DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21743/S-018

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING COMMITMENT

OSI Pharmaceuticals, LLC
Attention: Derek Williams
Senior Director, Regulatory Affairs
Astellas Pharma Global Development, Inc.
1 Astellas Way
Northbrook, IL, 60062

Dear Mr. Williams:

Please refer to your Supplemental New Drug Application (sNDA) dated November 15, 2013, received November 16, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tarceva (erlotinib) tablets, 25mg, 100mg and 150mg.

We acknowledge receipt of your amendments dated December 7, 2012 (2); December 10, 2012; December 14, 2012; December 19, 2012; December 21, 2012; January 2, 2013; January 3, 2013; January 4, 2013, January 7, 2013; January 8, 2013; January 17, 2013; January 28, 2013; January 29, 2013; February 4, 2013; February 8, 2013; February 13, 2013; February 27, 2013; March 18, 2013; March 28, 2013; April 11, 2013; April 22, 2013; April 30, 2013; May 2, 2013; May 3, 2013; May 7, 2013; May 13, 2013; and May 14, 2013.

(b) (4)

This “Prior Approval” supplemental new drug application proposes a new indication for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test. Limitation of use: Safety and efficacy of TARCEVA have not been evaluated as first-line treatment in patients with metastatic NSCLC whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution.

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.

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 the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable because the disease/condition does not exist in children.

FULFILLMENT OF POSTMARKETING COMMITMENTS

We have also reviewed your final study report submission dated February 19, 2013 cross-referencing the study reports submitted November 15, 2012 in this supplement for the following postmarketing commitment listed in the April 16, 2010 approval letter.

1628-2 A Phase 3, multicenter, open-label, randomized trial of erlotinib (Tarceva®) treatment versus chemotherapy in patients with advanced non-small-cell carcinoma of the lung who present with mutations in the tyrosine kinase (TK) domain of the epidermal growth factor receptor (EGFR). The primary endpoint is progression-free survival in patients who present with mutations in the tyrosine kinase domain of the EGFR. Other endpoints include objective response, overall survival, location of progression, safety profile, gene mutation analysis of EGFR in serum and Quality of life (LCSS). Eligible patients have a histologic diagnosis of non-small-cell lung cancer (NSCLC), stage IV or stage IIIB with malignant pleural effusion or N3 tumors that have not received prior chemotherapy and are not candidates for thoracic irradiation, who present with exon 19 deletions or exon 21 mutations in the tyrosine kinase domain of EGFR.

We have reviewed your submission and conclude that the above commitment was fulfilled.

We remind you that there are postmarketing commitments listed in the April 16, 2010 approval letter that are still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

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

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. 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.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any

new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Karen Boyd, Regulatory Project Manager, at (301) 796-7032.

Sincerely,

{See appended electronic signature page}

Patricia Keegan, M.D.
Director
Division of Oncology Products 2
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

PATRICIA KEEGAN
05/14/2013