



Brief Summary of the Circulatory System Devices Panel Meeting – July 20, 2011

Introduction:

The Circulatory System Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on July 20, 2011 to discuss, make recommendations, and vote on information related to PMA P100041 for the Edwards SAPIEN Transcatheter Heart Valve, model 9000TFX, sizes 23mm and 26mm and accessories.

Edwards Lifesciences is requesting an indication for transfemoral delivery of the SAPIEN THV in patients with severe aortic stenosis who have been determined by a cardiac surgeon to be inoperable for open aortic valve replacement and in whom existing co-morbidities would not preclude the expected benefit from correction of the aortic stenosis.

Panel Deliberations/FDA questions:

The Panel noted that the proposed indications for use statement was generally acceptable for this specific patient population (Cohort B) that are not candidates for open surgical aortic valve replacement, with the following additions to the existing language: the word “symptomatic” was added to the indications statement to adequately describe the patients in the trial; also, the Panel recommending specifically mentioning that the device could be implanted in a patient’s native valve as a way to address the lack of available data regarding the valve-in-valve implantation technique. There was also considerable discussion regarding available mechanisms for the sponsor, FDA, and clinical community to restrict commercial use of this device to the “inoperable” patient population studied in Cohort B.

The Panel generally agreed that the heterogeneity of the treatment options received by the Control group was not an issue due to the fact that it represented the standard of care. Some members expressed concern that the use of balloon aortic valvuloplasty (BAV) appeared to be higher than is normally done, and may have affected outcome, and should be noted in the labeling (Clinical Data section).

The Panel commented on the clinical significance of the increase of neurological adverse events occurring in the SAPIEN arm as compared to the Control arm. The Panel expressed concern regarding the neurological adverse event risk observed in the study, and agreed that the impact of stroke on the patient population needs to be correlated with the patient’s actual quality of life. The patient brochure should include explicit definitions of “neurological event” versus “stroke,” and modifications to the labeling should be made so that physicians and patients are clearly aware of these potential risks with use of this device. The Panel also agreed that the stroke risk is a complicated multifactorial issue that needs to be examined closely in the post-market setting.

The Panel commented on the proposed anticoagulation/antiplatelet protocol included in the post-approval study protocol, stating that it is a good starting point; however, a standardized anticoagulation/antiplatelet protocol should be implemented for all patients that receive this device, especially due to the risk of stroke. Over time, the sponsor should revisit whether or not any changes should be made to this protocol.

The Panel stated that the clinical significance of the vascular complications observed in patients treated with the SAPIEN THV is hard to translate due to the lack of data presented; however, the complications do not show a true signal that would raise concerns. Physician training, device experience, and advancements in technology could mitigate some of these vascular complications.

The Panel members commented that the training program for new practitioners proposed by the sponsor, which includes a minimum number of proctored procedures, bi-weekly complicated procedure meetings, and centers of excellence, is a good starting point. Accreditation by societies will also compliment the training program.

The Panel commented that we do have experience with pericardial bovine valves and that they are pretty robust in performance. The hemodynamic performance data presented so far, which include measurements of mean gradients, effective orifice area, and aortic regurgitation, support the notion that the device performs as intended. The hemodynamic performance should be monitored in the Post Approval Study to verify durability.

The Panel addressed the potential valve-in-valve use with the SAPIEN by stating that the labeling should include warnings that there is no data supporting valve-in-valve use. The Panel stressed that data should be collected in the form of a postmarket registry for all valve-in-valve use, if it should occur after device approval. In addition, the Panel recommended stipulating that the indication statement specify that the valve should be used to treat native aortic valve stenosis.

The Panel discussed the learning curve associated with TAVI, stating that patient selection should be strict and that new enrollment centers should be critiqued closely, by utilizing a phased enrollment model to avoid enrolling 75 centers at once. The Panel agreed that quality of life data should be collected in both proposed post-approval studies through 5 years of follow-up.

The Panel agreed that the PAS 2 registry should have a rigorous data collection at all 75 centers. The safety and effectiveness time points of 30 days and 1 year seemed appropriate; however, the patients should be followed out to 5 years. A 20% delta was recommended for the primary endpoints. A stroke neurologist should be on the DSMB. Some panelists felt that 20 patients per site may be too few in order to capture the learning curve. There was also consensus on the part of the Panel that all patients receiving this device should be enrolled in a national registry as a mechanism to capture overall device performance and monitor the patient population who receives the device.

Vote:

Question 1

The Panel voted **7 to 3 that the data does show** that there is reasonable assurance that the Edwards SAPIEN™ Transcatheter Heart Valve is safe for use in patients with severe symptomatic aortic stenosis who meet the criteria specified in the proposed indication.

Question 2

The Panel voted **9 to 1 that there is reasonable assurance** that the Edwards SAPIEN™ Transcatheter Heart Valve is effective for use in patients with severe symptomatic aortic stenosis who meet the criteria specified in the proposed indication.

Question 3

The Panel voted **9 to 0 (with 1 abstention)** that the benefits of the Edwards SAPIEN™ Transcatheter Heart Valve for use in the indicated patient population do outweigh the risks of the Edwards SAPIEN™ Transcatheter Heart Valve for use in the indicated patient population.

Contact: James Swink, Designated Federal Officer,
(301) 796- 6313 James.Swink@fda.hhs.gov

Transcripts may be purchased from: (written requests only)

Free State Reporting, Inc.

1378 Cape St. Claire Road

Annapolis, MD 21409

410-974-0947 or 800-231-8973 Ext. 103

410-974-0297 fax

Or

Food and Drug Administration

Freedom of Information Staff (FOI)

5600 Fishers Lane, HFI-35

Rockville, MD 20851

(301) 827-6500 (voice), (301) 443-1726