Brief Summary of the Circulatory System Devices Panel Meeting – December 11, 2013

Introduction:

The Circulatory System Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on December 11, 2013 to make recommendations and vote on information related to premarket approval application P130013 regarding the Boston Scientific WATCHMAN Left Atrial Appendage Closure Therapy. The WATCHMAN Left Atrial Appendage Closure Therapy is a percutaneously delivered permanent cardiac implant placed in the left atrial appendage.

The sponsor has proposed the following Indications for Use:

WATCHMAN LAAC Therapy is indicated to prevent thromboembolism from the left atrial appendage. It may be considered for use in patients with non-valvular atrial fibrillation who are eligible for warfarin therapy to reduce the risk of stroke and systemic embolism based on $CHADS_2$ or CHA_2DS_2-VASc scores.

Panel Deliberations/FDA Questions:

Panel Question 1: WATCHMAN Device Acute Procedural Outcomes
The panel believed that CAP and PREVAIL trial data appropriately address concerns regarding acute implantation procedural outcomes.

Panel Question 2: Evaluation of the PREVAIL First Primary Endpoint
There were several panel members that have ongoing concerns about the analysis of the first primary endpoint of PREVAIL. Other panel members were swayed by the totality of data, and some believe that the totality of the data is favorable or reasonable. Overall, there was a mixed response but the panel was mostly in favor of using the totality of the data instead of just looking at the fact that PREVAIL did not meet the first primary endpoint.

Panel Question 3: Evaluation of the PREVAIL Second Primary Endpoint
The panel felt that the data presented for this endpoint largely mitigate concerns about ischemic stroke, but there was some residual concern over the rate of all strokes. Ultimately, the panel believed that the PREVAIL data alone in regard to stroke is inconclusive.

Panel Question 4: Evaluation of Major Bleeding Events
There was nearly unanimous agreement from the panelists that the device is not intended to address bleeding, and while the observed bleeding is non-trivial, it does not raise significant safety concerns. The panel also noted that the bleeding rates are fairly consistent with those observed in clinical practice for other interventional procedures. However, the panel would like to see more bleeding data from post approval studies, and the sponsor may want to reevaluate their post-implantation protocol to potentially reduce drug therapy.

Panel Question 5: Evaluation of Long-Term Safety and Effectiveness
The panel agreed that, using the data derived from long-term follow-up of PROTECT AF, there is reasonable assurance of safety and effectiveness with this device.

Panel Question 6: Proposed Indications For Use
The panel believed that the indications for use is not acceptable as written and needs to be more prescriptive. The panel suggested emphasis on warfarin therapy eligibility, $CHADS_2$/CHA_2DS_2-VASc scoring, and a personalized approach including consideration of patient preference regarding long-term anticoagulation therapy. The panel suggested adding the statement "and who have reason not to remain on chronic warfarin therapy" to the end of the current indications for use.

Panel Question 7: Evaluation of the Totality of the Data from the WATCHMAN trials (Overall Benefit/Risk Assessment)
Regarding question 7, the panel generally believed that it is reasonably certain that the WATCHMAN studies have supported the statement in 7a, that the acute procedural success and safety results are acceptable, and that the device is a clinically reasonable alternative to warfarin therapy for some patients already indicated for warfarin therapy.

Panel Question 8: Labeling
Regarding the labeling, the panel believed the following should be addressed:

- Should include a contraindication for those ineligible for anti-coagulation therapy;
- Should include a statement that there should be a reasonable expectation of patient survival;
- Should be consistent with clinical trial medication guidelines regarding use of anti-platelet therapy and anti-coagulation therapy; and
- Should include a detailed characterization of attributes for success from experienced centers and implanters.

Panel Question 9: Proposed Post Approval Study (PAS)
Regarding the proposed post approval study, the panel believed that it is generally appropriate. It is reasonable to have a single arm study, but the sample size should be larger, there should be consecutive enrollment, and the patient population should be representative of the intended population.

The panel recommended additional consideration of the following:

- A separate observational registry run by a professional organization to further examine this transformative technology;
- Oversampling of some of the newer sites coming into the study;
- Information regarding device dislodgement or damage; and
- Enrollment of larger numbers of women and minorities.

Vote:
The panel voted on the safety, effectiveness, and risk benefit ratio of the Boston Scientific WATCHMAN® Left Atrial Appendage Closure Therapy.

On Question 1, the panel voted 13/1 that the data show reasonable assurance that the Boston Scientific WATCHMAN® Left Atrial Appendage Closure Therapy is safe for use in patients who meet the criteria specified in the proposed indication.

On Question 2, the panel voted 13/1 that there is reasonable assurance that the Boston Scientific WATCHMAN® Left Atrial Appendage Closure Therapy is effective for use in patients who meet the criteria specified in the proposed indication.

On Question 3, the panel voted 13/1 that the benefits of the Boston Scientific WATCHMAN® Left Atrial Appendage Closure Therapy do outweigh the risks for use in patients who meet the criteria specified in the proposed indication.

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