DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 208065/S-008

SUPPLEMENT APPROVAL

AstraZeneca Pharmaceuticals LP
Attention: Marilyn Tsourounis, Pharm.D., Ph.D.
Regulatory Affairs Director
1800 Concord Pike
Wilmington, DE 19803

Dear Dr. Tsourounis:

Please refer to your Supplemental New Drug Application (sNDA) dated October 18, 2017, received October 18, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tagrisso (osimertinib); 80 mg and 40 mg tablets.

This Prior Approval supplemental drug application provides for updates to the U.S. Prescribing Information (USPI) to:

- Revise the indication statement to allow for 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.

- Revise the Dosage and Administration, Patient Selection (2.1) subsection to allow for the selection of patients for first-line treatment of metastatic EGFR mutation-positive NSCLC based on the presence of an EGFR exon 19 deletions or exon 21 (L858R) substitution mutation in tumor specimens by an FDA-approved test [cobas® EGFR Mutation Test v2].

- Revise the Dosage and Administration, Dosage Modifications (2.4) subsection to remove the requirement for permanent discontinuation of Tagrisso in patients with asymptomatic left ventricular dysfunction that persists less than 4 weeks.

- Revise the Adverse Reactions (6) section to include the safety data from the FLAURA study, including laboratory abnormalities, and to remove safety information from single arm studies (AURA2 and AURA extension).

- Revise the Drug Interactions (7.3) Drugs that Prolong the QTc Interval subsection to include information regarding the effect of co-administration with medicinal products known to prolong the QTc interval.

- Revise the Clinical Studies (14) section to include a new subsection (14.1) Previously Untreated EGFR Mutation Positive Metastatic Non-Small Cell Lung Cancer subsection, to describe the data from the FLAURA study which demonstrated a statistically significant improvement in progression free survival (PFS) as compared to erlotinib or gefitinib and to remove the efficacy results from single arm studies (AURA2 and AURA Extension) supporting accelerated approval of Tagrisso for the treatment of patients with previously treated, EGFR mutation-positive, NSCLC.

In addition, the Patient Information was updated to reflect updates made in the package insert.

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.

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 and text for the patient 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 include 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 (which includes new salts and new fixed combinations), 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 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.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

3381-1 Submit the clinical report and datasets for the final analysis of overall survival, as well as updated duration of response data, for Study FLAURA (Protocol D5160C00007), "A Phase III, Double-Blind, Randomized Study to Assess the Efficacy and Safety of AZD9291 versus a Standard of Care Epidermal Growth Factor Receptor-Tyrosine Kinase Inhibitor as First-Line Treatment in Patients with Epidermal Growth Factor Receptor Mutation Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer," to update the label with mature duration of response and overall survival data.

The timetable you submitted via electronic mail on April 17, 2018, states that you will conduct this study according to the following schedule:

Study/Trial Completion:	06/2019
Final Report Submission:	12/2019

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:

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

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

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/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 NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Kristin Jarrell, Pharm.D., Regulatory Health Project Manager, at (301) 796-0137.

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(S):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
04/18/2018