



JUL 2 2008

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Ms. Kendra Basler
Regulatory Affairs Associate
Abbott Vascular
Cardiac Therapies
3200 Lakeside Drive
Santa Clara, CA 95054-2807

Re: P070015
XIENCETTM V Everolimus Eluting Coronary Stent System
PROMUSTTM Everolimus Eluting Coronary Stent System
Filed: June 1, 2007
Amended: July 5, September 4, November 8, and December 13, 2007; February 20,
April 2, May 12, May 13, June 9, June 23, and June 26, 2008
Procode: NIQ

Dear Ms. Basler:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the XIENCETTM V Everolimus Eluting Coronary Stent System, which will also be distributed as the PROMUSTTM Everolimus Eluting Coronary Stent System. This device is indicated for improving coronary luminal diameter in patients with symptomatic heart disease due to *de novo* native coronary artery lesions (length \leq 28 mm) with reference vessel diameters of 2.5 mm to 4.25 mm. We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions described below and in the "Conditions of Approval" (enclosed).

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that, to ensure the safe and effective use of the device, the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the periodic report (often referred to as annual report) requirements outlined in the enclosure, you have agreed to provide the following data in a separate postapproval study report:

1. You should collect and report to the Agency on an annual basis clinical outcomes through 5 years post-procedure on at least 80% of patients enrolled (excluding those discontinued due to death) from SPIRIT FIRST, SPIRIT II, SPIRIT III, and SPIRIT IV. When appropriate or as requested by FDA, you should submit PMA supplements requesting approval to update your Instructions for Use (IFU) to include these data.
2. You should collect clinical data on the implantation of the PMA-approved, commercially-distributed XIENCE V product in the U.S. The trial should be statistically powered to evaluate the annual rates of stent thrombosis, and the rate of cardiac death plus myocardial infarction (MI) through five years in patients treated with the XIENCE V stent according to its labeled indications. These data are needed to evaluate whether the rate of stent thrombosis plateaus or increases over time, and to evaluate the impact of stent thrombosis on rates of cardiac death and MI. These data are also needed to evaluate the potential for rare adverse events related to the drug substance and/or drug carrier that could not be detected in your initial clinical trials. You should also collect additional data on clinical outcomes (including target lesion revascularization rates at 12 months post-implantation) associated with use of the XIENCE V 4.0 mm diameter stent to confirm the outcomes observed in the 4.0 mm Arm of the SPIRIT III trial.

You have proposed collecting these data from at least 5000 patients enrolled in the XIENCE V USA Postmarket Registry. FDA agrees that the registry protocol submitted in Supplement 97 of your Investigational Device Exemption (IDE), G050050, with the planned modifications to the statistical analysis plan, is acceptable. Please provide progress reports at 6, 12, 18, and 24 months and annually thereafter through 5 years with data from your U.S. registry. When appropriate or as requested by FDA, you should submit PMA supplements requesting approval to update your IFU to include these data. Please note that if subsequent data analyses identify areas of significant off-label use, you should submit an IDE to conduct an appropriate study to evaluate the off-label use.

3. You should conduct or participate in a study that will develop clinical data to identify the optimal duration of dual antiplatelet therapy following percutaneous intervention with the XIENCE V drug-eluting stent.

The issue of the optimal duration of dual antiplatelet therapy following PCI with drug-eluting stents (DES) remains a key question that has not been addressed by any clinical trials conducted to date on the Cordis Cypher DES, the Boston Scientific Taxus Express² DES, the Endeavor DES, or the XIENCE V DES. At the December 7 – 8, 2006 meeting of FDA's Circulatory System Devices Advisory Panel meeting on DES thrombosis, the Panel recommended that the labeling for all marketed DES include the then-current ACC/AHA/SCAI guidelines for dual anti-platelet therapy, which specified that patients should receive aspirin indefinitely and clopidogrel for a minimum of 3 or 6 months for the Cypher or Taxus stents, respectively, after implantation, with this duration extended to 12 months in patients who are at low risk for bleeding complications.

However, it is important to recognize that the current recommendation for an extended duration of clopidogrel use reflects a consensus opinion among experts within cardiovascular professional societies based on limited data, rather than on rigorous randomized clinical trials. Further, it is not clear that 12 months is the optimal maximum duration of a dual anti-platelet therapy. In fact, the ACC/AHA/SCAI guidelines were recently revised to specify that patients with low bleeding risks should receive clopidogrel for at least 12 months post-procedure. While extending the duration of clopidogrel use may decrease the risk of very late stent thrombosis events, this strategy may also result in an increased risk for major bleeding complications and involves lifestyle modifications, such as deferral of surgical and dental procedures that may affect a patient's health and overall quality of life. Finally, it is known that stent thrombosis can occur in some individuals despite the continued use of dual antiplatelet therapy. With these considerations in mind, it is imperative that the risks and benefits of continued clopidogrel use be evaluated to determine with greater precision the optimal duration of dual anti-platelet therapy to ensure that these patients receive the best care possible.

Based on the important public health impact of this information, as stated above, you should collect clinical data to identify the optimal duration of dual anti-platelet therapy following PCI with the XIENCE V stent. Such an evaluation should encompass a consecutively enrolled patient population or utilize an approach to enroll patients representative of the actual use of your commercialized product. You may wish to limit your investigation to the XIENCE V stent, or your study may involve pooling with other approved drug-eluting stents. You may also choose to collect these data in a manner that would satisfy, wholly or in part, condition #2 above. When appropriate or as requested by FDA, you should submit PMA supplements requesting approval to update your IFU to include these data. You should submit your proposed plan to address this issue within six months of the date of this letter.

As FDA views the investigation of the optimal duration of dual anti-platelet therapy as a DES class effect, we are requesting that manufacturers of other approved DES collect the same information.

4. You should comply with the commitments made in Amendment 11 related to the implementation of updated final product testing methodologies.

Expiration dating for this device has been established and approved at 12 months.

CDRH does not evaluate information related to contract liability warranties, however you should be aware that any such warranty statements must be truthful, accurate, and not misleading, and must be consistent with applicable Federal and State laws.

CDRH will notify the public of its decision to approve your PMA by making available a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at <http://www.fda.gov/cdrh/pmapage.html>. Written requests for this information can also be made

to the Dockets Management Branch. (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with any postapproval requirement constitutes a ground for withdrawal of approval of a PMA. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

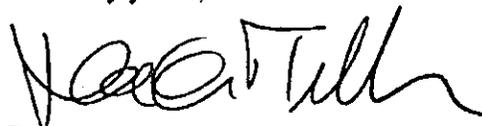
You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. The labeling will not routinely be reviewed by FDA staff when PMA applicants include with their submission of the final printed labeling a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Dr. Heather Agler at 240-276-4229.

Sincerely yours,



Donna-Bea Tillman, Ph.D., M.P.A.
Director
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

CONDITIONS OF APPROVAL

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e) or (f). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations that require a PMA supplement cannot be briefly summarized; therefore, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report (see below). FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

Alternate submissions permitted under 21 CFR 814.39(f) for manufacturing process changes include the use of a 30-day Notice. The manufacturer may distribute the device 30 days after the date on which the FDA receives the 30-day Notice, unless the FDA notifies the applicant within 30 days from receipt of the notice that the notice is not adequate.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

1. Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).
2. Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:
 - a. unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and
 - b. reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

1. A mix-up of the device or its labeling with another article.
2. Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and:
 - a. has not been addressed by the device's labeling; or
 - b. has been addressed by the device's labeling but is occurring with unexpected severity or frequency.

3. Any significant chemical, physical or other change or deterioration in the device, or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION.

The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984. This regulation was replaced by the reporting requirements of the Safe Medical Devices Act of 1990 which became effective July 31, 1996 and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to the FDA whenever they receive or otherwise become aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer or importer:

1. May have caused or contributed to a death or serious injury; or
2. Has malfunctioned and such device or similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for a PMA, the manufacturer shall submit the appropriate reports required by the MDR Regulation within the time frames as identified in 21 CFR 803.10(c) using FDA Form 3500A, i.e., 30 days after becoming aware of a reportable death, serious injury, or malfunction as described in 21 CFR 803.50 and 21 CFR 803.52 and 5 days after becoming aware that a reportable MDR event requires remedial action to prevent an unreasonable risk of substantial harm to the public health. The manufacturer is responsible for submitting a baseline report on FDA Form 3417 for a device when the device model is first reported under 21 CFR 803.50. This baseline report is to include the PMA reference number. Any written report and its envelope is to be specifically identified, e.g., "Manufacturer Report," "5-Day Report," "Baseline Report," etc.

Any written report is to be submitted to:

Food and Drug Administration
Center for Devices and Radiological Health
Medical Device Reporting
PO Box 3002
Rockville, Maryland 20847-3002

Additional information on MDR is available at <http://www.fda.gov/cdrh/devadvice/351.html>