

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

Most Recent REMS Update: 04/2020

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:

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.

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 [Patient Safety Card](#) and [Patient Safety Brochure](#). 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.

2. Patients who are prescribed ULTOMIRIS:

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 [Patient Safety Card](#) and [Patient Safety Brochure](#).

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 [Patient Safety Card](#) 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. 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 (12/21/2018). 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](#)