Circulatory System Devices Panel Meeting – March 18, 2010

Summary

A meeting of the Circulatory System Devices Panel Meeting was held on March 18, 2010, to discuss and vote on Boston Scientific's PMA application to request approval for an expansion of the indications for the company's Cardiac Resynchronization Therapy Defibrillators (CRT-D) based on the MADIT-CRT study. The Panel heard the Company and FDA presentations, discussed the clinical data presented from the MADIT-CRT study, addressed the FDA questions, and finally voted unanimously (11-0) to recommend that the PMA application as "Approvable with Conditions."

Device Description

The Boston Scientific Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) are indicated for patients with moderate to severe heart failure (NYHA III/IV) who remain symptomatic despite stable, optimal heart failure drug therapy and have left ventricular (LV) dysfunction (EF ≤ 35%) and QRS duration ≥120 ms.

The sponsor has proposed to expand the indications for use to include:

Mild heart failure (NYHA Class II) with EF ≤30% and QRS duration ≥130ms
and
Asymptomatic heart failure (NYHA Class I) of ischemic origin with EF ≤30% and QRS duration ≥130ms

VOTE

The Panel voted (11-0) to recommend that the PMA application for the expansion of indications for Boston Scientific's CRT-D devices to include the patients studied in the MADIT-CRT study be found "Approvable with Conditions." The panel recommended two conditions of approval:

1. The IFU includes a statement to include only patients with LBBB (left bundle branch block) and stable sinus rhythm

2. Post approval study with a meaningful comparator group that assesses the predictive values of subgroups and risk factors for safety issues.

Deliberations

The panel found the system-related complications related to the CRT-D system and left ventricular lead to be consistent with standard medical practice for these commercially-available devices. The panel agreed with the sponsor that the decrease in heart failure hospitalizations outweighs the increase in system-related complications. They discussed the fact that there is limited data capturing long term lead reliability, and this shortcoming is something that should be taken into consideration (perhaps in a PAS).

In general the panel agreed that the lack of patient and physician blinding could have biased the results, but blinding would have been very difficult to maintain over an extended period of time. In addition, the sponsor did their best to develop a robust study given this limitation and used a independent, blinded committee to review the supporting heart failure event data.

The hazard ratio, although weak, does support using this device in NYHA Class I patients. The panel thought that it was important to note that these patients are already indicated for ICD therapy and do not represent the subset of ICD patients that are generally less healthy that the average NYHA Class I-II patients in general. Many of these patients have been or will become NYHA Class II patients. The panel agreed that patients with chronic atrial fibrillation do not respond well to CRT-D therapy. Patients with LBBB receive the most benefit from the device, although the analyses supporting this conclusion are post-hoc.

The panel felt that the proposed indications for use for the expanded patient population are too broad and should be limited to left bundle branch block and stable sinus rhythm for patients with NYHA Class I-II.

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