DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-065

NDA APPROVAL

Bristol-Myers Squibb Company
5 Research Parkway
Signature 91, 3SIg-509
Wallingford, CT 06492

Attention: Heather Knight-Trent, PharmD
Director, Global Regulatory Sciences

Dear Ms. Knight-Trent:

Please refer to your new drug application (NDA) dated April 16, 2007, received April 16, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ixempra™ Kit (ixabepilone) for Injection.

We acknowledge receipt of your submissions dated June 27, July 6, 13, 17, August 7, 30, September 5, 6, 11, 14, 18, 20, 21, 24, October 3, 4, 5 and 10, 2007.

This new drug application provides for the use of Ixempra (ixabepilone) for Injection in combination with capecitabine for the treatment of patients with metastatic or locally advanced breast cancer resistant to treatment with an anthracycline and a taxane, or whose cancer is taxane resistant and for whom further anthracycline therapy is contraindicated. Anthracycline resistance is defined as progression while on therapy or within 6 months in the adjuvant setting or 3 months in the metastatic setting. Taxane resistance is defined as progression while on therapy or within 12 months in the adjuvant setting or 4 months in the metastatic setting.

This new drug application also provides for the use of Ixempra (ixabepilone) for Injection as monotherapy for the treatment of metastatic or locally advanced breast cancer in patients whose tumors are resistant or refractory to anthracyclines, taxanes, and capecitabine.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

This application was not taken to a meeting of the Oncologic Drugs Advisory Committee (ODAC) because, for the following reasons, we determined the application did not warrant ODAC review. The Office of Oncology Drug Products previously has accepted the endpoint of progression-free survival as an approval endpoint in the setting of refractory metastatic breast cancer. The two approved indications were supported by one large, well conducted randomized trial with clinically relevant and statistically significant findings, and several well conducted single arm trials. The toxicity profile is similar to that of other cytotoxic drugs, and the major

toxicities can be managed with dose modifications, dose interruption, and/or available supportive care measures as have been used previously with other cytotoxic drugs.

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/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert and text for the patient 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 20-065."

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

We remind you of your postmarketing study commitments in your submission dated October 4, 2007. These commitments are listed below.

1. To submit the complete study report and datasets for the ongoing clinical study CA163048 entitled "A Phase 3 Trial of Novel Epothilone BMS-247550 plus Capecitabine versus Capecitabine Alone in Patients with Advanced Breast CancerPreviously Treated with An Anthracycline and a Taxane" with a primary endpoint of overall survival following the collection of data for a prespecified number of events (deaths), or earlier if recommended by the independent data monitoring committee.

Protocol Submission:	June 2, 2003
Study Start:	November 11, 2003
Final Report Submission:	December, 2008

2. To submit the final study report and datasets for the study CA163046 "A Phase III Trial of Novel Epothilone BMS-247550 Plus Capecitabine Versus Capecitabine Alone in Patients With Advanced Breast Cancer Previously Treated With or Resistant To an Anthracycline and Who are Taxane Resistant" after collection of overall survival data following the prespecified number of deaths for a mature analysis.

Protocol Submission:	June 2, 2003
Study Start:	September 4, 2003
Final Report Submission and Datasets:	by October 2008

3. Submit the completed report for the rifampin drug-drug interaction evaluation and datasets for study CA163102.

Protocol Submission:	July 12, 2005
Study Start:	September 28, 2005
Final Report Submission:	by September 2009

4. An *in-vitro* assessment to determine if ixabepilone is a P-glycoprotein substrate or inhibitor needs to be conducted.

Protocol Submission:	Not applicable
Study Start:	April 2007
Final Report Submission:	by September 2009

5. To design, conduct and submit the completed study report and datasets for a study to assess the potential for ixabepilone to prolong the QT interval in patients.

Protocol Submission:	by May 2008
Study Start:	by September 2008
Final Report Submission:	by September 2009

6. Submit a packaging amendment to physically link the drug vial and diluent vial.

Protocol Submission:	by April 2008
Packaging Amendment Submission:	by April 2009

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 should be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) 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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

If you 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 an electronic copy of the letter to both this NDA and to the following address:

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

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Sharon Thomas, Regulatory Project Manager, at (301) 796-1994.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure

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

/s/

Karen Weiss

10/16/2007 02:55:24 PM