Appendix I—REMS document

BLA 125166 Soliris® (eculizumab)
Recombinant Humanized Monoclonal Antibody

Alexion Pharmaceuticals, Inc.
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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S):

The goals of the REMS are:

- To limit the occurrence and morbidity associated with meningococcal infections
- To mitigate serious outcomes for patients who develop infection with *Neisseria meningitidis* and other systemic infections
- To impart important safety information before initiating treatment with Soliris and ensure proper use of Soliris while patients remain on therapy by:
    - informing and educating Healthcare Professionals (HCP) and Patients or Caregivers on the important safety information associated with the use of Soliris with an emphasis on meningococcal infection *(Neisseria meningitidis),* other serious infections, and possible serious hemolysis post-discontinuation

II. REMS ELEMENTS

A. Medication Guide

Alexion will ensure that a Medication Guide is dispensed with each prescription of Soliris and in accordance with 21 CFR 208.24.

The Medication Guide is part of the REMS and is appended.

B. Elements To Assure Safe Use

Healthcare providers who prescribe Soliris are specially certified and patients are monitored for adverse events under Food, Drug, and Cosmetic Act (FDCA) section 505-1.

a) Prescriber certification is based on attestation that the prescriber will:
    i) Counsel patients and provide the patient educational materials to the patient, including the Soliris Patient Safety Card and the Medication Guide;
    ii) Provide the Medication Guide to the patient prior to each infusion;
    iii) Review the educational materials (Soliris Patient Safety Card, Prescriber Introductory Letter, Prescriber Safety Brochure, *Important Safety Information about Soliris,* and Dosing and Administration Guide) and the product labeling and comply with the directions for safe use including ensuring meningococcal vaccination status;
    iv) Monitor patients following completion of the infusion and for signs and symptoms of serious infections; and
    v) Promptly report to the Sponsor at 1-800-765-4747 or to the FDA at 1-800-332-1088, cases of meningococcal infection, other serious infections, serious hemolysis post

discontinuation, including the patients' clinical outcomes, and deaths of patients receiving Soliris, including the cause of death, if known.

b) The prescriber will fax the completed enrollment form to 1-800-FAX ALXI, e-mail the completed form to OSSP@alxn.com, or mail the form to Alexion at Alexion Pharmaceuticals, 352 Knotter Dr, Cheshire, CT 06410, Attn: OneSource Safety Support Program.

c) Alexion will contact certified prescribers annually and provide the educational materials (Medication Guide, Soliris Patient Safety Card, Prescriber Safety Brochure, *Important Safety Information about Soliris,* Patient Safety Brochure, *Important Safety Information about Soliris,* and Dosing and Administration Guide).

d) The following materials are part of the REMS and are appended

(1) Soliris Patient Safety Card,

(2) Prescriber Introductory Letter

(3) Patient Safety Brochure, *Important Safety Information about Soliris*

(4) Prescriber Safety Brochure, *Important Safety Information about Soliris*

(5) Prescriber Enrollment Form

(6) Dosing and Administration Guide

e) Alexion will maintain a database of certified prescribers in the REMS program, and will ensure that Soliris is distributed only to certified prescribers. Alexion will ensure that prescribers comply with the requirements of the REMS Program.

C. Timetable for Submission of Assessments

REMS assessments will be submitted to the FDA every six months for one year, and then annually thereafter from the date of the 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 days before the submission date for that assessment. Alexion will submit each assessment so that it will be received by the FDA on or before the due date.

Appendix II - REMS Supporting Document