



NDA 21-923/S-004  
NDA 21-923/S-005  
NDA 21-923/S-006  
NDA 21-923/S-007

Bayer Pharmaceuticals Corporation  
Attention: Yamin Wang, Ph.D.  
Associate Director, Global Regulatory Affairs/Therapeutic Area Oncology  
400 Morgan Lane  
West Haven, CT 06516

Dear Dr. Wang:

Please refer to your supplemental new drug applications dated November 17, 2006 (S-004); March 1, 2007 (S-005); June 12, 2007 (S-006) and June 20, 2007 (S-007), received respectively on November 20, 2006 (S-004); March 2, 2007 (S-005); June 13, 2007 (S-006) and June 20, 2007 (S-007), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nexavar (sorafenib) 200 mg tablets.

We acknowledge receipt of your submissions dated May 7, 2007 (S-004); August 16, August 17, August 28, August 29, September 10, September 11, September 19, October 3, October 5, and November 2, November 15 (facsimile) and November 16 (2 electronic), 2007.

We note that supplements 004, 005 and 006 have been superseded by supplement 007.

Supplemental new drug application 007 provides for the use of Nexavar (sorafenib) 200 mg tablets for the treatment of unresectable hepatocellular carcinoma.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the enclosed labeling text for the package insert and text for the patient package insert.

Within 21 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/oc/datacouncil/spl.html>, that is identical in content to the enclosed labeling text dated November 16, 2007. 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 supplement NDA 21-923/S-007."

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved supplement NDA 21-923/S-007.**" Approval of this submission by FDA is not required before the labeling is used.

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We have received your submission dated June 20, 2007, reporting on the following postmarketing commitments.

6. Complete the ongoing study examining rifampin's effects on sorafenib pharmacokinetics.

Protocol submission: October 3, 2005 (IND 60,453, serial number 1109)

Study start: October 27, 2005

Final report submission: June 2006

7. Complete the ongoing study examining sorafenib pharmacokinetics in patients with renal impairment.

Protocol submission: April 4, 2005 (IND 60,453, serial number 798)

Study start: June 3, 2005

Final report submission: September 2006

We have reviewed your submission and have concluded that the above commitments were fulfilled.

We remind you of your postmarketing study commitment #5 agreed upon in your submission dated December 19, 2005. This commitment, along with the completion dates agreed upon, is listed below.

5. Complete the ongoing investigation of biomarkers to identify patients who respond to sorafenib. This request will be fulfilled based on data from studies 100391 and 11213.

Study 100391

Protocol Submission: April 12, 2002 (IND 60,453, serial number 67)

Study start: September 25, 2002

Final report submission: September 2006

Study 11213

Protocol Submission: October 16, 2003 (IND 60,453, serial number 317)

Study start: November 15, 2003

Final report submission: September 2006

We remind you of your postmarketing study commitment #4 in your submission dated December 19, 2005. The original commitment is listed below.

4. Complete the ongoing study of the effect of sorafenib on paclitaxel (a CYP 2C8 substrate) pharmacokinetics: Study 100375

Protocol Submission: November 29, 2001 (IND 60,453, serial number 038)

Study Start: July 15, 2002

Final Report Submission: June 2006

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The above postmarketing study commitment has been revised and agreed upon per your November 15, 2007, letter and is listed below.

4. Complete the ongoing study of the effect of sorafenib on paclitaxel (a CYP 2C8 substrate) pharmacokinetics: Study 11988 (Phase 1 study with sorafenib in combination with carboplatin and paclitaxel to evaluate the safety and pharmacokinetics of this combination in patients with solid tumors).

Protocol Submission: November 29, 2006 (IND 60,453, serial number 2364)

Study Start: June 29, 2007

Final Report Submission: March 31, 2009

We also remind you of your postmarketing commitment agreed upon per your November 16, 2007, letter. This commitment, along with the completion dates agreed upon, is listed below.

8. Design and conduct a study of sorafenib in non-HCC patients with and without hepatic impairment in a sufficient number of subjects to determine the effect of hepatic impairment on differences in Cmax and AUC. The study should include a control group, a group with Child-Pugh A impairment, and a group with Child-Pugh B impairment, and if necessary, an additional group of impaired patients treated with an adjusted dose of sorafenib to maintain Cmax/AUC.

Protocol submission: February, 29, 2008

Study Start: October 31, 2008

Final Report Submission: March 31, 2011

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled **“Postmarketing Study Commitment Protocol”**, **“Postmarketing Study Commitment Final Report”**, or **“Postmarketing Study Commitment Correspondence.”**

Promotional materials should be submitted, in duplicate, directly to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Drug Marketing, Advertising, and Communications  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

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If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH  
Food and Drug Administration  
5515 Security Lane  
HFD-001, Suite 5100  
Rockville, MD 20852

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, please call Patty Garvey, Regulatory Project Manager, at (301) 796-1356.

Sincerely,

*{See appended electronic signature page}*

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

Enclosure

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Robert Justice  
11/16/2007 08:32:30 PM