St. Jude Medical
Cardiovascular & Ablation Technology
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January 17, 2013

To Physician Implanters of the AMPLATZER™ Septal Occluder:

This letter is to inform you about important information concerning the AMPLATZER Septal Occluder. On May 24, 2012, FDA held a meeting of its Circulatory System Devices Panel. The purpose of the meeting was to discuss current knowledge about the safety and effectiveness of the currently US marketed transcatheter Atrial Septal Defect (ASD) occluders used for the closure of secundum atrial septal defects. As one of the manufacturers of an FDA approved device for ASD closure therapy, St. Jude Medical attended this meeting to discuss its AMPLATZER Septal Occluder (ASO).

The FDA Panel reviewed safety and performance data of all approved occluders and concluded that the overall known safety profile of the class of devices has not changed since marketing approval; however, the awareness of the full spectrum of adverse events and outcomes has become clearer. In particular, the FDA Panel discussed ASO erosion events (defined as abrasion of the tissue of the atrium and/or adjacent aorta, primarily in the area where the roof of the atrium and the aortic root are in close approximation). Since these structures are separated by the free pericardial space, erosion results in either pericardial tamponade, or a fistula between either atrium and the aorta. While the FDA Panel agreed that the analyses of erosion events conducted by St. Jude Medical to date were reasonable, they also concluded that there are insufficient data, including inadequate echocardiographic information, about the cases already reported to determine the exact etiology. Specific patient or anatomical factors that may influence erosion are not fully understood today.

In addition to etiology of erosion, the incidence of these events was also discussed by the FDA Panel. Erosion remains a rare, although potentially serious, adverse event. The world-wide estimated incidence rate for erosion is between 0.1% and 0.3%. The risk for potential erosion has remained stable over time. Since CE-mark approval in 1998, there have been 97 world-wide cases of confirmed or presumed erosion (49 US and 48 OUS) in connection with the on-label use of the ASO device. Within the 97 erosion events, 8 deaths have occurred. No deaths associated with erosion occurred in patients younger than 16 years of age. The majority (almost 90%) of erosions occur within 1 year of being implanted, although one erosion was reported as late as 8.5 years after implant. To date, all reported deaths have occurred within 16-months of implant. Erosion, though rare, is a potentially serious life threatening event with symptomatic signals including chest pain, shortness of breath, fainting, and difficulty breathing. If erosion occurs, emergency surgery may be required for a successful outcome.

Although a very low incidence event, St. Jude Medical is dedicated to continuous improvement and actively seeks out data to enhance our understanding of erosion etiology and its potentiating factors in order to reduce patient risk and provide education and guidance to physicians to reduce the occurrence of erosion. In consultation with the FDA, St. Jude Medical is taking the following steps to increase physician and patient awareness and education in the use of the ASO device for atrial septal defect closure:

First, we are modifying the Instructions for Use (IFU). Upon the recommendation from the FDA Panel, the IFU has been updated and clarified as follows:

- The contraindication requiring a 5mm anterior-superior aortic rim has been clarified and changed to a warning
- Clinical follow-up recommendations have been updated. Specifically, follow-up with a cardiologist and echocardiograms are recommended at implant, 1 day post-implant, pre-discharge, and again at 1 week, 1 month, 6 months, and 12 months post-implant. Clinical follow-up with a cardiologist annually thereafter is also recommended
- Patient awareness has been emphasized. Specifically, patients should be educated to seek immediate medical attention, that includes an echocardiogram, if they develop cardiovascular symptoms such as chest pain, arrhythmias, shortness of breath or fainting

- Patients with an ASO in place who present with hemodynamic instability or compromise consistent with the possibility of cardiac tamponade should have an immediate and thorough evaluation, including an echocardiogram and/or CT for definitive evaluation of the possibility of erosion
- Echocardiographic guidance has been clarified regarding proper device placement

It is important for you to review the updated IFU prior to your next implant (www.amplatzer.com/products).

Second, we support FDA's initiative to immediately implement mandatory device tracking for all ASD closure therapy devices.[1] Device tracking will assist in calculating more accurate incidence rates, and enhance the ability to evaluate the effectiveness of the steps we are taking to better understand and reduce the incidence of erosion. The process of patient registration has not changed from what you are already familiar with. Please ensure your patients are registered, which can be accomplished through our website at http://health.sjm.com/device-registration or by completion of the registration form packaged with the device.

Third, St. Jude Medical believes that standardized and consistent imaging is necessary to understand the etiology of erosion events. Accordingly, St. Jude Medical is taking an active role in partnering with the FDA and echocardiography societies to develop standardized echocardiographic imaging techniques and guidance for ASD procedures. These techniques will provide much needed information toward understanding pre-, peri-, and post-procedural anatomical characteristics of patients with atrial septal defects and the operation of the device in use. Once defined, standardized imaging protocols will be incorporated into our IFU and further clinical investigations conducted by St. Jude Medical and will provide a sound baseline in prospective registries.

Fourth, we will participate in further FDA-regulated study of the ASO device. As recommended by the FDA Panel, further study will facilitate better understanding of the etiology of erosion which will result in reduction of this adverse event.

Fifth, further information for patients and physicians will be provided on the St. Jude Medical website. Despite the rare occurrence of erosion, it remains a potentially serious and life-threatening adverse event. Patients should be informed of the potential warning signs of erosion, including direction to seek immediate medical assistance in the event they experience any of the symptoms or warning signs. We highly encourage physicians to have available and provide current and future patients with complete information about the risks and benefits of transcatheter closure with the ASO device. The St. Jude Medical website has a link with additional resources and information for patients implanted with or considering ASO devices. Please make your patients aware of this site: www.atrialseptaldefectanswers.com.

Finally, we remind our physicians of the importance and necessity of timely and accurate adverse event reporting. If erosion is suspected in one of your patients, please immediately report this event to St. Jude Medical via the established adverse event reporting process. Additionally, please ensure that all necessary records (including, but not limited to implant and event images, surgical records, catheterization reports, etc.) are provided to facilitate a complete assessment of the event. These records and data will facilitate St. Jude Medical's ongoing internal investigation efforts as well as our independent adjudication board's continued surveillance and analysis of these events.

St. Jude Medical is committed to providing the highest quality products and support for the benefit of your patients. Your cooperation will help us continue to actively monitor and ensure the ongoing safety and effectiveness of the ASO device.

Sincerely,

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1. The FDA has also implemented device tracking for the AMPLAZTER Multi-Fenestrated Septal Occluder "Cribriform" and the AMPLATZER Muscular VSD Occluder. St. Jude Medical continues to encourage registration of all patients who receive an implantable AMPLATZER device.