DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Our STN: BL 125166/44

APPROVAL
June 4, 2010

Alexion
Attention: Mary F. Lyons
Manager, Regulatory Affairs
352 Knotter Drive
Cheshire, CT 06410

Dear Ms. Lyons:

Please refer to your supplemental biologics license application (BLA) dated March 25, 2009, received March 27, 2009, submitted under Section 351 of the Public Health Service Act for Soliris® (eculizumab).

This supplemental application contains your proposed Risk Evaluation and Mitigation Strategy (REMS) for Soliris (eculizumab), submitted in response to our letter dated November 25, 2008.

This letter corrects the approval letter issued on June 4, 2010 which included incorrect telephone numbers in Appendix 1 of the Risk Evaluation and Mitigation Strategies (REMS) Document as follows:

B. Elements to Assure Safe Use
   a) v) Promptly report to the Sponsor at 1-800-765-4747 or to the FDA . . .”
   b) The prescriber will fax the completed enrollment form to 1-800-FAX ALXI, e-mail the completed form . . .”

We acknowledge that the correct telephone numbers are:

B. Elements to Assure Safe Use
   a) v) “Promptly report to the Sponsor at 1-888-765-4747 or to the FDA . . .”
   b) “The prescriber will fax the completed enrollment form to 1-877-580-2586 (ALXN), email the completed form . . .”

The effective date of approval will remain June 4, 2010.

We also refer to your correspondence submitted on April 30, 2010, which included revisions to your proposed REMS.

Under section 505-1 of FDCA, one element of a REMS that FDA may require is a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has

determined that Soliris® (eculizumab) poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Soliris® (eculizumab). FDA has determined that Soliris® (eculizumab) is a product for which patient labeling could help prevent serious adverse effects, that has serious risk(s) (relative to benefits) of which patients should be made aware because information concerning the risk(s) could affect patients' decisions to use, or continue to use Soliris® (eculizumab). Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Soliris® (eculizumab).

Pursuant to 505-1(f)(1), we have also determined that elements necessary to assure safe use are required as part of a REMS to mitigate the risk of meningococcal infection and hemolysis post-discontinuation listed in the labeling. The elements to assure safe use will assure that prescribers are educated about the safety risks.

Your proposed REMS is approved. The REMS consists of a Medication Guide, elements to assure safe use, and a timetable for submission of assessments of the REMS.

The REMS assessment plan should include but is not limited to the following information:

1) Assessment of enrollment and discontinuation data for prescribers
    a) The number of prescribers who enrolled (including new enrollment) and who discontinued enrollment in the OneSource Safety Support Program during the reporting period and cumulatively
    b) The number of prescribers actively prescribing Soliris during the reporting period
    c) The number of prescribers who have ordered/prescribed Soliris who were not enrolled during the reporting period and cumulatively
2) An assessment of use data establishing the circumstances of the use of Soliris:
    a) The extent of use in the indicated population
    b) The extent of treatment for other reasons
    c) The extent of pediatric use
    d) The extent of meningococcal vaccination among patients
3) A narrative summary and analysis of the following adverse events during the reporting period:
    a) Meningococcal infection
    b) Serious infection
    c) Serious hemolysis post-discontinuation of Soliris
4) Medication Guide distribution data, including the number of Medication Guides dispensed in comparison to the number of prescriptions shipped during the reporting period, a report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24, a report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance.
5) An assessment of prescriber and patient understanding regarding the safe use of Soliris, i.e., the results of surveys administered to prescribers and patients. This will include any known

data about patients/prescribers who refuse to participate in the surveys, any known data about survey participants considered lost (drop-outs), basic demographics of patients completing questionnaires (age, gender) and prescribers (specialty, number of patients on Soliris compared to those not surveyed).

6) What is known about patients receiving Soliris, including the number of patients receiving Soliris, the number of patients who discontinued treatment with Soliris, a summary of the reasons for discontinuation, the number of patients enrolled in the OneSource Safety Support Program and receiving Soliris treatment (during the reporting period and cumulative), the number of patient person-years for enrolled patients on Soliris, the number of new patients enrolled during the reporting period, the number of patients who received Soliris who were not enrolled (during the reporting period and cumulative), and the number of patients who were lost to follow up (during the reporting period and cumulatively).

7) With respect to the REMS goals, an assessment of the extent to which the elements to assure safe use are meeting the goals or whether the goals or such elements should be modified.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(A), an assessment of the extent to which the elements to assure safe use are meeting the goal or goals to mitigate a specific serious risk listed in the labeling of the drug, or whether the goal or goals or such elements should be modified.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(B) and (C), requirements for information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 601.70 and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in Section 505-1(g)(2)(A) of the FDCA.

Prominently identify the submission containing the REMS assessments and/or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission:

STN 125166 REMS ASSESSMENT

NEW SUPPLEMENT FOR STN 125166
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)

FOR STN 125166
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

Please refer to http://www.fda.gov/cder/biologics/default.htm for information regarding therapeutic biological products, including the addresses for submissions.

If you have any questions, please contact the Regulatory Project Manager, Ebla Ali-Ibrahim, at (301) 796-3691 or the Safety Regulatory Project Manager, Diane Leaman, at (301) 796-1424.

Sincerely,

/Ann Farrell/
Ann Farrell, M.D.
Director
Division of Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Appendices:
REMS
Medication Guide