DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125326/S-60

SUPPLEMENT APPROVAL
PMR FULFILLMENT

Glaxo Group Limited d/b/a GlaxoSmithKline
Attention: Philip A. Witman, MPH, MPhil
Director, Global Regulatory Affairs - Oncology
P.O. Box 5089
1250 South Collegeville Road
Collegeville, PA 19426-0989

Dear Mr. Witman:

Please refer to your Supplemental Biologics License Application (sBLA), dated October 18, 2013, received October 18, 2013, submitted under section 351(a) of the Public Health Service Act for ARZERRA® (ofatumumab) Injection.

We acknowledge receipt of your amendments dated November 19, and 20, 2013; December 6, 10, and 23 (2), 2013; January 2, 6, 15, and 16, 2014; February 7, 12, 18 (2), 25, and 27, 2014; March 4, 7, 14, 19, 21, and 25, 2014; and April 1, 4 (2), 7, 8, 11, 14, 15, and 16, 2014.

This Prior Approval supplemental biologics application provides for:

- New indication: ofatumumab, in combination with chlorambucil, for the treatment of previously untreated patients with chronic lymphocytic leukemia (CLL) for whom fludarabine-based therapy is considered inappropriate.

- Postmarketing study to fulfill Postmarketing Requirement (PMR-1) to confirm the clinical benefit of Arzerra, and to convert the accelerated approval under Subpart E into full approval.

- Final immunology report for Postmarketing Requirement (PMR-3), “an assessment of anti-drug antibody (ADA) response to ofatumumab with a validated assay capable of sensitively detecting ADA responses in the presence of ofatumumab levels that are expected to be present at the time of patient sampling.”

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert), and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in MS Word format that includes the changes approved in this supplemental application.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels submitted on October 18, 2013, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)". Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labels for approved BLA 125326/S-60**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with final printed labeling (FPL) that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

SUBPART E FULFILLED

We approved this BLA under the regulations at 21 CFR 601 Subpart E for Accelerated Approval of Biological Products for Serious or Life-Threatening Illnesses. Approval of this supplement fulfills your commitments made under 21 CFR 601.41.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

We refer to your Supplemental Biologics License Application (sBLA) submitted under section 351 of the Public Health Service Act for ARZERRA (ofatumumab) Injection.

We have received your submission dated October 18, 2013, containing the final reports for the following postmarketing requirement and commitment listed in the October 26, 2009 approval letter for BLA 125326.

PMR-1: To submit a final report for ongoing clinical trial OMB110911, entitled, "A Phase 3 Open-label, Randomized, Multicenter Trial of Ofatumumab Added to Chlorambucil versus Chlorambucil Monotherapy in Previously Untreated Patients with Chronic Lymphocytic Leukemia" which is intended to verify the clinical benefit of ofatumumab through demonstration of a clinically meaningful effect on progression-free survival. The protocol for clinical trial OMB110911 was submitted to FDA on October 24, 2008 and began patient accrual on December 22, 2008. We also acknowledge receipt of the amended protocol submitted August 21, 2009.

The timetable you submitted on October 6, 2009 states that you will conduct this trial according to the following milestones:

Patient Accrual 50% Completed (222 pts)	by August 30, 2010
Patient Accrual 75% Completed (333 pts)	by March 30, 2011
Patient Accrual Completed	by November 30, 2011
Trial Completion Date:	by October 14, 2013
Final Report Submission:	by June 30, 2014

PMR-3: To conduct an assessment of anti-drug antibody (ADA) response to ofatumumab with a validated assay (required in PMR 2) capable of sensitively detecting ADA responses in the presence of ofatumumab levels that are expected to be present at the time of patient sampling. ADA response will be evaluated in at least 300 patients**,** including ofatumumab-treated patients enrolled in clinical trial OMB110911. The final report will include information on the level of ofatumumab in each patient's test sample at each sampling time point.

The timetable you submitted on October 6, 2009 states that you will conduct this assessment from clinical trial data according to the following milestones:

Patient Accrual Completed:	by November 30, 2011
Final Report Submission:	by December 31, 2013

We have reviewed your submission and conclude that the above requirements were fulfilled.

We remind you that there are postmarketing commitments listed in the October 26, 2009, June 1, 2010 and April 1, 2011 approval letters that are still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Laura Wall, Regulatory Project Manager, at (301) 796-2237.

Sincerely,

{See appended electronic signature page}

Ann T. Farrell, MD
Division Director
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Carton and Container Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ANN T FARRELL
04/17/2014