DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021938/S-010, S-011, S-014, and S-015

SUPPLEMENT APPROVAL

Pfizer, Inc.
Attention: Ann Carey
Sr. Director-Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017

Dear Ms. Carey:

Please refer to your supplemental New Drug Applications (sNDA) dated July 10 and July 31, 2009, received July 10 and July 31, 2009, respectively; February 9, 2010, received February 9, 2010; and May 6, 2010, received May 6, 2010 submitted under section 505(b), of the Federal Food, Drug, and Cosmetic Act (FDCA) for Sutent® (sunitinib malate) Capsules, 12.5 mg, 25 mg, 37.5 mg, and 50 mg.

We acknowledge receipt of your submissions dated September 3 and 29, 2009; November 9, 2009; December 14, 2009; March 12, 2010; May 6 and 10, 2010, and June 29, 2010.

Reference is also made to our letter dated April 7, 2010 notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for Sutent® (sunitinib malate) Capsules. This information pertains to the risk of hepatotoxicity.

The Prior Approval supplemental new drug application (S-010) provides for updated safety and efficacy data for the final report for Protocol A6181034 (renal cell carcinoma) as well as updates from the final report for Protocol A6181004 (gastrointestinal stromal tumor).

The Changes Being Effected supplemental new drug application (S-011) provides for the addition of adverse events language to the ADVERSE REACTIONS, Post-marketing Experience section of the package insert (cases of renal impairment and/or failure, in some cases with fatal outcome, hypersensitivity reactions; including angioedema, and cases of fistula formation).

The Changes Being Effected supplemental new drug application (S-014) provides for the addition of postmarketing safety information to the WARNINGS AND PRECAUTIONS section (left ventricular dysfunction and hemorrhagic events), as well as to the ADVERSE REACTIONS, Post-marketing Experience section (cases of fatal hemorrhage associated with thrombocytopenia, and pulmonary embolism, in some cases with a fatal outcome).

The Prior Approval supplemental new drug application (S-015) provides for revisions to the labeling for Sutent® (sunitinib malate) Capsules consistent with our April 7, 2010 letter. The

agreed upon changes to the language included in our April 7, 2010, letter are as follows (additions are noted by double underline and deletions are noted by ~~strikethrough~~).

1. Addition of a Boxed Warning

WARNING: HEPATOTOXICITY

See full prescribing information for complete boxed warning

(b) (4) **Hepatotoxicity has been observed in clinical trials and post-marketing experience.** (b) (4) **- This hepatotoxicity may be severe and** (b) (4) **deaths have been reported.** ***[See Warnings and Precautions (5.1).]***

2. Addition of new section in **WARNINGS AND PRECAUTIONS** section entitled, "**5.1 Hepatotoxicity**" that included the following language:

   SUTENT has been associated with hepatotoxicity resulting in death and liver failure. Liver failure signs include jaundice, elevated transaminases and/or hyperbilirubinemia in conjunction with encephalopathy, coagulopathy, and/or renal failure. Monitor liver function tests (ALT, AST, bilirubin) before initiation of treatment, during each cycle of treatment, and as clinically indicated. SUTENT should be interrupted for Grade 3 or 4 hepatic related adverse events and discontinued if there is no resolution. Do not restart SUTENT if patients experience severe changes in liver function tests or have other signs and symptoms of liver failure.

   Safety in patients with ALT or AST >2.5 x ULN or, if due to liver metastases, >5.0 x ULN has not been established.

3. In Highlights, summarize hepatotoxicity under **WARNINGS AND PRECAUTIONS** as follows:

   Hepatotoxicity, including liver failure has been observed. Monitor liver function tests before initiation of treatment, during each cycle of treatment, and as clinically indicated. SUTENT should be interrupted for Grade 3 or 4 hepatic related adverse events and discontinued if there is no resolution. Do not restart SUTENT if patients experience severe changes in liver function tests or have other signs and symptoms of liver failure.

4. In Section **6.5**, **Pancreatic and Hepatic Function**, add the following as the last sentence:

   SUTENT has been associated with hepatotoxicity *[See Boxed Warning and Warnings and Precautions (5.1)].*

5. Conversion of the Patient Package Insert to a Medication Guide

We have completed our review of these supplemental applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), 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, except with the revisions listed, the enclosed labeling (text for the package insert, Medication Guide) 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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days from the date of this letter, amend all pending supplemental applications for this NDA, including pending CBE supplements, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format that includes the changes with the revisions listed approved in this supplemental application.

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

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FDCA authorizes FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). The details of the REMS requirements were outlined in our letter dated April 7, 2010.

Since Sutent® (sunitinib malate) Capsules was approved on January 26, 2006, we have become aware of Adverse Events Reporting System (AERS) reports of hepatotoxicity, including death, associated with Sutent® (sunitinib malate) Capsules. We considered this information to be "new safety information" as defined in section 505-1(b)(3) of FDCA.

Your proposed REMS, submitted on May 6, 2010, and appended to this letter, is approved. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS.

The REMS assessment plan should include but is not limited to the following:

a. An evaluation of patients' understanding of the serious risks of Sutent® (sunitinib malate) Capsules

Assessments of an approved REMS must also include, under section 505-1(g)(3)(B) and (C), information on the status of any post-approval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such post-approval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such post-approval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) including any significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

Prominently identify the submission containing the REMS assessments or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission:

NDA 021938
REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 021938
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 021938
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
5600 Fishers Lane
Rockville, MD 20857

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}

Robert L. Justice, M.D., M.S.
Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling
REMS

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21938	SUPPL-15	CP PHARMACEUTICALS INTERNATIONAL CV	SUTENT (SUNITINIB)
NDA-21938	SUPPL-14	CP PHARMACEUTICALS INTERNATIONAL CV	SUTENT (SUNITINIB)
NDA-21938	SUPPL-11	CP PHARMACEUTICALS INTERNATIONAL CV	SUTENT (SUNITINIB)
NDA-21938	SUPPL-10	CP PHARMACEUTICALS INTERNATIONAL CV	SUTENT (SUNITINIB)

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

/s/

ROBERT L JUSTICE
07/01/2010