DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022059/S-011
NDA 022059/S-012

SUPPLEMENT APPROVAL

SmithKline Beecham (Cork) Ltd, Ireland d/b/a GlaxoSmithKline
Attention: Richard Swenson, Ph.D., Senior Director, Regulatory Affairs
c/o GlaxoSmithKline UP 4110
1250 S. Collegeville Road, POB 5089
Collegeville, PA 19426-0989

Dear Dr. Swenson:

Please refer to your Supplemental New Drug Application (sNDAs) dated April 12, 2010 (S-011); and April 28, 2010 (S-012); received April 12, and 29, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tykerb® (lapatinib) Tablets.

We acknowledge receipt of your amendments dated May 25, 2011(2) and July 26, 2011(2).

We also acknowledge receipt of your submissions dated December 15, 2009 (PMC 977-3) and April 9, 2010, (PMC 977-1) containing the postmarketing commitment final reports.

The "Prior Approval" (S-011) supplemental new drug application provides the addition of results of a number of drug-drug interaction studies to the Drug Interaction section of the Tykerb® full prescribing information, and revised text in the Clinical Pharmacology section of the Tykerb® full prescribing information regarding inhibitory effects of GW572016 on human renal transporters.

The "Changes Being Effected" (S-012) supplemental new drug application provides for the addition of text to ensure the safe use of the product; explicitly, to the Overdosage section of the Tykerb® full prescribing information.

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.

FULFILLMENT OF POSTMARKETING COMMITMENTS

We have received your submissions dated December 15, 2009 and April 9, 2010, containing the final reports for the following postmarketing commitments listed in the March 13, 2007 approval letter.

977-1 Description of Commitment: Based upon the ability of lapatinib to act as a CYP 3A4 inhibitor in vitro, GSK agrees to perform an in vivo drug interaction study of the ability of steady-state lapatinib dosing to alter the pharmacokinetics of a single dose of midazolam. A positive finding in this study may initiate a need for further studies.

Protocol Submission:	October 1, 2005
Study Start:	Ongoing
Final Report Submission:	June 2008

977-3 Description of Commitment: Based upon the ability of lapatinib to act as a Pgp inhibitor in vitro, GSK agrees to perform an in vivo drug interaction study of the ability of steady-state lapatinib dosing to alter the pharmacokinetics of a single dose of digoxin. A positive finding in this study may initiate a need for further studies.

Protocol Submission: September 2007
Study Start: November 2007
Final Report Submission: December 2009

We have reviewed your submissions and conclude that the above commitments were fulfilled.

We remind you that there are postmarketing requirements listed in the January 29, 2010 approval letter that are still open.

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, 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 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).

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 Kim J. Robertson, Regulatory Project Manager, at (301) 796-1441.

Sincerely,

{See appended electronic signature page}

Amna Ibrahim, M.D.
Deputy Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

ENCLOSURES:
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/

AMNA IBRAHIM
08/12/2011