DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022059/S-007 **ACCELERATED APPROVAL**

SmithKline Beecham (Cork) Ltd d/b/a GlaxoSmithKline
Attention: Richard Swenson, Ph.D., Senior Director
GlaxoSmithKline UP4110
1250 S. Collegeville Road, POB 5089
Collegeville, PA 19426-0989

Dear Dr. Swenson:

Please refer to your supplemental new drug application dated March 31, 2009, received March 31, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tykerb® (lapatinib) Tablets, 250 mg.

We acknowledge receipt of your submissions dated April 28, 2009; June 3, 2009; July 2, and 29, 2009; August 6, 2009; September 10, 11(2), 14, 18, 28, and 29, 2009; October 2, 7, 9, and 30, 2009; November 11, 2009; December 21, 2009; January 12, 14, 18, 21, 27(2), and 28, 2010.

Please also refer to our approval letter dated January 29, 2010, for supplements (S-003) and (S-006).

This supplemental new drug application provides for the use of Tykerb® (lapatinib) tablets in combination with letrozole tablets for the treatment of postmenopausal women with hormone receptor positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated. Tykerb® in combination with an aromatase inhibitor has not been compared to a trastuzumab-containing chemotherapy regimen for the treatment of metastatic breast cancer.

We completed the review of this supplemental application, as amended. It is approved under the provisions of accelerated approval regulations, 21 CFR 314.510, effective on the date of this letter, for use as recommended in the enclosed labeling text. Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

POSTMARKETING REQUIREMENTS UNDER 21 CFR 314.510 (SUBPART H)

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled trials to verify and describe clinical benefit. We remind you of the following post marketing requirements specified in your submission dated January 21, 2010. Submit clinical protocols for at least two trials to confirm the clinical benefit of treatment with

Tykerb® (lapatinib). These requirements, along with any completion dates, are listed below.

1586-1. A randomized trial comparing lapatinib in combination with trastuzumab and an aromatase inhibitor versus trastuzumab in combination with an aromatase inhibitor versus lapatinib in combination with an aromatase inhibitor in postmenopausal women with hormone receptor positive metastatic breast cancer that overexpresses the HER2 receptor.

Description of the trial: This will be a Phase 3 randomized clinical trial in postmenopausal women with hormone receptor positive metastatic breast cancer that overexpresses the HER2 receptor and who had prior neo-adjuvant/adjuvant trastuzumab and endocrine therapy. The primary endpoint will be superiority in overall survival comparing lapatinib in combination with trastuzumab and an aromatase inhibitor versus trastuzumab in combination with an aromatase inhibitor. The secondary efficacy endpoint will be overall survival comparing lapatinib in combination with trastuzumab and an aromatase inhibitor versus lapatinib in combination with an aromatase inhibitor.

The timetable you submitted on January 21, 2010, states that you will conduct this trial according to the following timetable:

Final Protocol Submission Date: May 31, 2010
Trial Completion Date: March 31, 2016
Final Report Submission Date: May 31, 2018

1586-2. EGF108919 is an ongoing collaborative trial between NCIC and GSK. It is a randomized trial comparing lapatinib in combination with a taxane versus trastuzumab in combination with a taxane in patients with metastatic breast cancer that overexpresses the HER2 receptor.

Description of the trial: This will be a Phase 3, randomized clinical trial in patients with metastatic breast cancer that overexpresses the HER2 receptor. Patients will be stratified by prior trastuzumab or taxane therapy, planned taxane treatment on study and liver metastases. The primary endpoint will be superiority in overall survival comparing lapatinib in combination with a taxane versus trastuzumab in combination with a taxane.

The timetable you submitted on January 21, 2010, states that you will conduct this trial according to the following timetable:

Final Protocol Submission May 31, 2010
Trial Completion Date: June 15, 2011
Final Report Submission Date: PFS: April 30, 2013
Final Survival Report Submission: July 31, 2016

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to these postmarketing requirements must be clearly designated "**Subpart H Postmarketing Requirements**."

We also remind you that, under 21 CFR 314.550, after the initial 120 day period following this approval, you must submit all promotional materials, including promotional labeling as well as advertisements, at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

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.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] 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. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "**SPL for approved NDA 022059/S-007.**"

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

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Kim J. Robertson, Consumer Safety Officer, at (301) 796-1441**.**

Sincerely,

{See appended electronic signature page}

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

Enclosure (label)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22059	SUPPL-7	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLINE	TYKERB TABLETS

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
01/29/2010