will help them diagnose and treat you quickly.**
- Get treatment right away for any symptoms of a meningococcal infection even if you do not have your card on you.

### PATIENT SAFETY CARD



#### Important Safety Information for Patients Taking ULTOMIRIS

ULTOMIRIS can lower the ability of your immune system to fight infections, **especially meningococcal infection, which requires immediate medical attention.** If you experience any of the following symptoms, you should immediately call your doctor or seek emergency medical care, preferably in a major emergency medical care center:



ULTOMIRIS is only available through a restricted program called the ULTOMIRIS REMS (Risk Evaluation and Mitigation Strategy). All prescribers must be specially certified. To become certified, prescribers must:

- 1) **Review** the ULTOMIRIS Prescribing Information, [Prescriber Safety Brochure](#), [Patient Safety Brochure](#) and the [Patient Safety Card](#).
- 2) **Enroll** in the ULTOMIRIS REMS by completing this form.
- 3) **Counsel** patients and provide them with the Patient Safety Brochure and Patient Safety Card.

**There are 2 pages to this form. Complete page 1. Read the agreements and sign page 2.** Return BOTH pages to ULTOMIRIS REMS.

You may complete this form

- online at [www.ultomirisrems.com](http://www.ultomirisrems.com)
- by fax at 1-877-580-2596 (ALXN)
- by scanning and emailing to [REMS@alexion.com](mailto:REMS@alexion.com)
- by mailing to Alexion Pharmaceutical, Inc. ATTN: REMS Program, 121 Seaport Boulevard, Boston, MA 02210

**Prescriber Information: (please print)**

First Name: \_\_\_\_\_ MI: \_\_\_\_ Last Name: \_\_\_\_\_

Prescriber NPI #: \_\_\_\_\_

Office Address: \_\_\_\_\_

City: \_\_\_\_\_ State: \_\_\_\_\_ ZIP: \_\_\_\_\_

Phone number: \_\_\_\_\_ Fax: \_\_\_\_\_

Email: \_\_\_\_\_

**Continue to page 2 to read the agreement and sign the form. You must return BOTH sides of this form.**

**By completing, signing and submitting this form, I acknowledge and agree that:**

- I have read and understand the ULTOMIRIS Prescribing Information (PI), *Prescriber Safety Brochure*, *Patient Safety Brochure*, and the *Patient Safety Card*.
- I understand the:
  - risk of meningococcal infections associated with ULTOMIRIS.
  - early signs of meningococcal infections
  - need for immediate medical evaluation of signs and symptoms with possible meningococcal infections
- Before treatment initiation at least 2 weeks prior to the first dose, I will:
  - Assess the patient's meningococcal vaccine status and immunize patients unless the risks of delaying ULTOMIRIS therapy outweigh the risks of developing meningococcal infection.
  - Provide the patient with a prescription for a two-week course of antibiotic prophylaxis if ULTOMIRIS must be started right away.
  - Counsel the patient about the signs and symptoms of meningococcal infections using the *Patient Safety Card*, and *Patient Safety Brochure*. Provide a copy of these materials to the patient. Instruct the patient to carry the *Patient Safety Card* at all times.
- During treatment, I will:
  - Assess the patient for early signs of meningococcal infection and evaluate immediately if infection is suspected.
  - Consider discontinuation of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infections.
  - Revaccinate patients according to the Advisory Committee on Immunization Practices recommendations.
- I will report cases of meningococcal infection including the patient's clinical outcomes to Alexion Pharmaceuticals, Inc.
- I understand that if I do not maintain compliance with the requirements of the ULTOMIRIS REMS, I will no longer be able to prescribe ULTOMIRIS.
- I understand that ULTOMIRIS REMS and its agents or contractors may contact me to support the administration of the ULTOMIRIS REMS.

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**Prescriber Signature**

**Date**

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**Print Name**

### Adverse Event Experiences

To report any suspected adverse event experience, contact Alexion Pharmaceuticals Inc. at 1.844.259.6783 or report to the FDA at 1.800.FDA.1088.

This guide does not provide all risk information for ULTOMIRIS.

Please see full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious meningococcal infection for more detailed safety information.

## ULTOMIRIS™ REMS

### Prescriber Safety Brochure

#### This brochure provides information on:

- The risk of meningococcal infection
- Patient meningococcal vaccination recommendations
- Monitoring Patients
- Counseling and providing your patients with a Patient Safety Brochure and Patient Safety Card

## Risk of Serious Meningococcal Infections

- Life-threatening meningococcal infections/sepsis have occurred in patients treated with ULTOMIRIS.

## Immunization

- Immunize all 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 risks of developing a meningococcal infection.
- Provide 2 weeks of antibacterial drug prophylaxis to patients if ULTOMIRIS must be initiated immediately and vaccines are administered less than two weeks before starting ULTOMIRIS therapy.
- Do not initiate ULTOMIRIS therapy in patients with unresolved serious *Neisseria meningitidis* infection or who are not vaccinated, unless the risks of delaying ULTOMIRIS treatment outweigh the risk of developing a meningococcal infection.
- If urgent ULTOMIRIS therapy is indicated in an unvaccinated patient, administer meningococcal vaccines(s) as soon as possible.
- Vaccination reduces, but does not eliminate, the risk of meningococcal infections.
- Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies. Revaccinate patients in accordance with ACIP recommendation, considering the duration of ULTOMIRIS therapy.

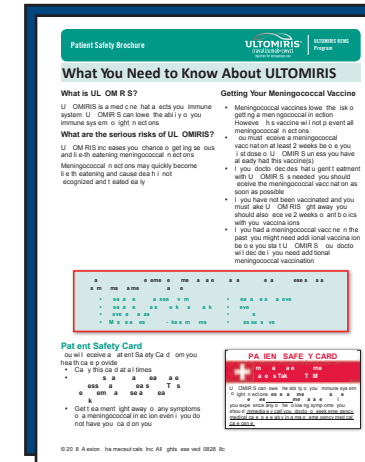
## Monitoring Patients

- Monitor patients for early signs of meningococcal infections, and evaluate immediately if infection is suspected.
- Consider discontinuation of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection.

## Patient Counseling

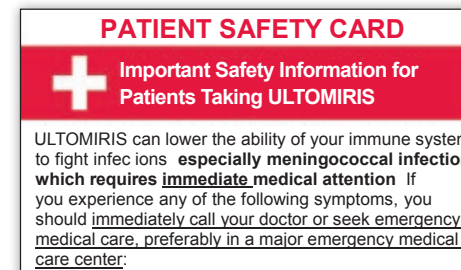
Counsel and provide your patients with both the **Patient Safety Brochure** and **Patient Safety Card**.

- Tell your patients about the risk of meningococcal infections and that this risk may continue for several weeks after the last dose of ULTOMIRIS.
- Instruct your patients to seek immediate medical attention if they develop any of the following symptoms:
  - Headache with nausea or vomiting
  - Headache with a stiff neck or stiff back
  - Fever and rash
  - Muscle aches with flu-like symptoms
  - Headache and a fever
  - Fever
  - Confusion
  - Eyes sensitive to light



## Patient Safety Card

The card has important safety guidance for both patients and any healthcare provider that may see or treat your patient for medical care.



- Discuss the importance and the proper use of this safety card with every patient.
- Tell your patients to carry this card at all times.**
- Instruct patients to show the card to any healthcare professional involved in their care.

## ULTOMIRIS REMS (Risk Evaluation and Mitigation Strategy)

A REMS is a program required by the FDA to manage known or potential serious risk associated with a drug program. ULTOMIRIS is available only through a restricted program under a REMS. Healthcare providers who prescribe ULTOMIRIS must be specially certified. Certification consists of review of REMS education materials and enrollment in the ULTOMIRIS REMS program.



Visit [www.ultomirisrems.com](http://www.ultomirisrems.com) or call 1-888-765-4747 to learn more about the ULTOMIRIS REMS. Enrollment can also be completed online at [www.ultomirisrems.com](http://www.ultomirisrems.com).

## Indication and Usage

ULTOMIRIS is indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

## Limitation of Use

ULTOMIRIS is not indicated in patients less than 18 years old.

# ULTOMIRIS REMS (Risk Evaluation and Mitigation Strategy)

## What is ULTOMIRIS REMS ?

A REMS (Risk Evaluation and Mitigation Strategy) is a program required by the Food and Drug Administration (FDA) to manage known or potential serious risks associated with a drug product

The purpose of the ULTOMIRIS REMS is to mitigate the occurrence and morbidity associated with meningococcal infections by informing healthcare providers and patients about the:

- Increased risk of meningococcal infections with ULTOMIRIS
- Early signs of invasive meningococcal infections, and
- Need for immediate medical evaluation of signs and symptoms consistent with possible meningococcal infections.

## PROGRAM REQUIREMENTS

ULTOMIRIS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).




HCPs who prescribe ULTOMIRIS must be specifically certified. Certification consists of review of REMS educational materials and enrollment in the ULTOMIRIS REMS program.

## HEALTHCARE PROVIDER CERTIFICATION

Certification in the ULTOMIRIS REMS includes the following steps:

STEP  
**01**

### Review the ULTOMIRIS REMS HCP Educational Materials

-  Prescribing Information
-  Prescriber Safety Brochure
-  Patient Safety Brochure
-  ULTOMIRIS Patient Safety Card

STEP  
**02**

### Enroll in the ULTOMIRIS REMS

[Click here to complete the ULTOMIRIS REMS Prescriber Enrollment online](#)

Or

[Print and sign the Prescriber Enrollment Form](#)

- Mail the form to Alexion Pharmaceutical, Inc.  
ATTN: REMS Program, 121 Seaport Boulevard, Boston, MA 02210
- Fax the form to ULTOMIRIS REMS at 1-877-580-2596
- Scan and email the form to [rems@alexion.com](mailto:rems@alexion.com)

## PATIENT COUNSELING

HCPs should

- Counsel patients using both the Patient Safety Brochure and Patient Safety Card. Provide these materials to your patients.
- Remind patients to carry the Patient Safety Card with them at all times
- Advise their patients that this safety card contains important safety information about the risk of meningococcal infection that they need to be aware of before they are given ULTOMIRIS and during their treatment with ULTOMIRIS
- Remind their patients to show this card to any doctor involved in their treatment
- Explain to their patients that if they cannot reach their doctor, they should go to the emergency room immediately and show the emergency room staff the ULTOMIRIS Patient Safety Card. Even if a patient stops using ULTOMIRIS, they should keep their ULTOMIRIS Patient Safety Card with them.

To order a ULTOMIRIS Patient Safety Card, contact ULTOMIRIS REMS at 1-888-765-4747

The Spanish versions of the Patient education material can be downloaded from below:

-  [Spanish ULTOMIRIS Patient Safety Card](#)
-  [Spanish Patient Safety Brochure](#)

## REPORTING ADVERSE EVENTS

HCPs should report all suspected adverse events, including reports of meningococcal infection by contacting Alexion Pharmaceuticals, Inc. at 1-844-259-6783 or reporting the information to the FDA MedWatch Reporting System by phone at 1.800.FDA.1088 (1.800.332.1088) or by mail using Form 3500 at <http://www.fda.gov/MedWatch>



**DOWNLOAD THE  
PATIENT SAFETY CARD**




**DOWNLOAD PATIENT  
SAFETY BROCHURE**




### ULTOMIRIS REMS

Contact us

 **Phone**  
1-888-765-4747

 **FAX**  
1-877-580-2596 (ALXN)

 **Hours of Operation**  
Monday – Friday  
8:30 am – 5:00 pm  
Eastern Time

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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
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/s/  
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AMY E MCKEE  
12/21/2018