Risk Evaluation and Mitigation Strategy (REMS) Document

Soliris (eculizumab) REMS Program

I. Administrative Information

Application Number: BLA 125166
Application Holder: Alexion Pharmaceuticals Inc.
Initial REMS Approval: 06/2010
Most Recent REMS Update: 04/2020

II. REMS Goal(s)

The goals of the REMS are:

- To mitigate the occurrence and morbidity associated with meningococcal infections
- To educate Healthcare Professionals (HCPs) and Patients regarding:
  - the increased risk of meningococcal infections with Soliris
  - 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, patients, and wholesaler-distributors comply with the following requirements:

1. Healthcare Providers who prescriber Soliris 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	4. Assess the patient's meningococcal vaccine status and immunize

Reference ID: 4592667

weeks prior to first dose	patients. 5. Provide the patient with a prescription for a two-week course of antibiotic prophylaxis if Soliris 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. Discontinue Soliris in patients who are being treated for serious meningococcal infections. 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 Soliris:

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 Soliris right away. 3. Receive counseling from the prescriber using the Patient Safety Card and Patient Safety Brochure.

Reference ID: 4592667

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 Soliris.

The training includes the following educational material(s): 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.solirisrems.com. The REMS program website must include the capability to complete the prescriber certification or enrollment online, and the option to print the PI and REMS materials. All 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 30 calendar days of REMS modification (06/28/2019).
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 Soliris REMS Program.
5. Ensure prescribers are able to enroll by fax, mail, email, and online.
6. Provide the 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 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,

Reference ID: 4592667

including, but not limited to records of: Soliris 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 every two years beginning June 1, 2015. 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 Soliris 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. Soliris REMS Program Website

Reference ID: 4592667